ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 1
January 1979
Pages 1–90

From the Principle of Areno-Analogy to Heterocyclopolyaromatic Compounds[**]

By Thomas Kauffmann[*]

Dedicated to Georg Wittig

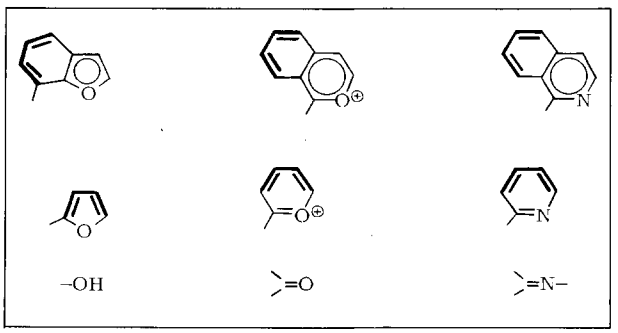
Organometallic linkage of heteroaromatic compounds provided a means of synthesizing complicated combinations of heteroaromatic compounds; not only nucleophilic aromatic substitution, but also "Ar—Cu/Ar—Hal linkage", "organometallic oxidative linkage", and "metal amide linkage" have been employed. The heterocyclopolyaromatic compounds are made of one, two, or three kinds of heteroaromatic species as ring members. These syntheses illustrate the construction of heterocycles from large, preformed structural units. Competition experiments showed that the reactivity typical of the individual species is enhanced in open-chain combinations $(Ar_{Nu})_n$ and $(Ar_E)_n$ (Ar_{Nu}, Ar_E: nucleo- and electrophilic heteroaromatic systems, respectively); the opposite situation is mostly encountered in the case of Ar_{Nu}—A_E combinations.—Cycloocta[1,2-*b*:4,3-*b'*:5,6-*b''*:8,7-*b'''*]tetrathiophene, the only heterocyclopolyaromatic system yet to have been studied in detail, proved surprisingly inclined to undergo monosubstitution reactions.

1. Motivating Influence of the Principle of Areno-Analogy

The existence of nucleophilic and electrophilic functional groups permits highly selective reactions to be performed in organic chemistry and biochemistry. Carbon chains furnished with groups of one kind or the other can be linked together without interference by formation of side products (*e.g.* ester formation from carboxylic acids and alcohols).

A second set of nucleophiles and electrophiles is available in the nucleophilic and electrophilic heteroaromatic compounds (π-electron-excess and π-electron-deficient heteroaromatic compounds[1]). With regard to their reactions and the effect on their substituents, they show a clear resemblance to nucleophilic and electrophilic functional groups (see below) and thus call for analogous applications in organic synthesis (principle of areno-analogy[2,3]).

The underlying reason for the relationship between heteroaromatic compounds and functional groups—the analogy between pyridine and the carbonyl group had already been pointed out prior to the formulation of the principle of areno-



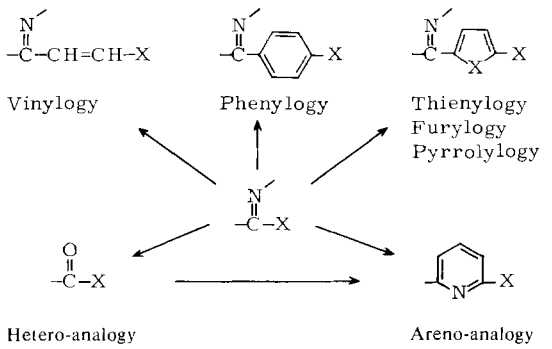
Scheme 1. Functional groups and their areno-analogs.

[*] Prof. Dr. Th. Kauffmann
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

[**] Heterocyclopolyaromatic Compounds, Part 8.—Part 7: ref. [40a].

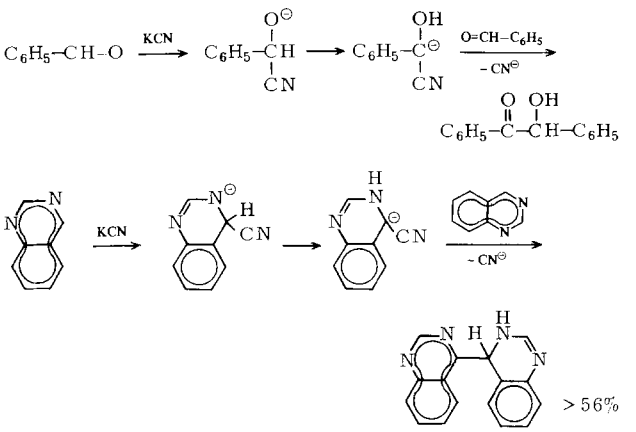
analogy[4]—can be considered[3] to lie in the possibility of formally deriving the simple heteroaromatic systems from the functional groups by incorporation of a C_4 unit possessing 4π electrons (Scheme 1). Although this leads to a drastic modification of the properties of the system, its nucleophilic or electrophilic activity and other essential features[2, 3] are retained.

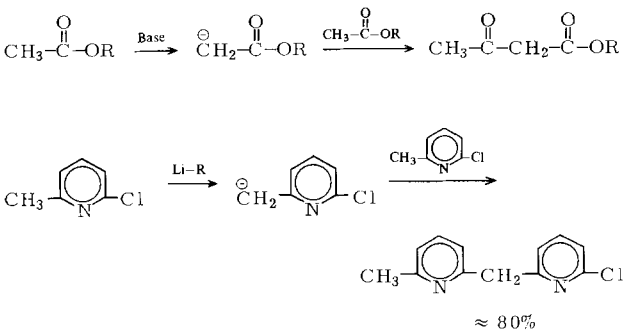
As may be seen in Scheme 2, areno-analogy corresponds rather to hetero-analogy than to vinylogy. We therefore prefer the term "areno-analogy" over the originally chosen term "arenology"[2, 3]. Scheme 2 also underlines the difference between areno-analogy and phenylogy, thienylogy, *etc.* (see Section 2.2).



Scheme 2. Heuristically valuable analogies as illustrated for the CN double bond.

Use of the principle of areno-analogy often involves several conceptual steps; the pairs of reactions shown in Scheme 3 serve as examples. If classical heteroaromatic compounds





Scheme 3. Normal and areno-analogous benzoin and Claisen condensations [5, 3].

are viewed as higher homologs of functional groups, a number of interesting questions arise: Is the reactivity of the individual systems altered on linking heteroaromatic compounds to give open-chain or macrocyclic compounds in the same way as in the case of functional groups (see Section 2.2)? Are there hetero-aromatic counterparts of important specific reactions of organic molecules containing functional groups (see Scheme 3)? What heteroaromatic groups are particularly well suited for the linkage of hydrocarbon chains to give compounds such as Alk—Ar_{Nu}—Ar_E—Alk (see Section 2.1.4)? Can the bond between a nucleophilic and an electrophilic heteroaromatic unit be broken specifically (see Section 3.3.3)?

Questions of this kind and the favorable synthetic scope to be expected from the very existence of nucleophilic and electrophilic heteroaromatic compounds instigated the studies surveyed in the present article[6].

2. Heteropolyaromatic Compounds

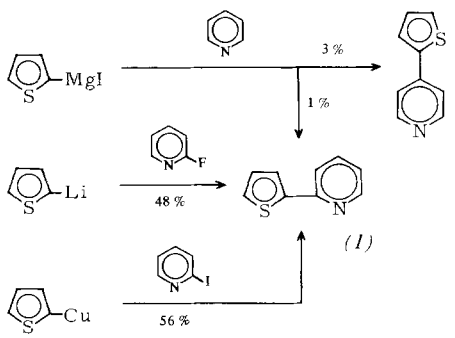
2.1. Syntheses

2.1.1. Linkage of Heteroaromatic Units by Nucleophilic Substitution

Unlike functional groups, nucleophilic and electrophilic heteroaromatic compounds do not react together without prior activation. However, the activity of the nucleophilic heteroaromatic systems can readily be enhanced by introduction of a metal atom; such an example is seen in the reaction of thiophene with *n*-BuLi to give 2-lithiothiophene or with *n*-BuLi+CuCl to form 2-cuprothiophene. This enhancement of nucleophilicity is straightforward because nucleophilic heteroaromatic compounds exhibit a relatively high CH acidity and—in contrast to electrophilic heteroaromatic compounds—show no tendency to add the metalation reagent or the product of metalation.

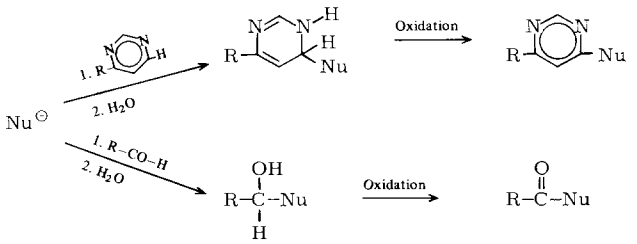
Addition of one of the more strongly electrophilic heteroaromatic systems to a lithiated nucleophilic heteroaromatic unit generally leads to fast specific linkage.

At the outset of our studies seven years ago, little was known about the combinations of nucleophilic and electrophilic heteroaromatic compounds. The simplest uncharged representative, *viz.* 2-(2-furyl)pyridine was unknown and *(1)*, the corresponding thiophene derivative, was accessible in only about 1% yield (Scheme 4)[7]. Replacement of the magnesium iodide group by lithium[8, 9] or copper[10], as well as an H atom of the electrophilic component by halogen significantly raised the yield of *(1)* (Scheme 4).



Scheme 4. Synthesis of 2-(2-thienyl)pyridine *(1)*.

While the reaction of anionic nucleophiles such as 2-lithiothiophene with *halogenated* electrophilic heteroaromatic compounds like 2-fluoropyridine is known to proceed in full analogy to nucleophilic substitution with addition-elimination mechanism of *acyl halides*, the reaction of *non-halogenated* electrophilic heteroaromatic substances corresponds to the nucleophilic substitution of *aldehydes* which is much less familiar to the organic chemist (Scheme 5): in each case a stable adduct is formed which must be oxidized to regenerate the 6π- and 2π-electron system. Regeneration of the 6π system is usually easier (oxidation with nitrobenzene or with $KMnO_4$ in acetone) and sometimes even occurs of its own accord. Substitution with aldehyde-analogous electrophilic heteroaromatic compounds is of great importance in heteropolyaromatic chemistry; pyrimidine, quinoxaline, and quinoline are particularly well suited for this purpose.



Scheme 5. Nucleophilic substitution in non-halogenated electrophilic heteroaromatic compounds.

As may be seen in Table 1 (second line), *electrophilic* heteroaromatic compounds can be linked analogously if one of the two components—preferably that of lower electrophilicity—is first subjected to "umpolung". In contrast to the carbonyl compounds[11], *direct* umpolung generally proceeds without difficulty at low temperatures. However, the yields

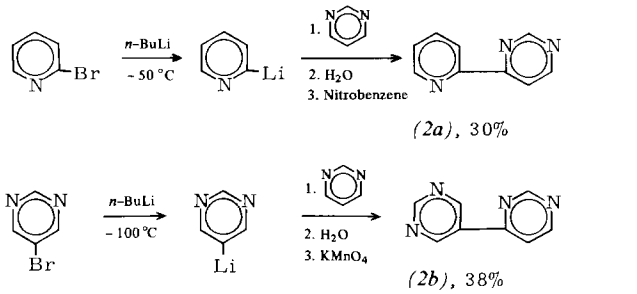


Table 1. Proven methods of linking heteroaromatic units.

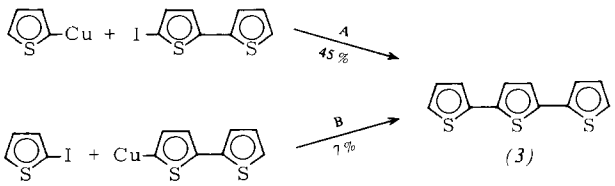
Kind of linkage	Reactants	Product
Nucleophilic aromatic substitution	Ar_{Nu}—Li + Ar_E (or Hal—Ar_E) Ar_E—Li + $Ar_{E'}$ (or Hal—$Ar_{E'}$)	Ar_{Nu}—Ar_E Ar_E—$Ar_{E'}$
Ar—Cu/Ar—Hal linkage	Ar_{Nu}—Cu + Hal—Ar_E (Hal = Br, I) Ar_{Nu}—Cu + Hal—$Ar_{Nu'}$ (Hal = Br, I)	Ar_{Nu}—Ar_E Ar_{Nu}—$Ar_{Nu'}$
Organometallic oxidative linkage	Ar_{Nu}—M + transition metal halide (M = Li, MgX) Ar_E—M + transition metal halide	Ar_{Nu}—Ar_{Nu} Ar_E—Ar_E
Metal amide linkage	Ar_E + $LiN(iPr)_2$	Ar_E—Ar_E
Areno-analogous benzoin condensation (see Scheme 3)	Ar_E + KCN	Ar_E—Ar_E

of linkage products are mostly lower than from corresponding substitutions with lithiated *nucleophilic* heteroaromatic compounds.

The syntheses of *(2a)*[12] and *(2b)*[13] are examples of substitutions with electrophilic heteroaromatic compounds after umpolung.

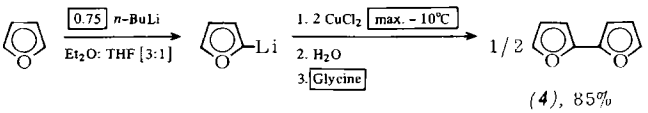
2.1.2. Other Methods of Linking Heteroaromatic Units

Ar—Cu/Ar—Hal linkage[14], the mechanism of which has still not been elucidated[15], has been used primarily by *Nilsson et al.*[16] to join nucleophilic aromatic compounds (benzene and its derivatives, nucleophilic heteroaromatic compounds) symmetrically and unsymmetrically. We found the method to be suitable for the synthesis of Ar_{Nu}—Ar_E combinations too[17] (an example is shown in Scheme 4), and to permit a convenient ring-linking synthesis of *all*-α-terthiophene *(3)*[10,18] (Scheme 6): pathway A proves much more favorable than B for reasons that are still not fully understood.



Scheme 6. Ring-linking synthesis of terthiophene.

Organometallic oxidative linkage is employed for symmetrically uniting nucleophilic heteroaromatic compounds. The reaction is normally accomplished smoothly by reaction of the lithium or magnesium compounds with $CuCl_2$, $CuCl/O_2$, $NiCl_2$, or $FeCl_3$ (for a survey, see ref. [6c]). Ring-linking synthesis of 2,2'-bifuran *(4)* (yield 85 %)[19], the best synthesis presently available for this sensitive compound[20], is particularly instructive: the reaction temperature should be about −10 °C; *n*-BuLi may only be used in the given molar ratio in order to ensure its complete consumption and to preclude its participation in the linkage process. Moreover, the bifuran-copper complex formed must be decomposed under mild conditions (addition of glycine). Analogous linkages led to the formerly unknown *all*-α-quaterfuran (53 %)[19], but for poorly understood reasons not to *all*-α-octifuran[21] (for further applications, see Sections 2.1.4, 3.2, and 3.4).



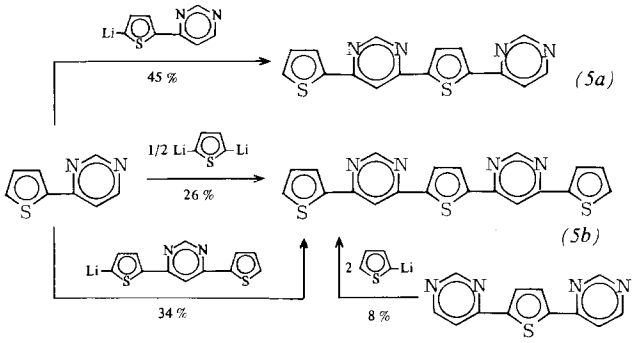
After umpolung, *electrophilic heteroaromatic compounds* can be linked analogously[6c] (a recent example is the synthesis of 5,5'-bipyrimidine, see Section 3.4).

Metal amide linkage permits linkage of electrophilic heteroaromatic compounds (pyridine, quinoline, isoquinoline) by reaction with $LiN(iPr)_2$ in tetrahydrofuran (THF)/hexamethylphosphoric triamide (HMPA) according to *Clarke, McNamara*, and *Meth-Cohn*[22]. Analogous linkages of quinoxaline ($NaNH_2$ in dimethylaniline[23]) and 3-fluoropyridine ($NaNH_2$ in liquid NH_3[24]) have been described on previous occasions. The formation of a carbanion assumed to occur in the initial reaction step (*e.g.* formation of 2-lithiopyridine) should then

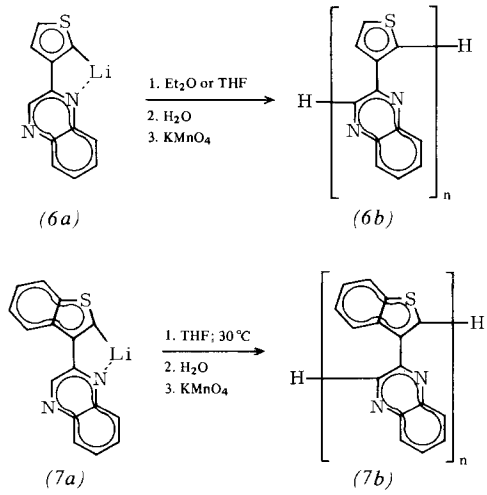
initiate a nucleophilic addition or substitution[22, 30]. However, trapping experiments failed to reveal carbanionic intermediates[22]. We have applied the linkage reaction with $LiN(iPr)_2$ to 3-bromopyridine, -quinoline (see Section 3.2), 5,5′-bipyrimidine, 3,3′-bi- and 4,4′-bipyridine, and to the tri- and tetraaromatic compounds *(52)* and *(49a)* (see Section 3.4). In some case a dihydro-product, requiring oxidation to the aromatic system, was formed, while in other cases the desired aromatic system is obtained directly. In spite of modest yields, these linkages are of preparative value because they provide ready access to suitable starting materials for heterocyclo-polyaromatic compounds and to such compounds themselves.

2.1.3. Linkage of Several Nuclei

It is relatively easy, by means of the methods described in Section 2.1.2, to prepare heteropolyaromatic compounds. Apart from compounds having *nucleophilic nuclei of the same kind*, which are conveniently preparable by organometallic oxidative linkage (see Sections 2.1.2 and 2.1.4), combinations of heteroaromatic systems having an *alternant* arrangement of nucleophilic and electrophilic nuclei are most readily accessible. The pyrimidine and quinoxaline systems are especially suited as electrophilic structural units, and thus permitted preparation of, *e.g.*, the yellow thiophene-pyrimidine combinations *(5a)* and *(5b)*[13] and the likewise yellow thiophene-quinoxaline combinations *(6b)*, $n = 2$—6 (yields 22, 12, 13, 9, 5 %)[25], and benzo[*b*]thiophene-quinoxaline combinations *(7b)*, $n =$ 2—4 (yields 24, 11, 4 %)[26, 27] (Schemes 7 and 8).

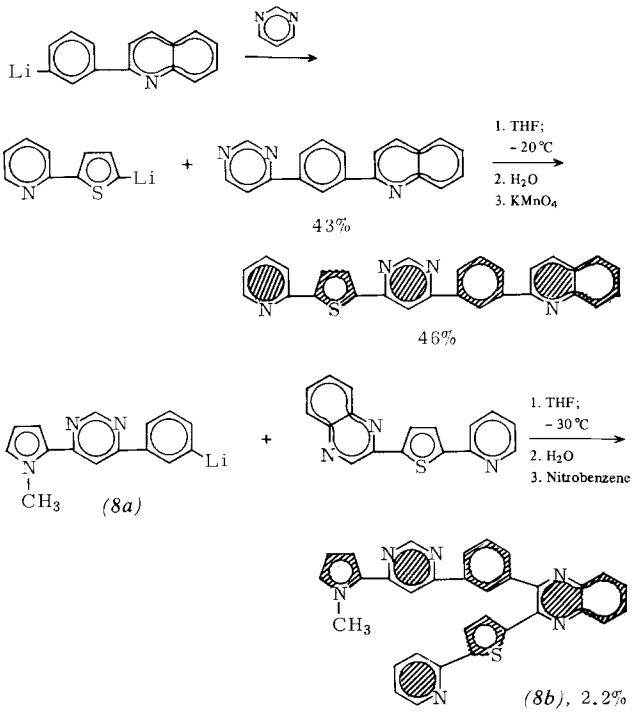


Scheme 7. Alternant thiophene-pyrimidine combinations.



Scheme 8. Alternant thiophene-quinoxaline and benzo[*b*]thiophene-quinoxaline combinations (see Section 3.3.1 regarding the mechanism of oligomerization).

Attempts to link four, five, or even six different aromatic species, undertaken with the aim of developing the synthetic approach, gave the desired products[12, 28] (Scheme 9). The resulting compounds, which contain a benzene ring (hatching in the formulae emphasizes the alternance between Ar_{Nu} and Ar_E) show the term "heteropolyaromatic" to be a more fitting general designation than "polyheteroaromatic".



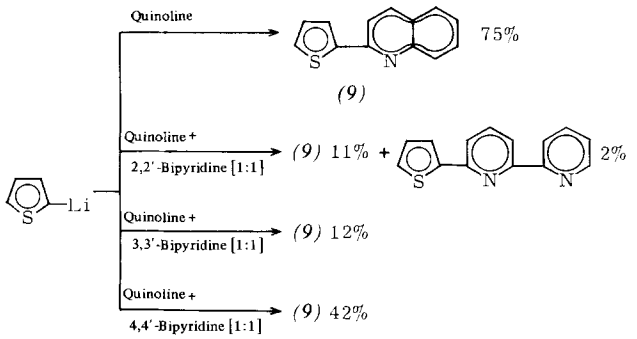
Scheme 9. Heteropolyaromatic compounds made up of many different components.

The low yield of the hexaaromatic compound *(8b)* is probably due, at least in part, to crowding on the quinoxaline group[29]. Crowding on the quinoxaline group appears to have a much less pronounced effect in the synthesis of the polyaromatic compounds *(6b)* and *(7b)* and of the protophane formulated in Scheme 14, possibly due to the greater mobility of the groups: in the synthesis of compounds *(6b)* and *(7b)* $n-1$ quinoxaline groups are present in the dihydro form prior to the oxidation step.

2.1.4. Fundamental Difficulties Besetting Synthesis

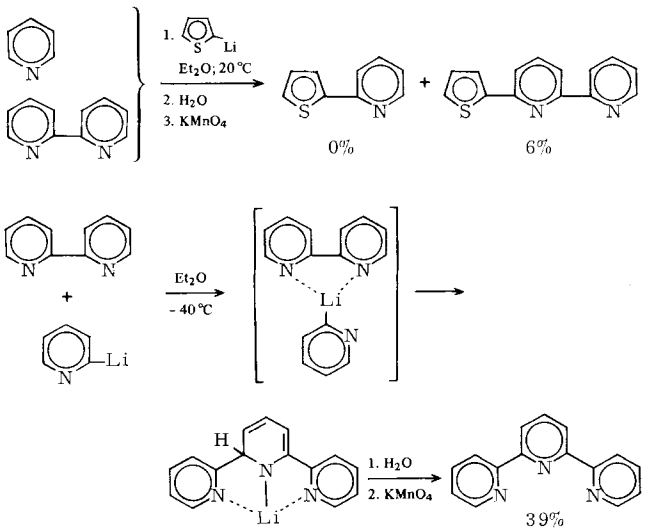
Deactivation by complexation: On attempted linkage of a lithiated nucleophilic heteroaromatic system with a combination of two or more heteroaromatic compounds, it was not uncommon for the lithiated species to be deactivated by complexation. This danger is particularly acute when two electrophilic heteroaromatic nuclei are joined together directly in the substrate.

Scheme 10 illustrates the deactivation of 2-lithiothiophene by bipyridines: the reaction with quinoline to give *(9)* is largely suppressed by addition of 2,2′- and 3,3′-bipyridine. The reason is undoubtedly to be sought in complexation since hardly any thienyl-bipyridine is formed.



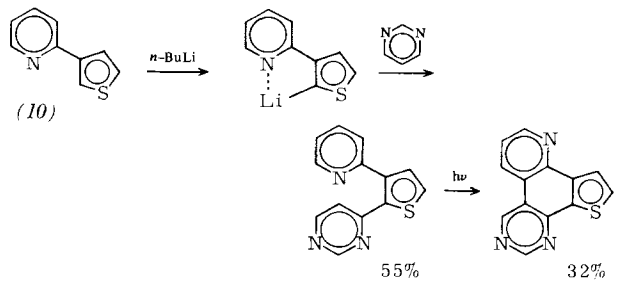
Scheme 10. Deactivation of 2-lithiothiophene by bipyridines [9].

Complexation of 2-lithiothiophene by 2,2'-bipyridine also explains why this diaromatic species, although extremely reactive towards *n*-BuLi (see Section 2.2), shows a similar resistance towards 2-lithiothiophene as pyridine (Scheme 11)[9]. Lithiated *electrophilic* heteroaromatic compounds appear to be less readily deactivated by 2,2'-bipyridine and similar systems than are lithiated nucleophilic heteroaromatic compounds. Thus, attempts to link lithiated pyridine with 2,2'-bipyridine by nucleophilic substitution are relatively successful (Scheme 11)[30, 31].



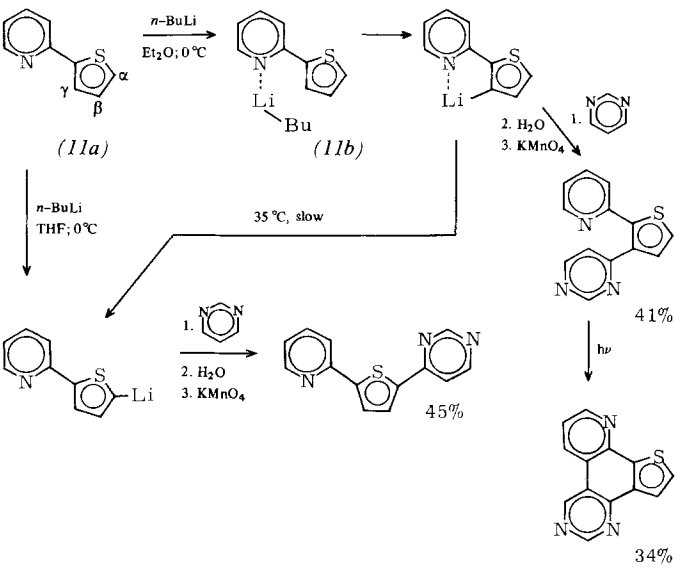
Scheme 11. Reactivity of 2,2'-bipyridine towards lithiated heteroaromatic compounds.

Nonspecific lithiation: If the nucleophilic component to be activated in a synthesis consists of two or more heteroaromatic units, then specific lithiation of a single position often proves impossible because two or more CH bonds of comparable acidity are present. This does not apply to compound *(10)* because lithiation at C-2 of the thiophene ring gives a thermodynamically stable chelated lithium compound. This phenomenon can be utilized in the synthesis of condensed heteroaromatic compounds[33, 34].



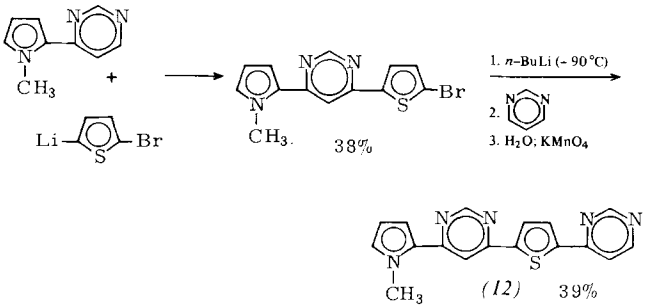
In contrast, the diaromatic compound *(11a)* possesses two positions of comparable acidity. The site of lithiation is strongly influenced by the solvent: in THF *n*-BuLi metalates almost exclusively in the α- position, and in ether mainly in the γ-position (γ:α-lithiation = 62:13)[32, 34]; *t*-BuLi even effects exclusive γ-lithiation in ether[34]. The lithioalkanes are presumably first attached as shown in *(11b)* and then effect H/Li exchange at the spatially proximate γ-C atom. It appears plausible that the tendency to form complex *(11b)* is reduced on use of the better-coordinating solvent THF. On heating of the ethereal solution of the γ-lithiation product to boiling, the lithium atom gradually shifts to the α-position, thus indicating kinetic control of γ-lithiation[35].

Solvent-controlled lithiations permit synthesis of the isomeric triaromatic compounds shown in Scheme 12[32, 34], as well as the photocyclization product[33, 34] (for further solvent-dependent lithiations and preparative applications, see ref. [32, 36]).



Scheme 12. Solvent-controlled α- and γ-lithiation of 2-(2-thienyl)pyridine.

Polyaromatic compounds containing more than two heteroaromatic members usually possess several CH groups of comparable acidity. In such cases, it is advisable to introduce the lithium atom in the manner shown for the synthesis of *(12)*[13], *i.e.* by *halogen/Li exchange* (essentially quantitative in this example; other examples are given in ref. [13]).



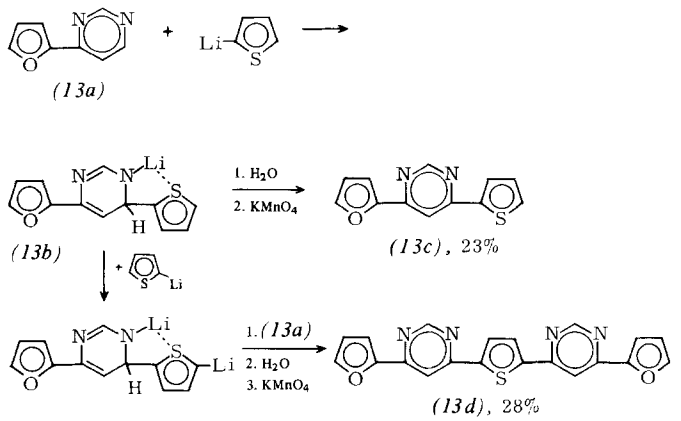
Transmetalation: Translithiations frequently impair the yields of heteropolyaromatic syntheses, and lead to undesired

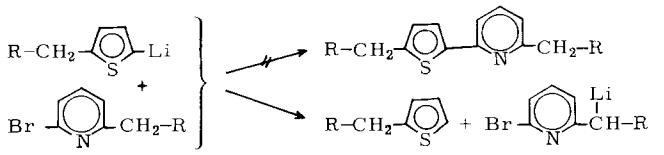
side products. In the synthesis of the triaromatic compound *(13c)* selected as example, the less acidic five-membered ring was first linked to pyrimidine, thus hindering further complication due to translithiation. Nevertheless, there is some interference from a transmetalation reaction: the adduct *(13b)* is lithiated by 2-lithiothiophene and reacts to give the side product *(13d)*[13].

Translithiation is a very real danger when dealing with *alkyl*-substituted *electrophilic* heteroaromatic compounds. Instead of linkage between heteroaromatic compounds, translithiation usually occurs (Scheme 13, below) and initiates secondary reactions. The linkage of two alkyl groups according to

$$Alk{-}Ar_{Nu}{-}Li + Ar_E{-}Alk \rightarrow Alk{-}Ar_{Nu}{-}Ar_E{-}Alk$$

which is areno-analogous to the formation of carboxylic esters or carboxamides (see Section 1) is possible only in exceptional cases[6a, 37].





Scheme 13. Interference by translithiation.

In contrast, alkyl groups attached to *nucleophilic* heteroaromatic systems do not have any interfering effect in organometallic syntheses of polyaromatic systems owing to their modest acidity. Thus alkyl groups can be joined *via* a group of three heteroaromatic nuclei ($Ar_{Nu}{-}Ar_E{-}Ar_{Nu}$) (Scheme 14, above)[9], which is areno-analogous to the formation of carboxylic diesters according to

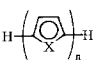
$$2\,Alk{-}OH + Cl{-}O{-}Cl \rightarrow Alk{-}O{-}CO{-}O{-}Alk$$

It also follows from Scheme 14[38] that this mode of linkage can be utilized in protophane syntheses.

Sparing solubility: Organometallic syntheses of heteropolyaromatic compounds have often been thwarted by the sparing solubility of the polyaromatic precursors in THF, benzene, or ether. Thus it proved impossible to effect oxidative linkage of *all*-α-octithiophene to give *all*-α-sexidecithiophene[39]. *all*-α-Octi(*N*-methylpyrrole), which is much more soluble owing to the methyl groups, underwent linkage to give the hexadecamer (Table 2). In general, alkyl groups attached to Ar_{Nu} rings, and thus non-acidic, should help to overcome solubility problems in organometallic syntheses of heteropolyaromatic compounds.

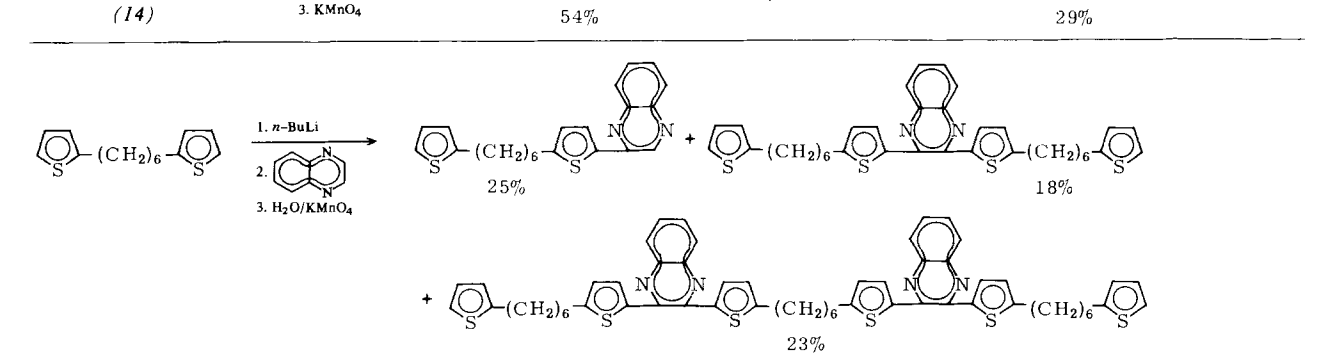
all-α-Poly(*N*-methylpyrrole) (Table 2), of which only the representative having $n=2$ was formerly known[16c], differ not only in their solubility but expectedly also in their melting points (Table 2) and UV spectra (Fig. 4) from the *all*-α-polythiophenes known as far as the octamer.

Table 2. Melting points of *all*-α-polythiophene [41] and *all*-α-poly(*N*-methylpyrroles) [40].



n	M.p. [°C] X=S	M.p. [°C] X=NCH3	X=NCH3, yield [%] $CuCl_2$ [a]	X=NCH3, yield [%] $NiCl_2$ [a]
2	33	14—15	52	82
4	214	134	40	53
5	253	145	0.3[b]	
6	305—307	160	1.0 [c]	
8	338	178—182	29	21
16	—	240—256	10	7

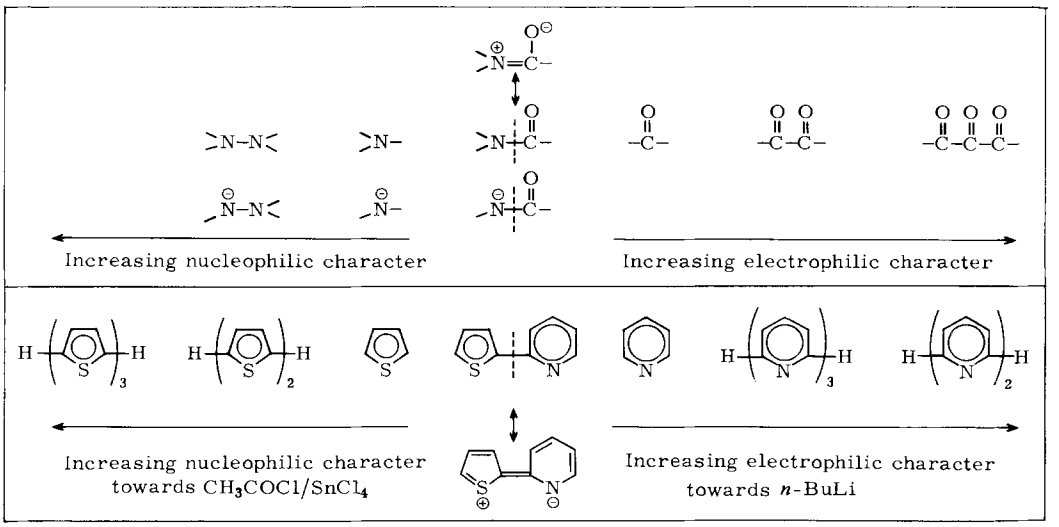
[a] Oxidative linkage with $CuCl_2$ or $NiCl_2$ analogous to the synthesis of *(4)*. [b] Side product in the oxidative linkage of 2-lithio(*N*-methylpyrrole). [c] Side product in the oxidative linkage of 5-lithio-2,2'-bi(*N*-methylpyrrole).



Scheme 14. Linkage of alkyl groups *via* heteroaromatic groups and protophane syntheses.

2.2. Reactivity[42]

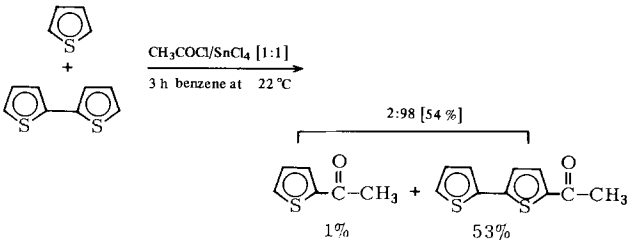
Combinations of functional groups are of considerable significance in organic chemistry. The results compiled in the upper part of Scheme 15 thus belong to the basic armamentarium of the organic chemist: linkage of groups of the same kind (nucleophilic or electrophilic), for instance of amine or carbonyl functions, leads to an enhancement of the reactivity typical of the individual group; on linkage of a nucleophilic group with an electrophilic one, however, the reactivity of individual groups is lowered by mesomeric interaction. In this connection, the reader's attention is called to the pronounced electrophilicity of triketones, which is manifested in their tendency to add water at the central carbonyl group.



Scheme 15. Relative reactivity of combinations of functional groups and of heteroaromatic compounds.

Our studies have shown that the question, raised in the Introduction, whether an analogous situation is encountered in heteroaromatic combinations can be answered essentially in the affirmative if *thiophene* and *pyridine* are chosen as representative systems and acetyl chloride/$SnCl_4$ and *n*-BuLi as reagents. The only deviation from the situation described in the upper part of Scheme 15 is that *all*-α-terpyridine lies between pyridine and 2,2'-bipyridine on the electrophilicity scale. This deviation is probably due to the formation of the very stable *n*-BuLi-terpyridine complex *(15)* and the *m*-position of the terminal nuclei on the central ring of terpyridine, which hinders mesomeric interaction between the terminal rings.

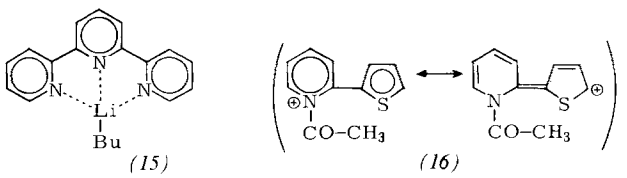
The information shown in the lower part of Scheme 15 was gained in competition experiments with the reagents mentioned according to Scheme 16, giving practically only monosubstitution products. The individual results are shown in Schemes 17—20. The figures above the brackets are the ratios in which the monosubstitution products are formed in the competition experiments (slow dropwise addition of reagent



Scheme 16. Typical competition experiment [43].

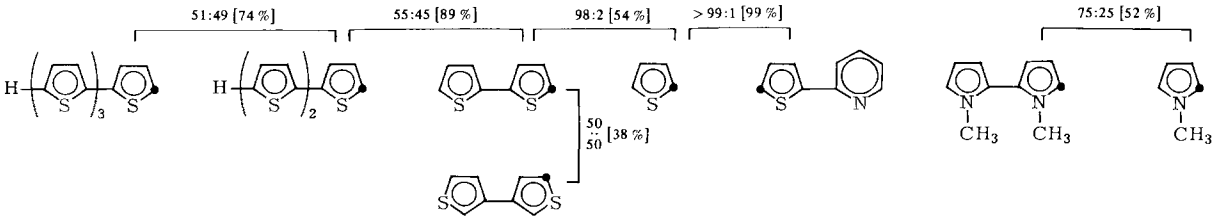
solution to the aromatic pair[42]); the overall yields of the two monosubstitution products are given in square brackets.

We attribute the apparent drastic weakening of the *nucleophilic* activity in the combination of nucleophilic and electrophilic nuclei as compared with thiophene (Schemes 17 and 19) to the formation of *N*-acetyl compounds, *e.g. (16)*, in which the electron-withdrawing effect of the electrophilic nucleus is greatly increased. Accordingly, acetylation of one mole

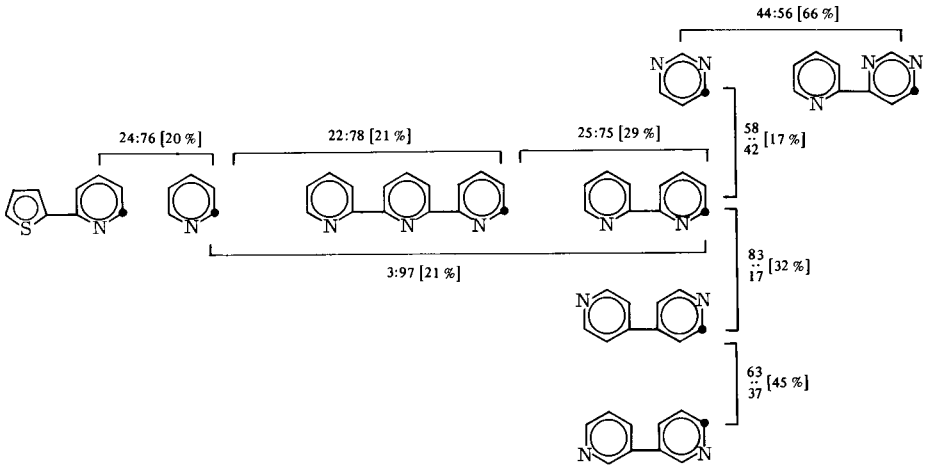


(15) *(16)*

of this combination requires two moles of acetyl chloride (but only one mole of $SnCl_4$)[43].

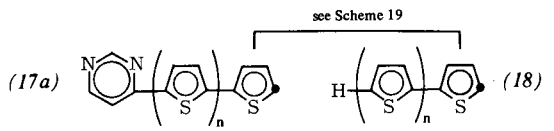


Scheme 17. Competition experiments with $CH_3COCl/SnCl_4$ as reagent (acetylation at ●).



Scheme 18. Competition experiments with *n*-BuLi as reagent (butylation at •).

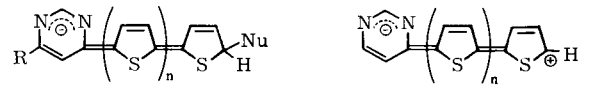
Scheme 19 shows that the drop in nucleophilicity at the thiophene nucleus of *(17a)*, $n=0$, due to the pyrimidine nucleus can extend over two further thiophene nuclei and is completely attenuated only after the third additional nucleus[39]. The ratio of 32:68 almost corresponds to the statistical ratio since *(17a)*, $n=3$, possesses *one* nucleophilic α-position whereas *(18)* has *two* such positions; acetylation is apparently subject to kinetic control.



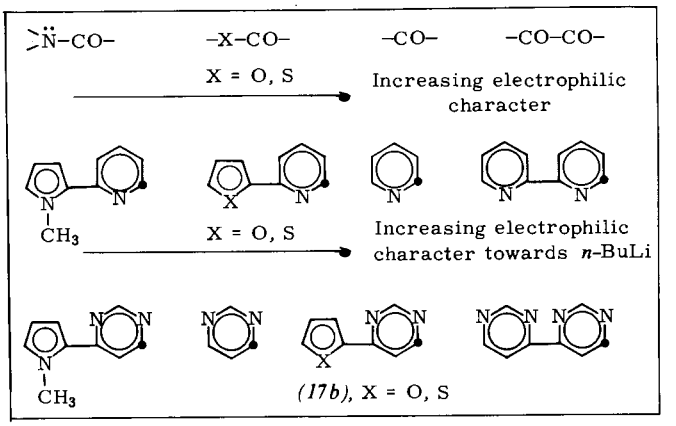
Scheme 19. Competition experiments on "thienylogous pyrimidines" with $CH_3COCl/SnCl_4$ as reagent (acetylation at •) [39].

$n=0$	$n=1$	$n=2$	$n=3$
<1:99 [99 %]	<1:99 [99 %]	24:76 [49 %]	32:68 [96 %]

Compounds *(17a)* can be regarded as thienylogs of pyrimidine (cf. Scheme 2). The nucleophilicity of their terminal thiophene nuclei does not exhibit umpolung under the influence of the pyrimidine nucleus—no formation of adducts *(19a)* has been observed so far—but is significantly lowered, partly due to charge shifts according to *(19b)*.



Further results of competition experiments are summarized in Scheme 20 (for details see ref. [42]): the increase in carbonyl activity on going from left to right in line 1 has long been known. The "pyridine activity" (towards *n*-BuLi) of the compounds in line 2 show a similar gradation. However, the "pyrimidine activities" (towards *n*-BuLi) in the compounds of line 3 do not correspond entirely to expectation, for reasons yet unknown[44], since in competition experiments with pyrimidine *(17b)* the diaromatic compounds *(17b)* underwent butylation almost to the same extent as pyrimidine although they have only one site susceptible to attack by *n*-BuLi compared with the two of pyrimidine[45].



Scheme 20. Electrophilicity of carbonyl compounds and areno-analogous systems (butylation at •) [42].

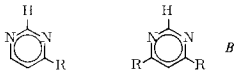
It was established in the competition experiments with $CH_3COCl/SnCl_4$ that the resulting monoacetyl compounds are stable under the experimental conditions. In competition experiments with *n*-BuLi the lithium derivatives of dihydroheteroaromatic compounds appear as primary products, and have to be hydrolyzed and oxidized for the synthesis of the aromatic monosubstituted products. Presumably the lithiated dihydroheteroaromatic species are largely stable under the experimental conditions and are transformed into the substitution products on hydrolysis and oxidation. However, this assumption has yet to be confirmed.

2.3. Spectra

2.3.1. NMR Spectra[49]

The diminished chemical reactivity of Ar_{Nu}—Ar_E combinations usually observed on comparison with the individual aromatic compounds suggests that electron density is transferred from the nucleophilic to the electrophilic nuclei. This can be confirmed by ^{1}H-NMR spectroscopy[46]. The 2-H atom of the pyrimidine nucleus is particularly suitable as a probe because its signal (Table 3) is hardly ever masked by other proton signals[13,43].

Table 3. ^{1}H-NMR signal of 2-H in pyrimidine derivatives *A* and *B* (*ca.* 0.12 M solution, TMS as int. standard, 20°C, in $CDCl_3$) [43].



R	*A* δ	*B* δ
2-(*N*-Methylpyrrolyl)	9.04	8.94
2-Thienyl	9.13	9.03
2-Furyl	9.14	9.00
H	9.22	9.22
2-Pyridyl	9.29	
2-Pyrimidinyl	9.35	

The redistribution of electron density is even clearer in the ^{13}C-NMR spectra[47]: the chemical shifts shown in Figures 1 and 3 can be viewed, to a first approximation, as a measure of the change in electron density at the C atoms. The signals of C-3 and C-5 of the pyridine ring (Fig. 1) and of C-5 of the pyrimidine ring (Fig. 2) are shifted upfield owing to enhanced electron density and those of the nucleophilic heteroaromatic nuclei downfield. The effects are very pronounced in the triaromatic systems of Figure 2 because a stronger acceptor nucleus is linked to two donor nuclei.

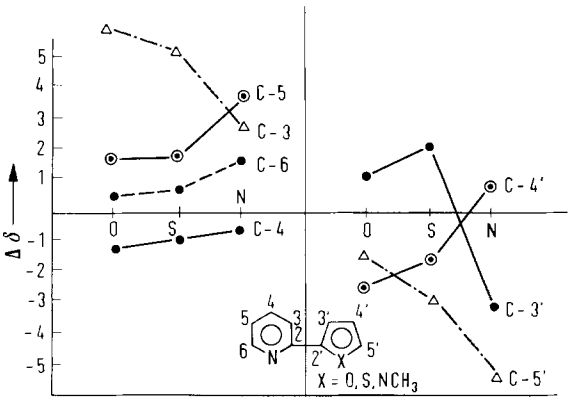


Fig. 1. ^{13}C-NMR of diaromatic compounds: chemical shifts relative to furan, thiophene, *N*-methylpyrrole, or pyridine (*ca.* 0.4 M solution, 20°C, in [D_6]dimethyl sulfoxide, standard TMS, upfield shift shown positive) [47].

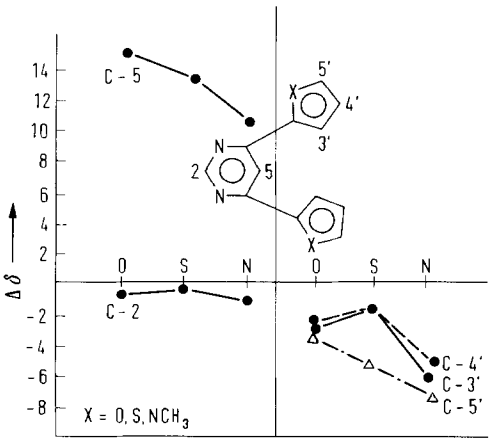


Fig. 2. ^{13}C-NMR of triaromatic compounds: chemical shifts relative to furan, thiophene, *N*-methylpyrrole, or pyrimidine (*ca.* 0.4 M solution, 20°C, in [D_6]dimethyl sulfoxide, standard TMS, upfield shift shown positive) [47].

2.3.2. UV Spectra

In this Section mention is made only of the difference in spectra between *all*-α-poly(*N*-methylpyrroles)[40] on the one hand and *all*-α-polythiophenes[48], -furans[19], and -pyrroles[48] on the other (Fig. 3). The convergence of the absorption wavelengths in *all*-α-poly(*N*-methylpyrroles), which is more pronounced than in the case of the poly-*p*-benzenes[48], is due to the greater torsional angle between the planes of adjacent nuclei.

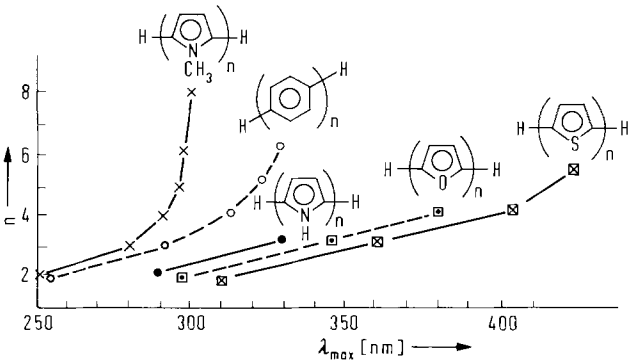
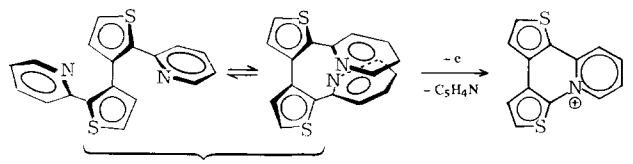


Fig. 3. λ_{max} in the UV spectrum of combinations $(Ar_{Nu})_n$; solvent $CHCl_3$.

2.3.3. Mass Spectra[49]

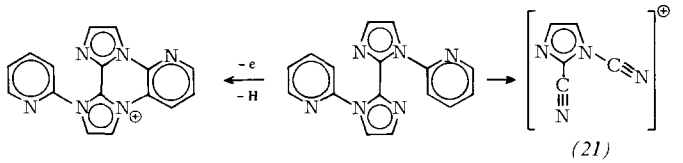
The mass spectra (70 eV) of heteropolyaromatic compounds do *not* normally contain fragment ions indicating the elimination of individual aromatic nuclei; intranuclear bonds are apparently broken much faster than internuclear ones. Exceptions are encountered in heterotetraaromatic compounds with terminal nuclei in the *o,o'*-position relative to the central internuclear bond ("*o,o'*-linkage"). In such a case, *e.g.* in *(20)*, an intense $(M^+ - Ar)$ peak regularly appears which is usually also the base peak (Table 4). Knowledge of this phenomenon is useful in structure elucidation.

The mass number of the $(M^+ - Ar)$ peak of tetraaromatic compounds which consist, like *(20)*, of two kinds of aromatic species, show that one *terminal* nucleus each is eliminated. A fused aromatic compound is probably formed, for an intense peak for $(M^+ - Ar)$ occurs only if cyclization to give a condensed aromatic molecule is formally possible (further arguments, see [49]).



(20) [49]

Heterotetraaromatic compounds having *o,o'*-linkage in which the terminal nuclei are attached by CN bonds to the central portion also eliminate a terminal nucleus in the mass spectrometer (Table 4). However, the $(M^+ - Ar)$ peaks are relatively weak owing to competition by more favorable decomposition pathways [H elimination, HCN elimination, formation of fragments such as *(21)*].



(21)

Table 4. ($M^+ - Ar$) peaks in the mass spectra of heteroaromatic compounds with "*o,o'*-linkage".

Compound	Relative intensity [%]			
	(M^+)	($M^+ - 1$)	($M^+ - Ar$)	$M^+ - HCN$
2,2'-Di(2-pyridyl)-3,3'-bithiophene (*20*)	9	2	100	—
3,3'-Di(2-pyridyl)-2,2'-bithiophene	6	—	100	—
3,3'-Di(4-pyrimidinyl)-2,2'-bithiophene	18	—	100	—
3,3'-Di(2-pyrazinyl)-2,2'-bithiophene	16	1	100	—
3,3'-Di(2-quinoxalinyl)-2,2'-bithiophene	64	5	100	—
2,2'-Di(2-quinolyl)-3,3'-bi(benzo[*b*]thiophene)	23		100	—
5,5'-Di(5-pyrimidinyl)-4,4'-bipyrimidine [a]	35	15	100	—
3,3'-Di(3-pyridyl)-4,4'-bipyridine [b]	87	100	87	—
1,1'-Di(2-pyridyl)-2,2'-biimidazole	53	44	23	39
1,1'-Di(3-pyridyl)-2,2'-biimidazole	37	100	22	2
1,1'-Di(2-pyridyl)-5,5'-bipyrazole	100	65	6	90
1,1'-Di(2-pyridyl)-5,5'-bi(1,2,4-triazole)	100	45	22	72

[a] 5,5':4',4'':5''-Quaterpyrimidine. [b] 3,3':4',4'':3'',3'''-Quaterpyridine.

3. Heterocyclopolyaromatic Compounds

3.1. An Unattractive Class of Compounds?

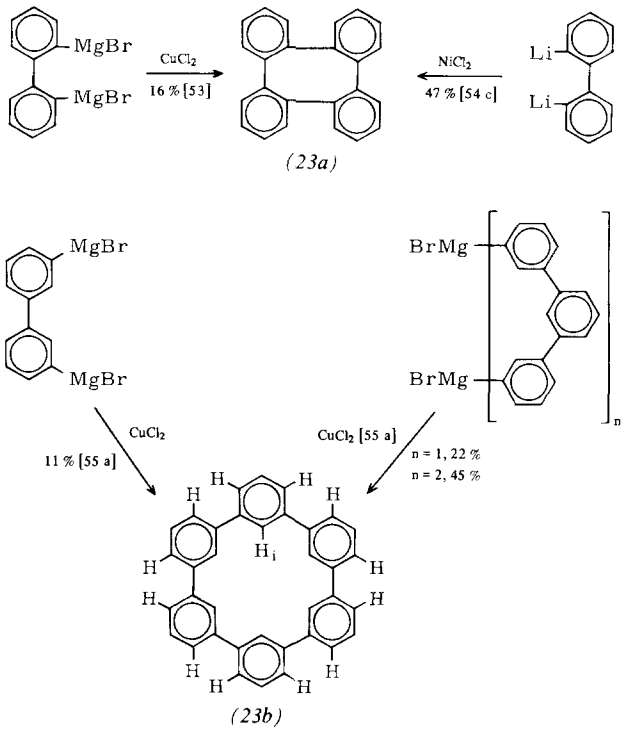
In contrast to the field of organoelement compounds, there are probably only few regions left to be discovered in the field of organic compounds proper. Nevertheless, the well-populated class of heterocyclopolyaromatic compounds was still unknown in 1973, apart from the heterocyclodiaromatic[52] compounds such as (*22a*)[50] or (*22b*)[51].



(*22a*) (*22b*)

Carbocyclic cyclopolyaromatic compounds have been known for several decades. The first example, cyclotetrabenzene (tetraphenylene) (*23a*) was prepared in 1943 by *Rapson, Shuttleworth*, and *van Niekerk*[53] by oxidative coupling of a di-Grignard compound (Scheme 21). Further syntheses and studies were performed primarily by research teams led by *Wittig*[54] and *Staab*[55]. The carbocyclic compounds were obtained mainly in modest yield by oxidative linkage of metalated starting compounds with transition metal halides; the properties of the products, *e.g.* (*23b*), correspond largely to expectations.

We attempted to gain an entry to heterocyclopolyaromatic compounds, which promise to be more interesting than their carbocyclic analogues with regard to their chemical reactivity because they are also expected to exhibit the interactions between neighboring nuclei (see Section 2.2) observed in open-chain heteropolyaromatic compounds. It might be expected that the reactivity typical of the individual nuclei would be enhanced in (*24a*) and (*25*), whereas mutual deactivation

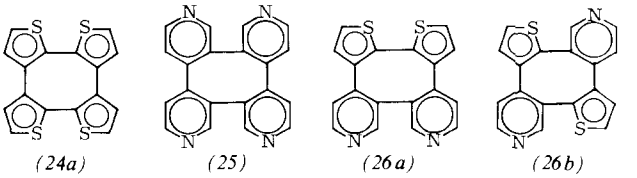


(*23a*)

(*23b*)

Scheme 21. Cyclopolybenzenes (polyphenylenes).

of the aromatic nucleophiles and electrophiles constituting the ring members could occur in (*26a*) and especially (*26b*).

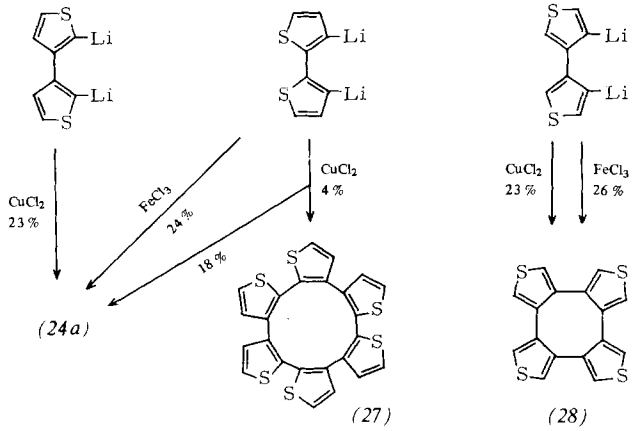


(*24a*) (*25*) (*26a*) (*26b*)

3.2. Organometallic Oxidative Linkage as Cyclization Step

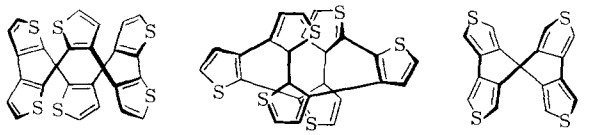
3.2.1. Similar Aromatic Ring Members

The method of oxidative linkage which proved of value in the preparation of cyclotetrabenzene was successfully applied to heterocyclic starting materials. Starting from the dibromides[56], Br/Li exchange and oxidative coupling initially gave the cyclotetrathiophenes *(24a)* and *(28)* (Scheme 22)[9, 13, 57, 58]. Cyclohexathiophene *(27)* was formed as side product in one case. Cyclodithiophenes, *i.e.* products analogous to *(22a)*, could not be detected.

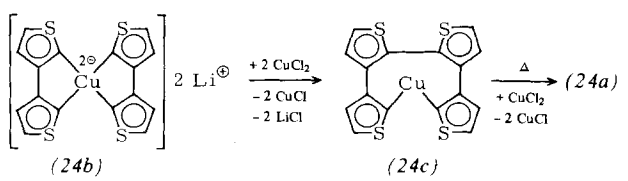


Scheme 22. Cyclopolythiophene syntheses.

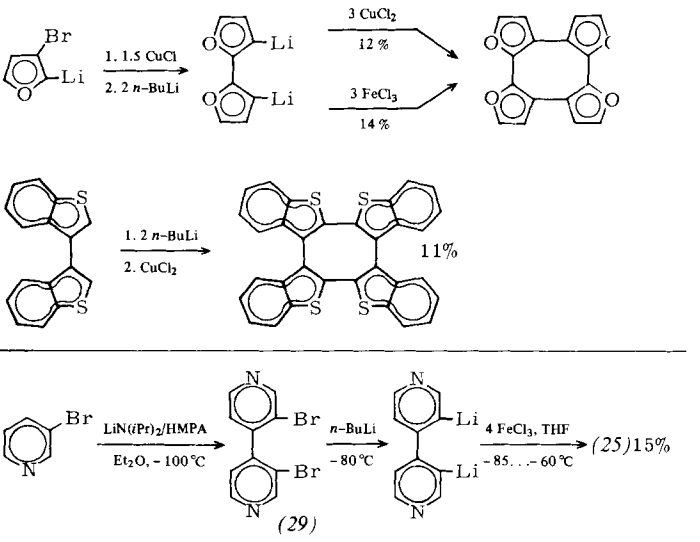
The three-dimensional structure *(28')* was found for *(28)* by X-ray structure analysis[59]. The angle between the planes of adjacent nuclei is 53.7° and is thus considerably smaller than in cyclotetrabenzene *(23a)* (*ca.* 70°)[60]. This complies with expectations, because less deformation of the bond angles is required to planarize *(28')* than *(23a)*. Analogous nonplanar structures are assumed for *(24a)* and the other heterocyclotetraaromatic compounds synthesized. The ^{1}H-NMR spectrum of the cyclohexathiophene *(27)* is almost identical with that of *(28')*. Hence *(27)* probably has the three-dimensional structure *(27')* rather than *(27'')*[61].



The mechanism of the linkages leading to *(24a)* and analogous compounds is still unclear. A reaction route analogous to that proposed and experimentally supported by *Wittig et al.*[54c] for the formation of cyclotetrabenzene would involve the intermediacy of the ate complex *(24b)* and metallocyclic species *(24c)* in the formation of *(24a)* by oxidation with $CuCl_2$.



Two further nucleophilic cyclotetraaromatic compounds (Scheme 23) could be prepared analogously[9, 13, 57, 58] from known precursors[62, 63]. The difficult synthesis of cyclotetrafuran[64] could be reproduced only after several attempts[65].



Scheme 23. Further homotypic [66] heterocyclotetraaromatic compounds by oxidative coupling: Top, aromatic nucleophiles as ring members; bottom, aromatic electrophiles as ring members.

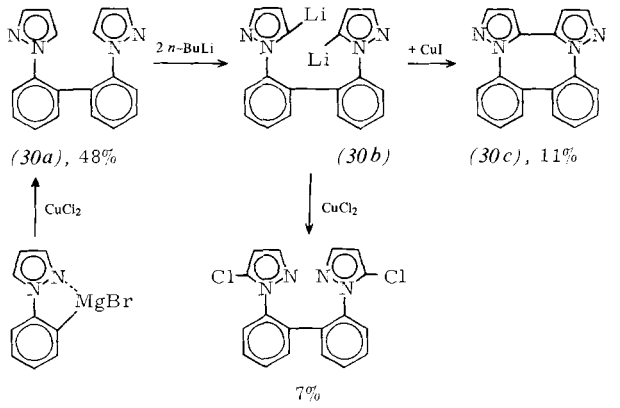
Analogous attempts to synthesize cyclopolyaromatic compounds made up exclusively of heteroaromatic *electrophiles* as ring members have so far succeeded only in the case of cyclotetrapyridine *(25)*. Metal amide linkage of 3-bromopyridine (cf. Section 2.1.2) led to *(29)*[31], which reacted with *n*-BuLi to form the corresponding dilithium compound. Addition of $FeCl_3$ gave the cyclotetrapyridine *(25)*. In contrast, only traces of *(25)* were formed on use of $CuCl_2$[67].

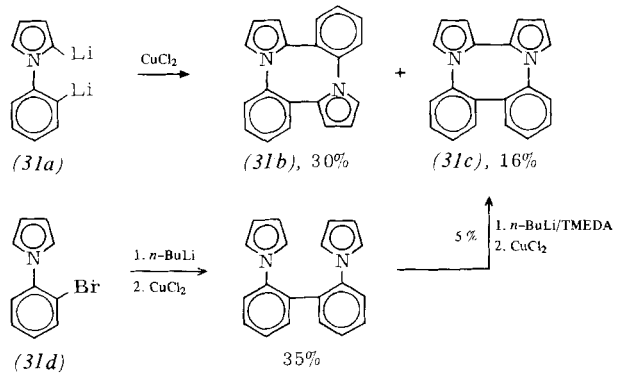
3.2.2. Two Different Kinds of Aromatic Ring Members

On synthesis of *(30c)*, the first heterocyclopolyaromatic compound containing unlike aromatic ring members (Scheme 24)[68, 69], selective linkage of pyrazole and benzene proved feasible because 1-phenylpyrazole is metalated specifically at the phenyl group by Grignard compounds[70] and the tetraaromatic compound *(30a)* specifically at the pyrazolyl group by *n*-BuLi[68]. $CuCl_2$, which is usually the reagent of choice for oxidative linkage *via* organocopper compounds, fails to effect cyclization of the dilithium compound *(30b)*; it acts as a chlorinating agent instead. There is a danger of explosion when cyclization is performed with CuI/O_2[71].

Cyclic pyrrole-benzene combinations were much more readily accessible (Scheme 24, below). On linkage of the dilithium compound *(31a)*, which arises almost quantitatively on reaction of 1 mol of 1-phenylpyrrole with 2 mol of *n*-BuLi/tetramethylethylenediamine (TMEDA)[40b, 72], the question whether *(31b)* or *(31c)* is formed preferentially was of particular interest. It is still unclear why the macrocycle with alternant arrangement of the nuclei happens to predominate. Structural assignment of the two cyclization products[40b] proved possible only after the isomer *(31c)* had been synthesized from *(31d)*[73].

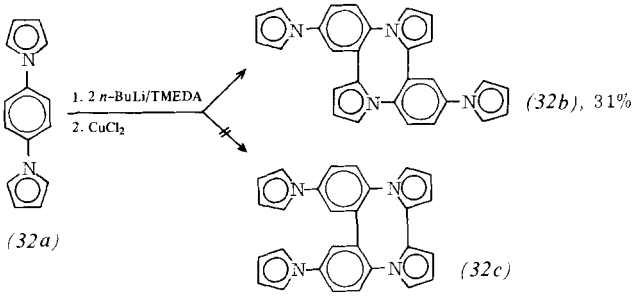
It was not possible to isolate the expected cyclohexaaromatic analog of *(36b)* or the cyclotetraaromatic compound *(32c)* from the mixture obtained on reaction[40b] of the triaromatic





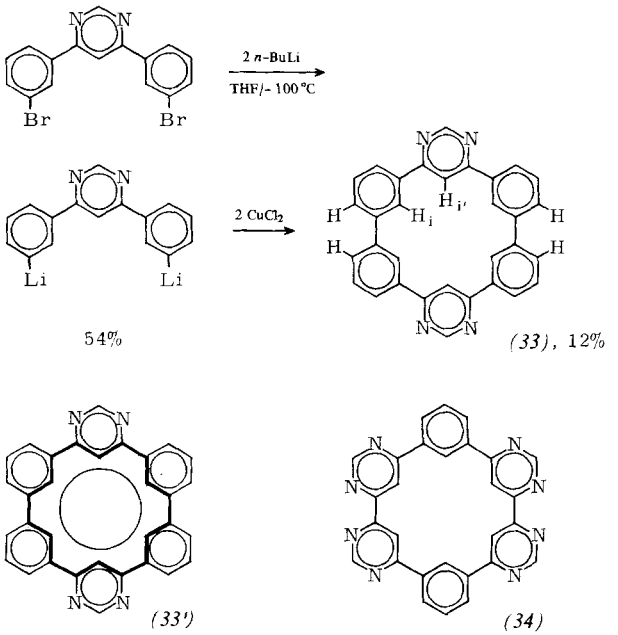
Scheme 24. Heterotypic [66] heterocyclotetraaromatic compounds by oxidative linkage.

species *(32a)*[73]. Compound *(32c)* should be formed less readily for steric reasons than the colorless, fairly soluble isomer *(32b)* formed in relatively good yield; the compound has the basic ring system of *(31b)*.



On synthesis of *(33)* (Scheme 25)[69, 74], the first heterocyclo*hexa*aromatic compound having different kinds of ring members, the double Br/Li exchange shown in the scheme must be carried out with cooling owing to the competing *n*-BuLi addition at the pyrimidine nucleus.

While the planes of adjacent benzene rings are twisted by *ca.* 30° relative to each other in hexa-*m*-phenylene *(23b)* (Scheme 21)[75], the corresponding angle in tetraazahexa-*m*-phenylene *(33)* is shown by X-ray structure analysis[76] not to exceed 1°. This is probably because six pairs of *o,o'*-protons in the outer sphere of *(23b)* hinder planarization while only two such pairs are present in the tetraaza compound. Intramolecular hydrogen bonds from benzene moieties to nitrogen atoms may also be effective.



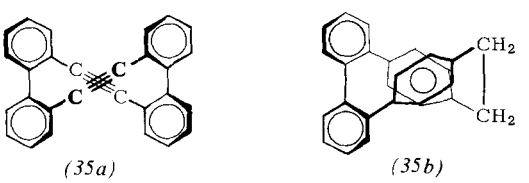
Scheme 25. Heterocyclohexaaromatic compounds with a crown-type structure.

X-Ray structure analysis of *(33)* also shows that a clear distinction in bond length remains (C—$C_{aromatic}$: 1.38 Å; C—$C_{internuclear}$: 1.40 Å) in the internal ring, which formally corresponds to an [18]annulene ring. Thus, as expected, the aromatic character of the individual benzene rings is not weakened in favor of an aromatic [18]annulene system. Any formulation as a condensed aromatic system *(33')* is therefore erroneous.

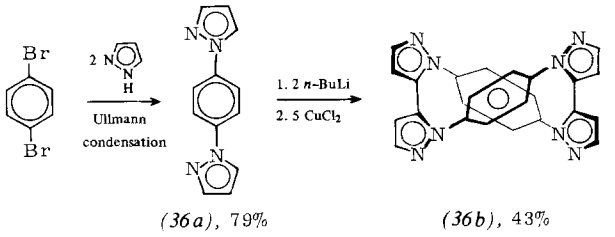
The ^{1}H-NMR spectrum of hexa-*m*-phenylene *(23b)* (Scheme 21) contains the signals of the internal protons at $\delta = 8.85$. The corresponding signals of the tetraaza compound *(33)* at $\delta = 9.42$ (H_i) and 9.51 ($H_{i'}$) show a significant downfield shift. This is probably partly due to the stronger mutual interaction (van der Waals). In the case of octaazahexa-*m*-phenylene *(34)* (synthesis in Section 3.4), the signals of the internal protons H_i and $H_{i'}$ appear at $\delta = 9.75$, *i.e.* even further downfield. This cyclohexaaromatic compound should therefore also be planar, which is understandable in view of the absence of steric hindrance between external *o,o'*-pairs of protons.

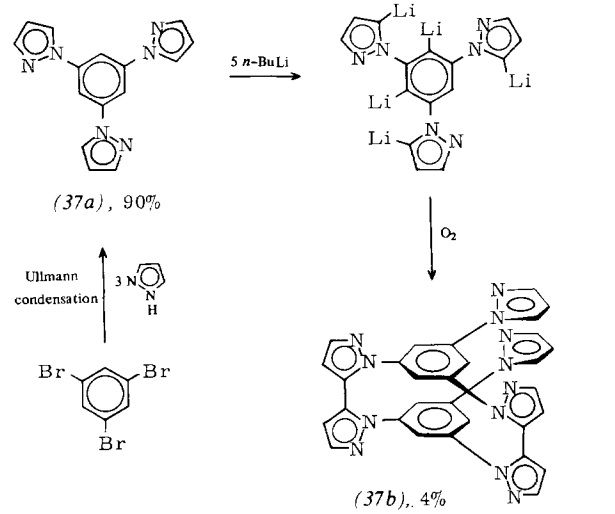
Since compounds *(35a)* and *(35b)* are known[77, 78], it was to be expected that not only crown-type cyclohexaaromatic compounds (Scheme 25) should be possible in which two nuclei are arranged face to face. The question of their chemical and spectroscopic properties makes such compounds interesting synthetic objectives.

It proved possible to synthesize compound *(36b)* as the first representative of this type in acceptable yield (Scheme 26)[40]. Attempted preparation of an analogous heterobicyclooctaaromatic compound having benzene rings linked *via* three bispyrazolyl bridges did not give the desired product but instead a disubstituted cyclohexaaromatic compound to



which we assign structure *(37b)*[79]. The yield of *(37b)* was only 1 % on oxidative coupling of the precursor with $CuCl_2$ instead of with O_2[40b].

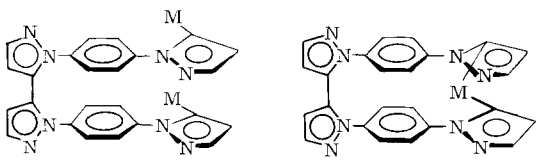




Scheme 26. Heterocycloaromatic compounds with face-to-face arrangement of two rings.

The signals of the phenylene protons (singlet, $\delta = 6.97$) in the ^{1}H-NMR spectrum (in $CDCl_3$) of *(36b)* are distinctly shifted upfield relative to those of the precursor *(36a)* ($\delta = 7.80$). This corresponds to the situation in [2.2]paracyclophane[80], in *(35b)*[78], and in other phanes, and can be explained in terms of the anisotropic effect of the neighboring phenylene group[80].

In the syntheses of heterocyclopolyaromatic compounds by oxidative linkage considered so far, the yield of the cyclization step was at most 31 %. The high yield of *(36b)*—43 %—is therefore surprising. Since the two CC bonds will hardly be formed simultaneously, we have to assume that the intermediate hexaaromatic compound occurs in the cisoid conformation *(38a)* or as metallocycle *(38b)*, or readily transforms into these structures (cf. ref. [49]).



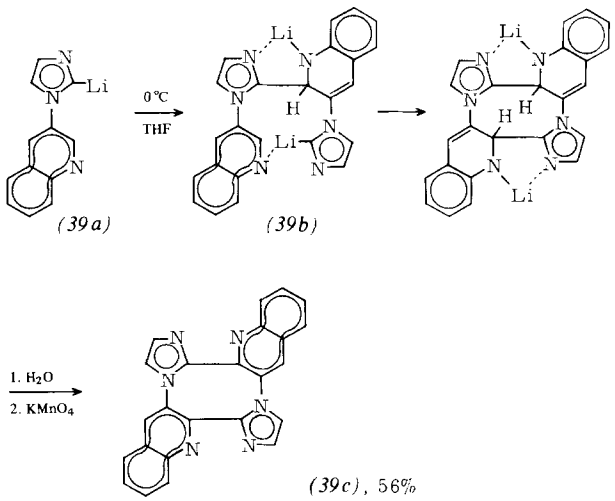
3.3. Nucleophilic Aromatic Substitution as Cyclization Step

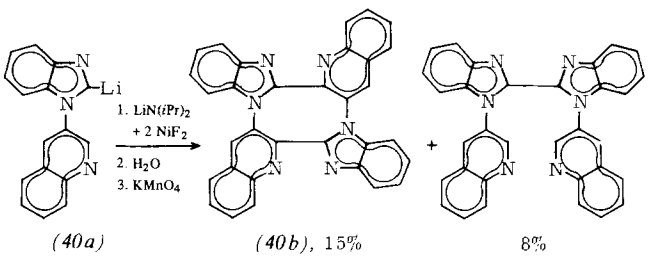
3.3.1. 2+2 Linkage

Since linkage of a heteroaromatic nucleophile with an electrophile is particularly facile (see Section 2.1.1), the cyclization of two molecules of a monolithiated diaromatic compound appears highly promising if it contains a strongly nucleophilic and a strongly electrophilic center like *(39a)*. This kind of cyclization proved successful in four cases.

Especially smooth cyclization was observed with lithiated 3-(1-imidazolyl)quinoline *(39a)* (Scheme 27)[68,81,82]. A contributory role is probably played by the chelate bridge assumed to occur in the intermediate *(39b)* which forces the terminal nuclei into spatial proximity. Unlike the syntheses of *(40b)*, *(41c)*, and *(42)*, that of *(39c)* fails to give better yields on addition of CuF_2 or NiF_2.

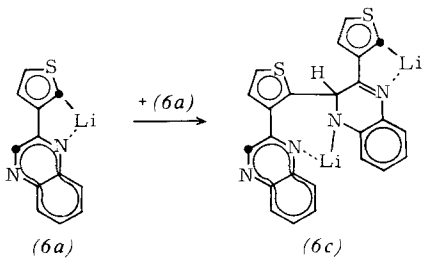
The analogous benzimidazole derivative *(40a)* gives the cyclotetraaromatic compound mentioned in a yield of only 3 %, for reasons which are still unknown; addition of 2 equiv. of NiF_2 *(vide infra)* to the reaction mixture raises the yield to over 15 %[68,81]. The higher electrophilicity of benzimidazole, compared with imidazole, is probably responsible for formation of the above side product (addition of *(40a)* to the corresponding nonlithiated compound).





Scheme 27. Cyclization of imidazolide-analogous [83] diheteroaromatic compounds.

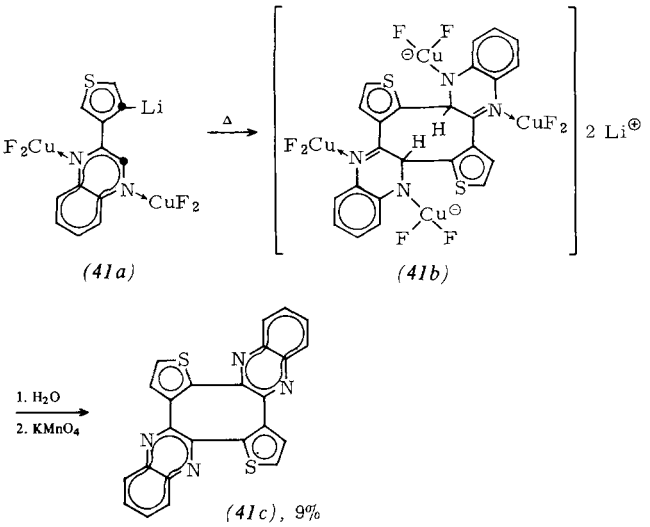
The corresponding cyclization of the lithiated thiophene-quinoxaline combination *(6a)* could not initially be performed since only the open-chain oligomers *(6b)* mentioned in Section

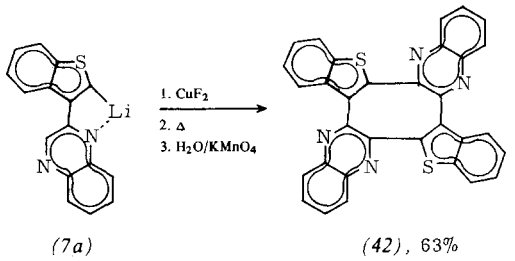


2.1.3 were formed on heating. We attribute this to the chelate bridges in *(6a)* and *(6c)* and analogous intermediates because they fix the two active centers (marked by a point) in the *trans* orientation which is unfavorable for cyclization.

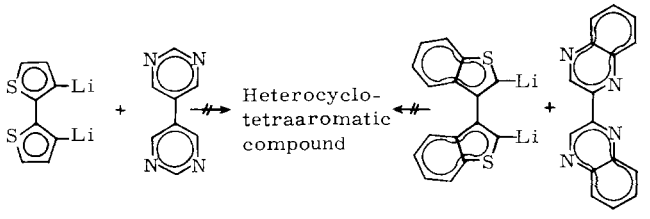
The desired cyclization to *(41c)* (yield 9%) occurred only on treatment of the THF solution of *(6a)* with 2 equiv. of CuF_2 (Scheme 28)[26, 27]. The effect of the CuF_2 can be rationalized by assuming it to complex the N atoms of the quinoxaline system according to *(41a)*, which should overcome the fixing of the "wrong" conformation of *(6a)* and also raise the electrophilicity. The speculative formula *(41b)* should illustrate the complexity of the reaction course.

The benzohomolog *(7a)* likewise mentioned in Section 2.1.3 also cyclizes without addition of CuF_2. Addition of 2 equiv. of anhydrous CuF_2 or NiF_2[84] raised the yield of cyclization product *(42)* from 12% to 63 and 26%, respectively[26, 27]. 63% is the highest yield yet obtained in a heterocyclopolyaromatic synthesis. It is remarkable that this yield and the second-best one [56% of *(39c)*] were both achieved by Ar_{Nu}—Ar_E linkages, which have also proved especially valuable in the synthesis of open-chain systems (cf. Section 2.1.3).



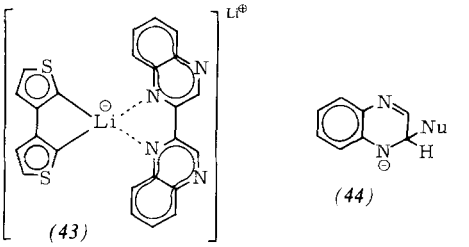


Scheme 28. CuF_2-assisted cyclotetraaromatic syntheses.



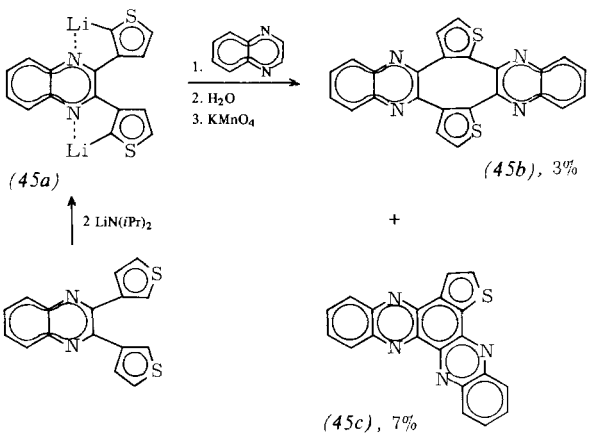
Scheme 29. Unaccomplished cyclizations [13, 26].

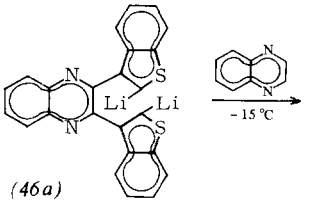
The reaction of a dilithiated nucleophilic diaromatic compound with an electrophilic diaromatic species, *e.g.* according to Scheme 29, also appeared promising as a method for the synthesis of heterocyclotetraaromatic compounds, but all attempts to carry out this reaction were unsuccessful. We suspect the dilithium compound to be deactivated by complexation, *e.g.* according to *(43)* (cf. Section 2.1.4).

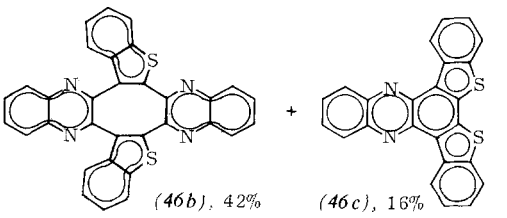


3.3.2. 3+1 Linkage

The quinoxaline system, whose adjacent electrophilic centers make it appear to be such a favorable structural unit for cyclotetraaromatic syntheses, is particularly advantageous for the critical cyclization step in cyclotetraaromatic syntheses. If one of the two electrophilic centers is attacked with formation of an adduct *(44)*, then the electrophilicity of the second center increases, since the "aromatic" CN double bond has been transformed into a "normal" CN double bond. Thus special measures are required (very slow addition of nucleophile to quinoxaline[85]) if single nucleophilic addition to the





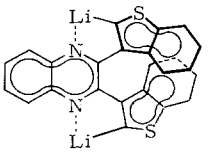


Scheme 30. Heterocyclotetraaromatic syntheses with dilithium compounds.

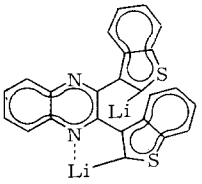
quinoxaline system is to be accomplished rather than double addition. Reaction of the lithiated triaromatic compound *(45a)* with quinoxaline does lead to the desired compound *(45b)* (Scheme 30), but only in poor yield[26].

The dilithium compound *(46a)* prepared analogously is a far better starting material[26,69]. Presumably, crowding of groups in the conformations *(46a')* and *(46a'')* leads to population of conformation *(46a)* which is more favorable for cyclization. The reaction temperature has a marked influence on the product ratio: at 20 instead of −15 °C (Scheme 30) the yield of *(46b)* and *(46c)* is 18 and 69 %, respectively. X-Ray structure analysis[76] confirms the expected double-boat structure analogous to *(28')*.

Reaction of *(47a)* with quinoxaline gives *(47b)*, the first heterocyclotetraaromatic compound to contain three kinds of ring members (Scheme 31)[26]. The by-product *(47c)* justifies the conclusion that the benzothienyl group is initially linked to the quinoxaline. This is expected, because chelation

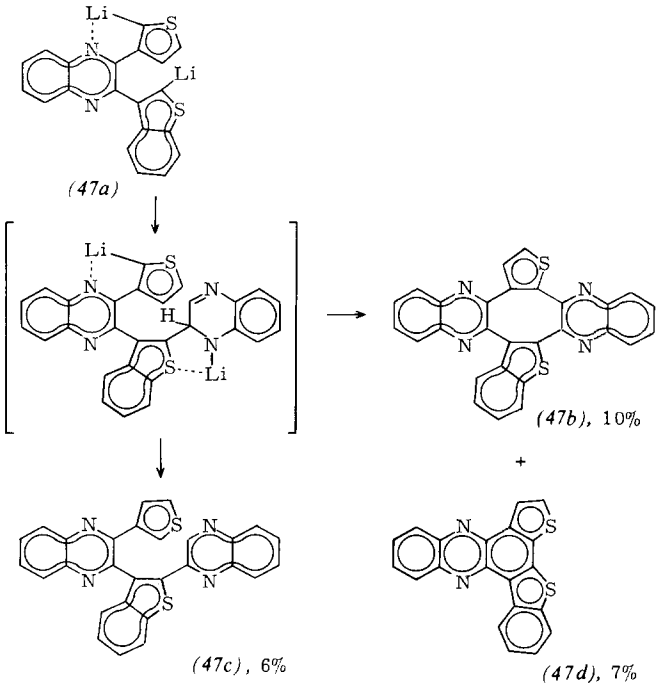


(46a')



(46a'')

to an N atom of the quinoxaline leading to a drop in nucleophilicity is more likely for steric reasons in the case of the thienyl group of *(47a)* than for the benzothienyl group.



(47a)

(47b), 10%

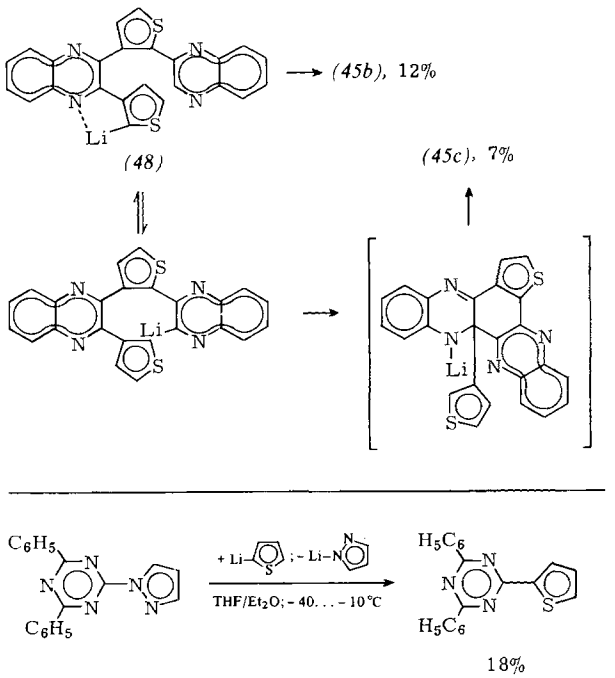
(47c), 6%

(47d), 7%

Scheme 31. Heterocyclotetraaromatic compound having three different kinds of ring members.

3.3.3. 4+0 Linkage

The yield obtained on cyclization of the lithiated tetraaromatic compound *(48)* to give the compound *(45b)* already mentioned was surprisingly low[26]. This may be partly because lithiation with lithium diisopropylamide leading to *(48)* does not occur specifically at the site given (cf. Section 2.1.4)[86]. A further detrimental effect on the yield is exerted by the unusual intramolecular nucleophilic substitution leading to the fused system *(45c)*, in which a 3-thienyl group replaces a 2-quinoxalinyl moiety (Scheme 32). Elimination of a nucleus from *(48)* (two terminal nuclei located in an *o,o'*-relationship to the central internuclear bond) is comparable with elimination of nuclei in the mass spectrometry of structurally analogous tetraaromatic compounds (cf. Section 2.3.3).



(48)

(45b), 12%

(45c), 7%

18%

Scheme 32. Cyclization of tetraaromatic compounds and replacement of one nucleus by another (see also Scheme 30).

In only one other case have we observed a similar nuclear substitution: the by-product *(45c)* of the reaction formulated in Scheme 30 must have been formed in this way. That such reaction must also be able to proceed intermolecularly follows from the 1-pyrazolyl/2-thienyl exchange shown in the bottom part of Scheme 32[87]. A common feature of these substitutions, which probably proceed *via* an addition-elimination mechanism, is their occurrence at a strongly electrophilic nucleus.

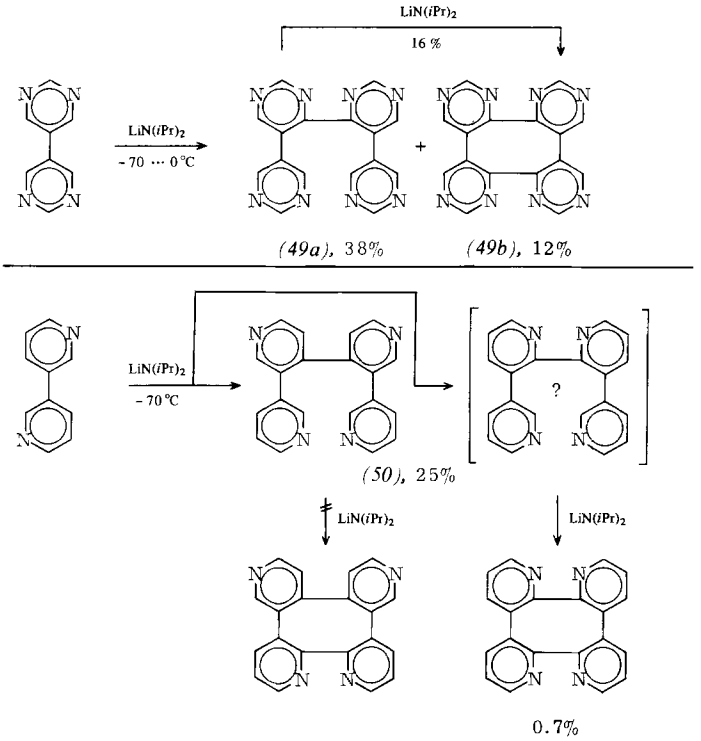
3.4. Metal Amide Linkage as a Cyclization Step[*]

The 5,5'-bipyrimidine obtained (57 %, Scheme 33)[13,57b,58] by oxidative linkage of 5-lithiopyrimidine[88] was transformed into quaterpyrimidine *(49a)* and cyclotetrapyrimidine *(49b)* on addition of lithium diisopropylamide. On further reaction with lithium diisopropylamide[13,57b,58], *(49a)* underwent cyclization, possibly involving fixation of the cisoid conformation by complexation with lithium diisopropylamide according to *(49c)*. This would explain why quaterpyridine *(50)*, which lacks the two nitrogen atoms required for such a complexation, cannot be cyclized analogously[31].

Linkage of 3,3'-bipyridine[31,57b] led to only a very modest yield of cyclotetrapyridine (Scheme 33). The much more readily

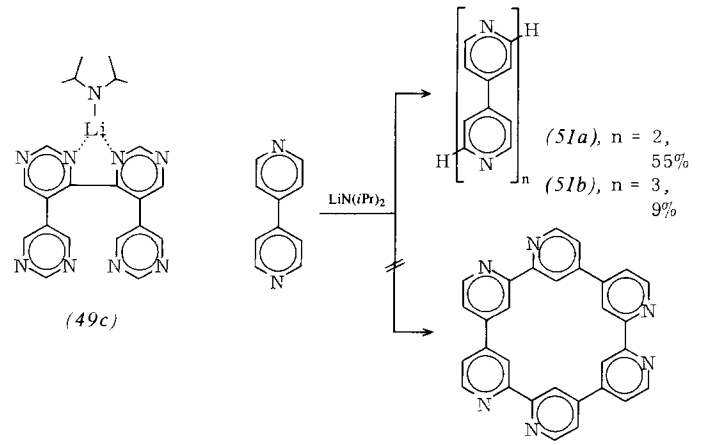
[*] Cf. Section 2.1.2.

accessible cyclotetrapyridine *(25)* was mentioned in Section 3.1.

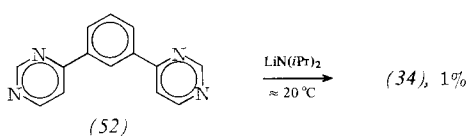


Scheme 33. Cyclization of electrophilic heterodiaromatic compounds.

Attempts to obtain cyclohexapyridine *(51c)* by treatment of 4,4'-bipyridine, alone or in admixture with *(51a)*, or of sexipyridine *(51b)* with lithium diisopropylamide were unsuccessful. Linkage gave only open-chain polypyridines[67].

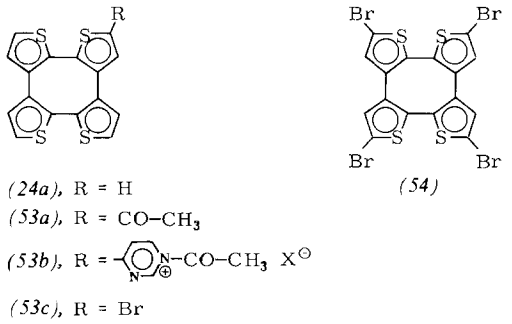


In contrast, the triaromatic compound *(52)* reacts to give octaazahexa-*m*-phenylene *(34)* already mentioned (see Section 3.2.2)[74]. The product of linkage was obtained directly in the "fully aromatic" form, albeit in very low yield.

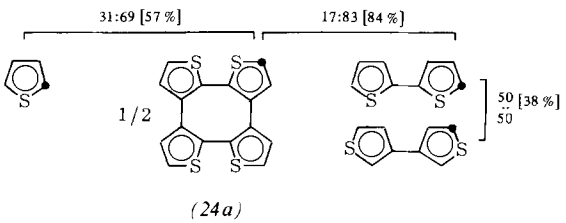


3.5. Detailed Studies on the Heterocyclotetraaromatic Compound *(24a)*

Among the heterocyclotetraaromatic compounds synthesized, only the cyclotetrathiophene cycloocta[1,2-*b*:4,3-*b'*:5,6-*b''*:8,7-*b'''*]tetrathiophene *(24a)* has been studied in detail. Nonavailability of suitable crystals precluded X-ray structure analysis; however, the three-dimensional structure will no doubt closely resemble that found for the isomer *(28)*[59] (see Section 3.2.1). In the UV spectrum ($CHCl_3$) of *(24a)* λ_{max} is observed at 278 nm, and thus lies between λ_{max} of 3,3'-bithiophene (263 nm) and of 2,2'-bithiophene (297 nm). Noncoplanarity of the nuclei apparently prevents extensive interaction between the π-electrons.



Reaction of *(24a)* with one mol. equiv. each of acetyl chloride and $SnCl_4$ leads to a 45% yield of the monoacetyl compound *(53a)*; less than 3% of diacetyl compounds were formed[89, 90]. Introduction of the electron-attracting acetyl group thus significantly reduces the nucleophilic character, not only of the acetylated thiophene ring but of the entire macrocycle, which seems surprising in view of the markedly nonplanar structure.—Competitive experiments with acetyl chloride/$SnCl_4$ show (Scheme 34) that *(24a)* lies between thiophene and 2,2'-bithiophene[89] on the nucleophilicity scale (regarding experimental conditions, see ref. [42]).



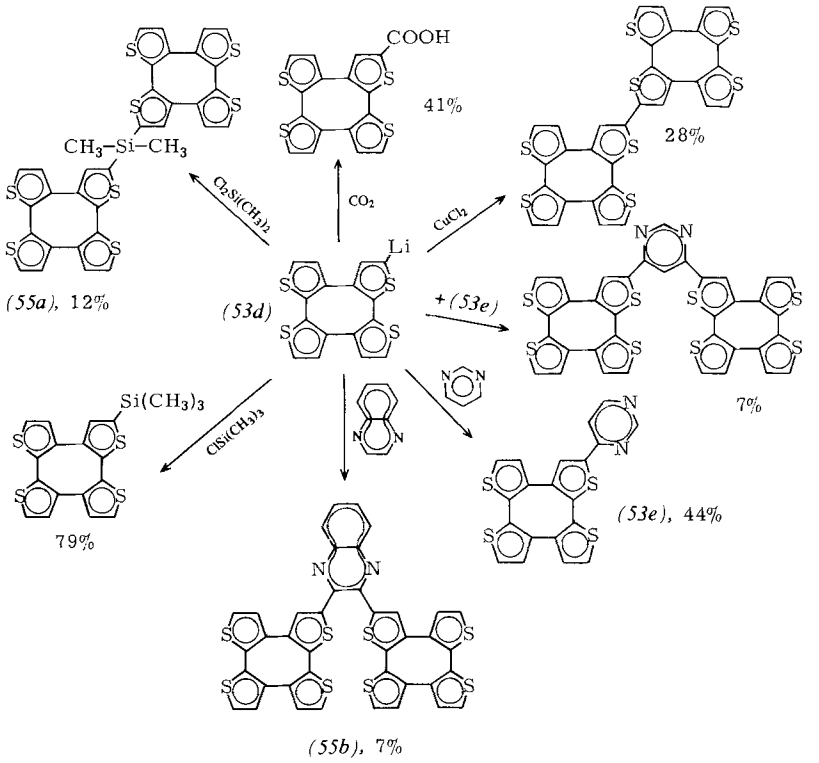
Scheme 34. Relative nucleophilicity towards acetyl chloride/$SnCl_4$: results of competitive experiments analogous to Scheme 16 [91].

The deactivating effect of electron-withdrawing substituents on the entire macrocycle manifests itself even more clearly in the failure of an excess of acetyl chloride and $SnCl_4$ to acetylate even one of the C atoms of the macrocyclic system of the pyrimidinyl-substituted cyclotetrathiophene *(53e)* (Scheme 35), whereas the pyrimidinyl-substituted (open-chain) quaterthiophene *(17a)*, $n=3$, is readily acetylatable under the same conditions (see Section 2.2). This is probably due to the formation of the *N*-acetyl compound *(53b)* and the resulting strongly enhanced electron attraction of the pyrimidinyl group.

While 2-bromothiophene effectively cannot be obtained by the action of bromine on thiophene, owing to fast incorporation of further bromine atoms[92], the reaction of *(24a)* with one mol. equiv. of bromine leads to a 29% yield [48% based on reacted *(24a)*] of the monobromine derivative *(53c)*. Reaction with an excess of bromine under more drastic conditions gave the tetrabromide *(54)* in 82% yield[89].

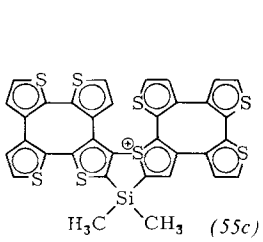
Weak electrophiles can be linked to the macrocycle by reaction with lithiated *(24a)*. It is most fortunate that the reaction of *(24a)* with one equivalent of n-BuLi surprisingly affords essentially only a monolithium derivative[9,89]. It also proves possible, *via* this compound *(53d)*, to oxidatively link two molecules of *(24a)* or to join them together by way of a linking group[89] (Scheme 35).

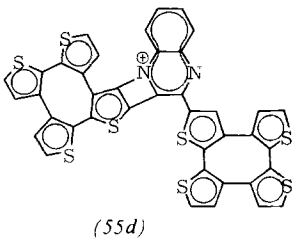
The mass spectrum of the bridged products, *e.g. (55a)* and *(55b)*, contain intense peaks suggestive of cyclization[89]; *(55c)* and *(55d)* (each of relative intensity 100%) are two



Scheme 35. Products obtained from lithiocyclotetrathiophene *(53d)*.

characteristic examples. We may expect that uncharged metallocycles analogous to *(55a)* will one day become readily accessible on a preparative scale from heterocyclopolyaromatic compounds.





The information obtained from a detailed study of cyclotetrathiophene *(23a)* is encouraging: although this macrocycle contains two sets of four equivalent nucleophilic and CH acid positions, monosubstitution products could be obtained with a surprising degree of selectivity by direct electrophilic substitution, by lithiation, or by electrophilic substitution of the lithiation product. The nonplanar structure endows the molecule with a relatively good solubility (*e.g.* 29.4 g/l in $CHCl_3$[93]), while still not effecting mutual isolation of the nuclei which would be of disadvantage on substitution of equivalent positions by random attack. The results suggest that selective and hence preparatively valuable reactions are also possible with other heteropolyaromatic compounds.

4. Outlook

The principle of areno-analogy, which prompted our investigations, will continue to stimulate research into organic chemistry. Developing trends can be seen in protophane (see Section 2.1.4) and phane syntheses[6], in which heteroatoms linked *via* carbon chains serve as nucleophilic and electrophilic functional groups; however, transmetalation reactions (see Section 2.1.4) could set narrow limits to the utility of these reactions. A further limitation comes from the generally irreversible nature of linkages between two heteroaromatic groups (exception: see Scheme 32), which contrasts with the linkage of most functional groups.

It should be mentioned in connection with the heterocyclopolyaromatic compounds that the large number of known hetero- and carbocyclic aromatic compounds and the great variety of possible linkages must, in principle, give rise to thousands of such compounds. In the long term, chemists will not wish to forgo this enormous potential. The years

to come will therefore see the synthesis of many new compounds of this kind. After introduction of suitable substituents to raise their solubility, some compounds of this class may also exhibit interesting physiological properties.

As shown in Section 3.5, monosubstitution does not cause any fundamental difficulties. Concerning the introduction of several substituents or side chains, we can expect that tetrasubstituted derivatives of *(24a)* should be preparable, *e.g.* from the tetrabromo compound *(54)*, by Br/Li exchange and reaction with electrophiles. Apart from subsequent introduction of substituents, it should also be possible to cyclize substituted di- and triaromatic compounds.

All the syntheses carried out so far are organometallic in nature, and often unsatisfactory with regard to yield. Thus, another future task is the development of less complicated, productive syntheses.

The pathway leading to heterocyclopolyaromatic compounds was smoothed by a team of capable co-workers, whose names are mentioned in the references cited. This report is their report. I wish to express my gratitude to all of them.—Thanks are also due to Prof. Dr. H. G. von Schnering, Max-Planck-Institut für Festkörperforschung, Stuttgart, and Priv.-Doz. Dr. H. Irngartinger, Organisch-chemisches Institut der Universität Heidelberg, for X-ray structure analyses. I am indebted to H. Niewind, Organisch-Chemisches Institut der Universität Münster, for preparation of starting materials.—Financial support of this work by the Deutsche Forschungsgemeinschaft (Ka 144/27 and Ka 144/30), the Ministerium für Wissenschaft und Forschung des Landes Nordrhein-Westfalen[94], and the Fonds der Chemischen Industrie is gratefully acknowledged.

Received: January 2, 1978 [A 252 IE]
German version: Angew. Chem. *91*, 1 (1979)

[1] *A. Albert:* Heterocyclic Chemistry. Athlone Press, London 1959; Chemie der Heterocyclen. Verlag Chemie, Weinheim 1962. – Nucleophilic and electrophilic aromatic moieties are designated as Ar_{N_0} and Ar_E, respectively.

[2] *Th. Kauffmann*, Angew. Chem. *83*, 798 (1971); Angew. Chem. Int. Ed. Engl. *10*, 743 (1971).

[3] *Th. Kauffmann*, Chimia *26*, 511 (1972).

[4] Cf. *A. R. Katritzky, J. M. Lagowski:* The Principles of Heterocyclic Chemistry. Methuen, London 1967.

[5] *W. L. F. Armarego, R. E. Willette*, J. Chem. Soc. *1965*, 1258; *T. Higashino, M. Gio, E. Hayashi*, Chem. Pharm. Bull. *22*, 2493 (1974).

[6] For studies on protophanes, phanes, heteroprotophanes, and heterophanes stimulated by the principle of areno-analogy, see: a) *Th. Kauffmann, A. Woltermann*, Angew. Chem. *84*, 824 (1972); Angew. Chem. Int. Ed. Engl. *11*, 842 (1972); b) *Th. Kauffmann, J. Jackisch, A. Woltermann, P. Röwemeier, ibid. 84*, 826 (1972) and *11*, 844 (1972), respectively; c) *Th. Kauffmann, ibid. 86*, 321 (1974) and *13*, 291 (1974), respectively; d) *Th. Kauffmann, G. Beissner, W. Sahm, A. Woltermann, ibid. 82*, 815 (1970) and *9*, 808 (1970); e) *Th. Kauffmann, G. Beissner, R. Maibaum, ibid. 83*, 795 (1971) and *10*, 740 (1971), respectively; f) *Th. Kauffmann, H.-H. Kniese*, Tetrahedron Lett. *1973*, 4043.

[7] *H. Wynberg, T. J. van Bergen, R. M. Kellogg*, J. Org. Chem. *34*, 3175 (1969).

[8] *Th. Kauffmann, E. Wienhöfer, A. Woltermann*, Angew. Chem. *83*, 796 (1971); Angew. Chem. Int. Ed. Engl. *10*, 741 (1971).

[9] *A. Woltermann*, Universität Münster, experiments 1971–1976.

[10] *H. Lücking*, Diplomarbeit, Universität Münster 1977.

[11] Indirect umpolung of carbonyl compounds: *B. T. Gröbel, D. Seebach*, Synthesis *1977*, 357, and references cited therein.

[12] *E. Wienhöfer*, Dissertation, Universität Münster 1974.

[13] *B. Greving*, Dissertation, Universität Münster 1976.

[14] *A. Cairncross, W. A. Sheppard*, J. Am. Chem. Soc. *90*, 2186 (1968).

[15] Addition-elimination mechanism in reactions of hetero-arylcopper compounds with 1,3,5-trinitrobenzene: *M. Nilsson, C. Ullenius, O. Wennerström*, Tetrahedron Lett. *1971*, 2713.

[16] a) *M. Nilsson, C. Ullenius*, Acta Chem. Scand. *24*, 2379 (1970); b) *M. Nilsson, O. Wennerström, ibid. 24*, 482 (1970); c) *N. Gjos, S. Gronowitz, ibid. 25*, 2596 (1971); d) *C. Ullenius, ibid. 26*, 3383 (1972).

[17] Analogy: reactions of phenylcopper with acyl halides: *H. Gilman, J. M. Straley*, Rec. Trav. Chim. Pays-Bas *55*, 821 (1936).

[18] Six-step ring-forming synthesis (overall yield 14 %): *H. J. Kooremann, H. Wynberg*, Rec. Trav. Chim. Pays-Bas *86*, 37 (1967).

[19] *H. Lexy*, Diplomarbeit, Universität Münster 1975.

[20] Four-step ring-forming synthesis (overall yield 16 %): *T. Reichstein, A. Grüssner, H. Zschokke*, Helv. Chim. Acta *15*, 1066 (1932); *R. Grigg, J. A. Knight, M. V. Sargent*, J. Chem. Soc. *C 1966*, 976.

[21] IUPAC rule A-54.1 requires use of the numerical prefixes bi, ter, quater, quinque, sexi, *etc.* for open and unbranched chains made up of identical ring systems. These requirements are not fulfilled by most of the conceivable polyaromatic systems owing to non-identical aromatic chain members, to cyclic or branched structures. In these cases and in the general terms such as tetraaromatic compounds or cyclotetraaromatic compounds we employ the set of prefixes di, tri, tetra, *etc.*

[22] *A. J. Clarke, S. McNamara, O. Meth-Cohn*, Tetrahedron Lett. *1974*, 2373.

[23] *B. C. Platt*, Nature *157*, 439 (1946). Dehydrodimerization products of electrophilic heteroaromatic compounds have been obtained on several occasions as side products of the Chichibabin reaction (cf. *H. T. Leffler*, Org. React. *1*, 91 (1942)).

[24] *R. J. Martens, H. J. den Hertog, M. van Ammer*, Tetrahedron Lett. *1964*, 3207.

[25] The yields given are the highest yields obtained in several experiments. Heating of *(6a)* in boiling ether afforded all the oligomers listed, while only *(6b)*, $n=1$ and 2, were formed if *(6a)* was allowed to react in THF at 0°C.

[26] *R. Otter*, Dissertation, Universität Münster 1978.

[27] *Th. Kauffmann, R. Otter*, Angew. Chem. *88*, 513 (1976); Angew. Chem. Int. Ed. Engl. *15*, 500 (1976).

[28] *E. Wienhöfer, Th. Kauffmann*, Tetrahedron Lett. *1974*, 2347.

[29] The reaction temperature cannot be increased since *(8a)* otherwise undergoes increased self-addition.

[30] *Th. Kauffmann, J. König, A. Woltermann*, Chem. Ber. *109*, 3864 (1976).

[31] *J. König*, Dissertation, Universität Münster 1977.

[32] *Th. Kauffmann, A. Mitschker*, Tetrahedron Lett. *1973*, 4039.

[33] *A. Mitschker, U. Brandl, Th. Kauffmann*, Tetrahedron Lett. *1974*, 2343.

[34] *A. Mitschker*, Dissertation, Universität Münster 1974.

[35] *A. Vahrenhorst*, Universität Münster, experiments 1977.

[36] *P. Ribereau, G. Nevers, G. Queguiner*, lecture at Réunion du Groupe Français de Chimie Hétérocyclique in Lille, Sept. 1977; *P. Ribereau, G. Nevers, G. Queguiner, P. Pastour*, C. R. Acad. Sci. Ser. *C 280*, 293 (1975).

[37] *J. Jackisch*, Dissertation, Universität Münster 1973.

[38] *U. Prager*, Dissertation, Universität Münster 1977.

[39] *D. Körber*, Dissertation, Universität Münster 1977.

[40] a) *Th. Kaufmann, H. Lexy*, Angew. Chem. *90*, 804 (1978); Angew. Chem. Int. Ed. Engl. *17*, 755 (1978); b) *H. Lexy*, Dissertation, Universität Münster 1978.

[41] The melting points given by *W. Steinkopf, R. Leitsman, K. H. Hofman*, Justus Liebigs Ann. Chem. *546*, 180 (1941), for *all*-α-polythiophenes have been improved on the basis of our own results [39]. *all*-α-Octithiophene [39] was previously unknown. The melting points given in Table 2 are corrected values.

[42] *Th. Kauffmann, J. König, D. Körber, H. Lexy, H.-J. Streitberger, A. Vahrenhorst, A. Woltermann*, Tetrahedron Lett. *1977*, 389.—In the competition experiments, several factors (failure of reaction to occur at low reagent concentrations owing to *N*-acetylation or H/Li exchange; poor availability of some compounds; necessity of high yields to facilitate evaluation) precluded choice of reaction conditions required for determination of competition constants (large excess of substrates relative to reagent; cf. *R. Huisgen, W. Mack, L. Möbius*, Tetrahedron *9*, 29 (1960)). Nevertheless, our aim of gaining some idea about the relative nucleo- or electrophilicity of the substrates has probably been accomplished.

[43] *H.-J. Streitberger*, Dissertation, Universität Münster 1975, and unpublished measurements performed in 1976.

[44] Calculations (Pariser-Parr-Pople) by *M. Klessinger* and *T. Ischebeck* (*T. Ischebeck*, Diplomarbeit, Universität Münster 1974) show that the nucleophilicity and electrophilicity of a combination $Ar_{Nu}-Ar_E$ should be greater than those of Ar_{Nu} and Ar_E.

[45] Given thermodynamic control, the number of sites open to attack would not play any role. However, kinetic control is to be assumed since no *n*-BuLi adduct of the diaromatic compound *(17b)*, X=S, was formed on its addition to the *n*-BuLi adduct of pyrimidine under the conditions of competition experiments [35].

[46] *Th. Kauffmann, P. Bandi, W. Brinkwerth, B. Greving*, Angew. Chem. *84*, 830 (1972); Angew. Chem. Int. Ed. Engl. *11*, 848 (1972).

[47] *H. Stöckelmann*, Diplomarbeit, Universität Münster 1976.

[48] UV spectra of *all*-α-polythiophenes (in $CHCl_3$), see [39]; of *all*-α-polypyrroles (in $CHCl_3$), see [40b]; of poly-*p*-benzenes (in $CHCl_3$), see *A. E. Gillan, D. H. Hey, A. Lambert, ibid. 1941*, 364.

[49] *Th. Kauffmann, A. Mitschker*, Tetrahedron Lett. *1977*, 393.—According to the ^{1}H-NMR spectra, heterotetraaromatic compounds with "*o,o'*-linkage", *e.g. (20)*, exist preferentially in the cisoid conformation in solution [40b, 68].

[50] *P. J. Garrat, K. P. C. Vollhardt*, J. Am. Chem. Soc. *94*, 7087 (1972).

[51] *J. M. Kramer, R. S. Berry*, J. Am. Chem. Soc. *93*, 1303 (1971).

[52] Heterocyclotriaromatic compounds such as the photocyclization product in Scheme 12 number among the fused heterocyclic compounds.

[53] *W. S. Rapson, R. G. Shuttleworth, J. N. van Niekerk*, J. Chem. Soc. *1943*, 326.

[54] a) *G. Wittig, G. Lehmann*, Chem. Ber. *90*, 875 (1957); b) *G. Wittig*, Q. Rev. Chem. Soc. *20*, 205 (1966); c) *G. Wittig, G. Klar*, Justus Liebigs Ann. Chem. *704*, 91 (1967); d) *G. Wittig, K.-D. Rümpler, ibid. 751*, 1 (1971); e) *G. Wittig, S. Fischer, G. Reiff, ibid. 1973*, 495.

[55] a) *H. A. Staab, F. Binnig*, Chem. Ber. *100*, 293, 889 (1967); b) *H. A. Staab, H. Bräunling, K. Schneider*, Chem. Ber. *101*, 879 (1968).

[56] *S. Gronowitz, H.-O. Karlsson*, Ark. Kemi *17*, 89 (1961); *R. M. Kellogg, A. P. Schaap, H. Wynberg*, J. Org. Chem. *34*, 343 (1969); *S. Gronowitz*, Acta Chem. Scand. *15*, 1393 (1961).

[57] a) *B. Greving, A. Woltermann, Th. Kauffmann*, Angew. Chem. *86*, 475 (1974); Angew. Chem. Int. Ed. Engl. *13*, 467 (1974); b) *Th. Kauffmann, B. Greving, J. König, A. Mitschker, A. Woltermann, ibid. 87*, 745 (1975) and *14*, 713 (1975), respectively.

[58] *Th. Kauffmann, B. Greving, R. Kriegesmann, A. Mitschker, A. Woltermann*, Chem. Ber. *111*, 1330 (1978).

[59] *H. Irngartinger*, 1976, personal communication. The results will be published in full.

[60] The value is taken from a molecular model [54d] based on electron diffraction studies by *I. L. Karle, L. O. Brockway*, J. Am. Chem. Soc. *66*, 1974 (1944).

[61] Cf. the analogous alternative for cyclohexa-*o*-benzene (hexa-*o*-phenylene): [54d] and *L. Ernst, A. Mannschreck, K.-D. Rümpler*, Org. Magn. Reson. *5*, 125 (1973).

[62] *G. M. Davies, P. S. Davies*, Tetrahedron Lett. *1972*, 3507.

[63] *L. J. Pandya, D. S. Rao, B. D. Tilak*, J. Sci. Ind. Res. Sect. *B 18*, 516 (1939); Chem. Abstr. *54*, 1739d (1960); for an improved preparation, see [58].

[64] *A. Mitschker*, Universität Münster, experiments performed in 1975.

[65] *R. Kriegesmann*, Diplomarbeit, Universität Münster 1976.

[66] We designate cyclopolyaromatic compounds having aromatic ring members of the same kind (not necessarily joined by the same kind of bond) as "homotypic" and those with different kinds of aromatic ring members as "heterotypic".

[67] *F. R. Sapi*, Dissertation, Universität Münster, projected for 1979.

[68] *D. Tigler*, Dissertation, Universität Münster 1977.

[69] *Th. Kauffmann, B. Muke, R. Otter, D. Tigler*, Angew. Chem. *87*, 746 (1975); Angew. Chem. Int. Ed. Engl. *14*, 714 (1975).

[70] *A. Marxer, M. Siegrist*, Helv. Chim. Acta *57*, 1988 (1974).

[71] After passage of oxygen into THF solutions of organocopper(I) compounds (*e.g.* 2-cuprothiophene) at *ca.* −60 °C the mixture exploded on three occasions when warmed to room temperature in our laboratory, probably due to decomposition of peroxides of THF. We have found room temperature oxidation of the organocopper(I) compounds with oxygen to be a more favorable method.

[72] *D. A. Shirley, B. H. Gross, P. A. Roussel*, J. Org. Chem. *20*, 225 (1955).

[73] Preparation of the new compound *(31d)* by reaction of *o*-bromoaniline with 2,5-dimethoxytetrahydrofuran in glacial acetic acid (yield 93 %) [40b]; corresponding preparation of *(32a)* (yield 36 %): *N. Elming, N. Clauson-Kaas*, Acta Chem. Scand. *6*, 867 (1952).

[74] *B. Muke*, Dissertation, Universität Münster 1976.

[75] *H. Irngartinger, L. Leiserowitz, G. M. J. Schmidt*, Chem. Ber. *103*, 1132 (1970).

[76] X-Ray structure analysis of *(33)* and *(46b)*: *H. G. von Schnering, G. Sawitzki*, 1976/77, personal communication. The results will be published in detail elsewhere.

[77] *H. A. Staab, E. Wehinger*, Angew. Chem. *80*, 240 (1968); Angew. Chem. Int. Ed. Engl. *7*, 225 (1968).

[78] *F. Vögtle, M. Atzmüller, W. Wehner, J. Grütze*, Angew. Chem. *89*, 338 (1977); Angew. Chem. Int. Ed. Engl. *16*, 325 (1977).

[79] The low yield of *(37b)* is probably due in part to the fact that *(37a)* is also lithiated at the benzene nucleus (threefold "external lithiation" is accompanied by double "internal lithiation"). The "*cis*" position of the two 1-pyrazole groups in *(37b)* is supported the significant upfield shift of the ^{1}H-NMR signals (in $CDCl_3$) of the pyrazole protons of *(37b)* ($\delta = 7.79$) relative to those of *(37a)* ($\delta = 7.98$) (cf. ref. [8]).

[80] ^{1}H-NMR signals (in $CDCl_3$) of the phenylene groups of [2.2]paracyclophane, [2.3]paracyclophane, and *p*-xylene: $\delta = 6.37$, 6.48, and 7.05 (*H. Hopf*, Angew. Chem. *84*, 471 (1972); Angew. Chem. Int. Ed. Engl. *11*, 419 (1972); *D. J. Cram, R. C. Helgeson*, J. Am. Chem. Soc. *88*, 3515 (1966); High Resolution NMR, NMR Spectra Catalog, Instrument Division of Varian Associates, Palo Alto, California 1962).—Concerning interpretation of the upfield shift for aromatic rings arranged face to face in phanes, see *M. Haenel, H. A. Staab*, Chem. Ber. *106*, 2203 (1973); *C. E. Johnson, Jr., F. A. Bovey*, J. Chem. Phys. *29*, 1012 (1958).

[81] *Th. Kauffmann, D. Tigler, A. Woltermann*, Tetrahedron Lett. *1977*, 741.

[82] Increase in yield from 35 % [68] to 56 % by lowering the reaction temperature from 20 to 0 °C; *H. Rohkrähmer*, Diplomarbeit, Universität Münster 1977.

[83] The *N*-acylimidazoles designated as imidazolides (see *H. A. Staab*, Angew. Chem. *74*, 407 (1962); Angew. Chem. Int. Ed. Engl. *1*, 351 (1962)) have a carbonyl activity resembling that of acyl halides. The electrophilicity of the electrophilic heteroaromatic species is correspondingly enhanced in heterodiaromatic compounds analogous to imidazolides [81].

[84] The favorable effect of CuF_2 or NiF_2 on cyclizations was discoved by accident on attempted coupling of lithiated heterodiaromatic compounds with these fluorides [26].

[85] Synthesis of Ar_{Nu}—Ar_E combinations of quinoxaline under these conditions, see: *M. Ghanem*, Diplomarbeit, Universität Münster 1974.

[86] Owing to the unfavorable position of this signal the site of lithiation could not be determined by ^{1}H-NMR spectroscopy of the deuterolysis product in this case.

[87] *W. Brinkwerth*, Dissertation, Universität Münster 1975.

[88] *S. Gronowitz, J. Röe*, Acta Chem. Scand. *19*, 1741 (1965).

[89] *H. P. Mackowiak*, Dissertation, Universität Münster 1977.

[90] The position of the acetyl groups in the two diacetyl compounds accessible in 20 % yield each under more drastic conditions could not be elucidated [89].

[91] The molar ratio *(24a)*: thiophene (bithiophene): acetyl chloride: $SnCl_4$ is 0.5:1:1:1 in the competition experiments with *(24a)* + thiophene or 2,2'-bithiophene. This ratio was chosen in order that the substrates should present equal numbers of active sites to attack by acetyl chloride (cf. ref. [42]).

[92] Monobromination succeeds with *N*-bromosuccinimide: *Ng. Ph. Buu-Hoi*, Justus Liebigs Ann. Chem. *556*, 1 (1944).

[93] *H. P. Mackowiak*, Universität Münster, unpublished measurements performed in 1977.

[94] Research report: *Th. Kauffmann*, Forschungsberichte des Landes Nordrhein-Westfalen, No. 2450. Westdeutscher Verlag, Opladen 1975.

The Art of Titration

From Classical End Points to Modern Differential and Dynamic Analysis[**]

By Ruthild Winkler-Oswatitsch and Manfred Eigen[*]

Gerold Schwarzenbach in memoriam

Titration represents the quantitative determination of a chemical change in response to the variation in concentration of a standard. Information on reaction parameters is usually obtained from an analysis of the shape of the titration curve. In this paper the derivatives of titration functions with respect to concentration variables and with respect to equilibrium parameters are compared with one another. The latter can be determined directly from amplitudes and time constants of the dynamic responses to equilibrium perturbations, brought about by fast alterations of temperature, pressure or electric field.

Three general situations have to be distinguished: 1. If the interaction is very strong (*i.e.* the complex stability is high: $K \rightarrow \infty$), the (average) number of sample particles can be counted directly by means of their reaction with a calibrated number of standard particles.—2. If, on the contrary, the interaction is weak (*i.e.* the complex stability is low), the sample will react quantitatively only in the presence of a large excess of standard; the half-way point of which provides a direct measure of the binding constant.—3. Only for moderate interactions can individual curves characteristic of the binding strength be observed. The limiting cases 1 and 2 yield titration curves which reflect only the general class to which the system belongs.

The dynamical procedures are fairly insensitive in case 1, which represents the classical end-point situation and is most suitable for quantitative analysis, *i.e.* for a determination of sample concentrations. For case 2, the classical and dynamical techniques yield comparable information: mass-action parameters are obtained from the extrema of the curves, which occur only in the presence of an excess of the standard. In case 3 the dynamical treatment provides a more direct access to the equilibrium constants, and also to the enthalpies or volumes of reaction as well as to the rate constants. The advantage of the dynamic method is due to the fact that in the two derivatives of the titration function $\mathrm{d}T_i/\mathrm{d}\ln q$ and $\mathrm{d}T_i/\mathrm{d}\ln p$ (where q is the titration variable, *i.e.* the ratio of standard and sample concentration, and p the mass-action parameter, *i.e.* a reduced binding constant) the terms resulting from a differentiation with respect to p are more closely related to the reaction parameters than those following from a variation of q.

The dynamic analysis is generalized for applications to multiple-step titration processes, where it allows for the measurement of equilibrium and rate parameters of *individual* steps. A uniform representation utilizing trigonometric functions was chosen which expresses clearly the singular character of the end-point. The relations are summarized in tabular form. They provide in conjunction with the illustrations the basis for a comparative discussion.

1. Introduction

Any complex system of matter is completely characterized by the spatial and temporal distribution of its various individual constituents, expressed in terms of their population densities. The determination of the population densities of the various molecular parts of the system is one of the fundamental tasks of chemistry. This is usually effected by "counting" utilizing chemical turnover: The species present in unknown number is allowed to react with a known or measurable number of specific partners. This procedure is called *titration.*

The *classical method* of titration is based on a more or less *complete turnover* of the sample to be analyzed yielding a well defined *end-point.* Of course, the only reactions suitable for titration are those which occur rapidly enough, *i.e.* within the time of observation. The "completeness" of the turnover is then solely determined by the magnitude of the equilibrium stability constant. In fact, a quantitative establishment of this parameter is very often the final object of the titration. It is therefore necessary to measure precisely the *concentrations of individual partners and products* involved in the reaction.

An alternative procedure for determining stability constants is to measure an *extensive thermodynamic quantity* as a function of the weighed-in concentrations of the reaction partners. It requires the precise measurement either of Gibb's free energy or of any of its first or higher derivatives with respect to

[*] Prof. Dr. M. Eigen, Dr. R. Winkler-Oswatitsch
Max-Planck-Institut für Biophysikalische Chemie,
Abt. Biochemische Kinetik
D-3400 Göttingen (Germany)

[**] This work is based on a thesis [1] carried out at the Max-Planck-Institut für Physikalische Chemie, Göttingen, and submitted at the Technische Hochschule, Wien, im November 1969.

an *intensive variable* (such as temperature T, pressure P, electrical field density $\boldsymbol{E}$).

The aim of the present paper is *to demonstrate the particular advantages of dynamic titration methods for the determination of binding constants from the time-dependent chemical increments of extensive thermodynamic functions*, and *to compare the results of the dynamical approach with those obtained by classical titration procedures.*

This article is particularly addressed to the chemist who has experienced that titration is by no means a matter of routine, requiring rather a procedure optimally adapted to suit each problem. For this purpose an understanding of the physical basis is necessary, and its principles will be developed in this paper. The "Art of Titration" is as little related to the mechanical execution of recipes as is the "Art of Cooking".

2. Binary Complex Formation

2.1. Stability Constants and Titration Curves

The progress of a chemical reaction can be followed (almost) instantaneously, if reaction partners and products show detectable changes in their electromagnetic properties upon reaction. As an example let us consider the binary association-dissociation process

$$A + B \rightleftharpoons AB \tag{2.1-1}$$

where A and B may represent an acid and a base, a metal ion and a ligand, an enzyme and a substrate, an antibody and a hapten, or any kind of reaction partners involved in a general coordination process. The example embodies equally the processes of electron, proton or ligand exchange, although these processes belong to the category of substitution rather than addition reactions.

If both weighed-in concentrations c_A^0 and c_B^0 are known, the law of mass action adopts the form

$$K = K_0 \Pi f \approx \frac{c_{AB}}{(c_A^0 - c_{AB})(c_B^0 - c_{AB})} \tag{2.1-2}$$

where K_0 is the thermodynamic equilibrium constant at the given values of the intensive thermodynamic variables, and $\Pi f = f_A f_B / f_{AB}$ is a term involving the activity coefficients of the reaction partners and products.

In the following we shall not deal explicitly with the term Πf. Its changes during the titration occurring especially when there is charge neutralization, can be taken into account wherever it turns out to be necessary; it is negligible at low concentrations of A, B and AB, or, in the presence of an excess of inert electrolyte, it can be included in K as a constant factor.

Eq. (2.1-2) provides explicit expressions for the equilibrium concentrations of all individual species in terms of c_A^0, c_B^0 and K:

$$c_{AB} = \frac{c_A^0 + c_B^0 + K^{-1}}{2} - \frac{1}{2}\sqrt{(c_A^0 + c_B^0 + K^{-1})^2 - 4 c_A^0 c_B^0} \tag{2.1-3}$$

$$c_A = c_A^0 - c_{AB} \tag{2.1-4}$$

$$c_B = c_B^0 - c_{AB} \tag{2.1-5}$$

Let A and/or B, upon its conversion into AB, show a measurable shift in the absorption spectrum, characterized by the (finite) difference of extinction coefficients: $\varepsilon_A + \varepsilon_B - \varepsilon_{AB}$. The optical density per unit length (E/l) can then be written as

$$\begin{aligned} E/l &= c_A \varepsilon_A + c_B \varepsilon_B + c_{AB} \varepsilon_{AB} \\ &= c_A^0 \varepsilon_A + c_B^0 \varepsilon_B + c_{AB}(\varepsilon_{AB} - \varepsilon_A - \varepsilon_B) \end{aligned} \tag{2.1-6}$$

If we denote the limiting values of the optical density for $c_{AB} = 0$ as:

$$E_0/l = c_A^0 \varepsilon_A + c_B^0 \varepsilon_B \tag{2.1-7}$$

or for $c_B = 0$, *i.e.* after complete conversion of B into AB in presence of an excess of A as:

$$E_\infty/l = c_A^0 \varepsilon_A + c_B^0(\varepsilon_{AB} - \varepsilon_A) \tag{2.1-8}$$

then the "degree of complexation" can be expressed by measurable extinction values as

$$\frac{c_{AB}}{c_B^0} = \frac{E - E_0}{E_\infty - E_0} \equiv \eta \tag{2.1-9}$$

Eq. (2.1-9), in combination with the law of mass action, provides useful relations for the determination of equilibrium constants from titration curves, *e.g.* the Hildebrand-Benesi equation or similar forms[2]:

$$\frac{c_A^0}{E - E_0} = \frac{c_B^0}{E_\infty - E_0} + \frac{K^{-1}}{E_\infty - E} \tag{2.1-10}$$

If we plot $c_A^0/(E - E_0)$ *versus* $1/(E_\infty - E)$ (cf. Fig. 1a), a straight line is obtained. Its slope yields the dissociation constant K^{-1}. Such a diagram does not even require a precise knowledge of c_B^0, which results from the intercept of the obtained line.

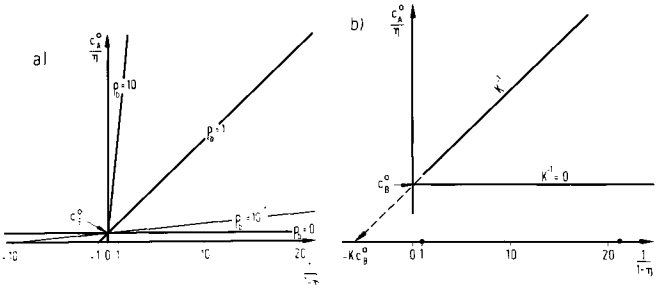
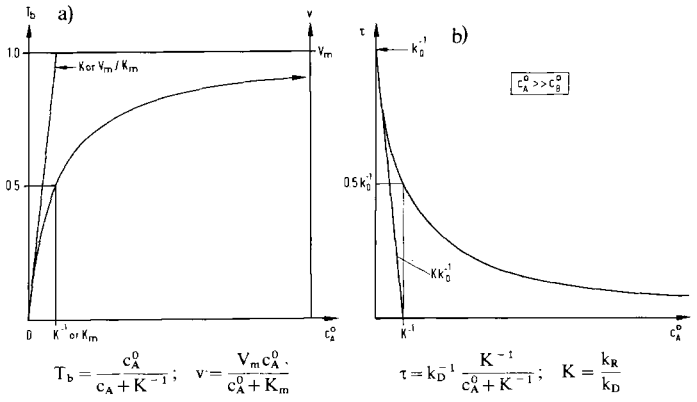


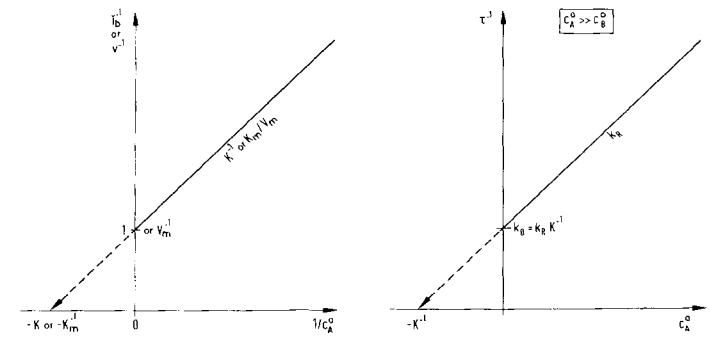
Fig. 1. a) Hildebrand-Benesi plot providing stability constants (K) from extinction ratios η or $1-\eta$ resp. (variation of c_A^0- or $q_b = c_A^0/c_B^0$- at constant c_B^0; parameter to be determined: $p_b = K^{-1}/c_B^0$). For η-values close to one or zero, the detection becomes insensitive. If p_b is large, the ratio $q_b = c_A^0/c_B^0$ can be adjusted to comparatively large values, which represent the sensitive range for changes of η. If p_b is small, however, there will be almost no change of c_A^0/η within the corresponding region of η (*i.e.* $\eta \sim c_A^0$). Hence very small values of p_b cannot be evaluated (cf. also Fig. 3).

b) The range between the two dots on the abscissa is most suitable for measurements.

A variety of similar equations may be derived which offer specific advantages (*e.g.* a suitable extrapolation in cases where $(E_\infty - E_0)$ is unknown), or which refer to parameters other than those of extinction. Biochemists have been especially successful in inventing all sorts of related plots for enzyme-

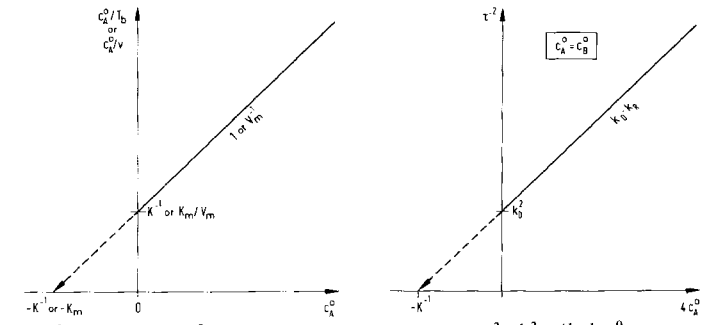


$$T_b = \frac{c_A^0}{c_A + K^{-1}}; \quad v = \frac{V_m c_A^0}{c_A^0 + K_m} \qquad \tau = k_D^{-1}\frac{K^{-1}}{c_A^0 + K^{-1}}; \quad K = \frac{k_R}{k_D}$$

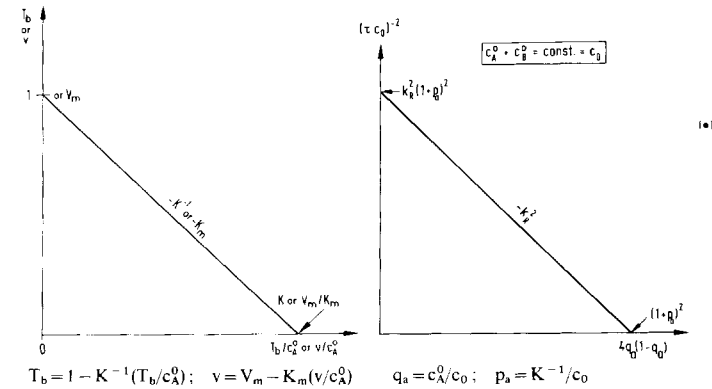


$$T_b^{-1} = K^{-1} c_A^{0\,-1} + 1 \qquad \tau^{-1} \approx k_R c_A^0 + k_D$$

$$v^{-1} = \frac{K_m}{V_m} c_A^{0\,-1} + V_m^{-1}$$



$$\frac{c_A^0}{T_b} = c_A^0 + K^{-1}; \quad \frac{c_A^0}{v} = \frac{1}{V_m} c_A^0 + \frac{K_m}{V_m} \qquad \tau^{-2} = k_D^2 + 4k_D k_r c_A^0$$



$$T_b = 1 - K^{-1}(T_b/c_A^0); \quad v = V_m - K_m(v/c_A^0) \qquad q_a = c_A^0/c_0; \quad p_a = K^{-1}/c_0$$

$$(\tau c_0)^{-2} = k_R^2[(1+p_a)^2 - 4q_a(1-q_a)]$$

Fig. 2. a) Illustrative plots for binding (T_b) and steady state rates (v), popular in enzymology. Various names are associated with such plots (from top to bottom): Michaelis-Menten, Lineweaver-Burk, Woolf, Angustinsson. All these plots suppose the concentration of free substrate to be known, which is fulfilled, if the total substrate concentration is large compared to total enzyme concentration, *i.e.* $c_A^0 \gg c_B^0$.

b) Analogous plots for the evaluation of relaxation times (τ). Again restricting assumptions—as quoted with the curves—are involved. (Note that similar linear plots do not hold for Γ_b, which can be expressed as a product of τ_b and T_b and therefore cannot easily be represented in a linear form.)

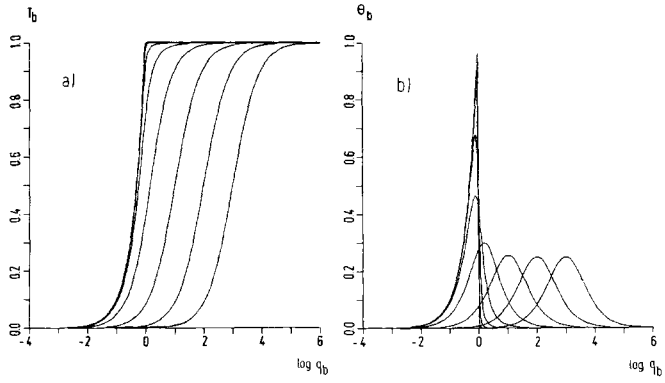
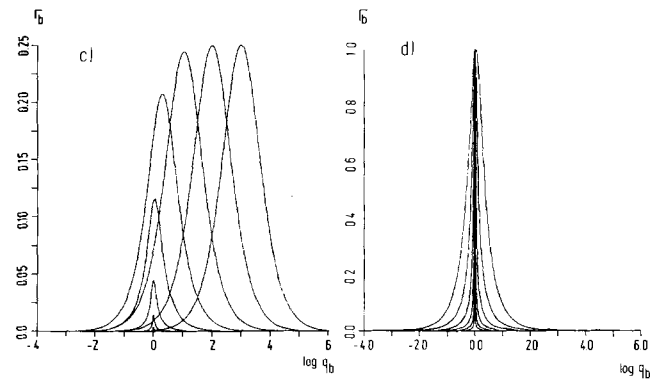


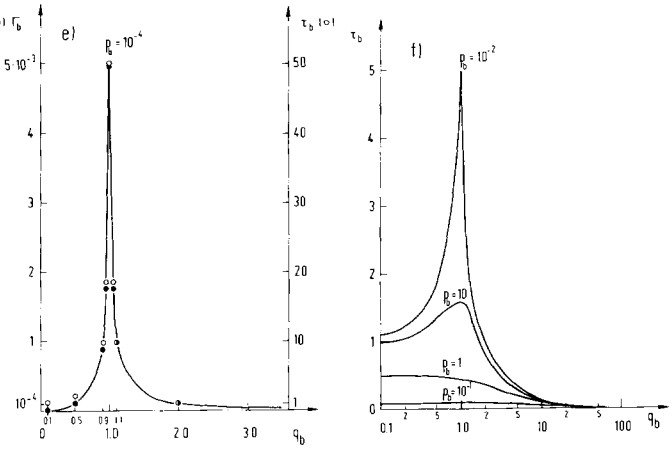
Fig. 3. a) Classical titration curves: plot of degree of binding (T_b) *vs.* logarithm of concentration ratio ($q_b = c_A^0/c_B^0$), A being the standard and B the sample (c_A^0 = const., c_B^0 = variable), for different parameters p_b (cf. Table 1).

b) Slopes of titration curves: $\theta_b = \mathrm{d}T_b/\mathrm{d}\ln q_b$. As is seen for $p_b > 1$, the position of the maximum slope, indicating the inflection point of the titration curve, is a direct measure of p_b. For $p_b \to 0$, however, a limiting curve is approached. The curve shapes show only relative differences, which cannot be improved by signal amplification.



c) For comparison, the amplitude factor $\Gamma_b = \partial T_b/\partial \ln p_b$ is plotted in the same way as θ_b. For $p_b \gg 1$ identical curves result for Γ_b and θ_b. Amplitude factors can be detected *directly* from relaxation amplitudes and do not have to be derived by differentiation procedures. For $p_b < 1$ the absolute values decrease in proportion to $1/\sqrt{p_b}$, but at the same time the curve shapes change characteristically. Signal amplification can truly enhance such effects to a level where they provide a sensitive measure of p_b.

d) The shifts of Γ_b with p_b amplified to the same maximum value (cf. Table 1).



e) Γ_b and τ_b (not normalized) plotted on a linear concentration axis for one example ($p = 10^{-4}$).

f) τ_b for various parameters p_b plotted on a logarithmic concentration axis (see also Table 1).

substrate interactions (cf. [3, 4]), usually supposing the substrate to be in excess of the enzyme ($c_S \approx c_S^0$). A compilation of those plots can be found in Figure 2a.

Useful as all those relations may be—wherever they apply—their validity with respect to a precise determination of stability constants becomes severely limited whenever K reaches excessively large values or, explicitly if

$$K(c_A^0 + c_B^0) \gg 1 \tag{2.1-11}$$

This can be immediately seen from Figure 1b, and even better from Figure 3a, where titration curves for different stability constants ($K c_B^0$ as parameter) are plotted against the logarithm of the titration variable $q_b = c_A^0/c_B^0$. These curves—or their first derivatives (Fig. 3b)—show that for $K c_B^0 \gg 1$ the region sensitive to K is more and more restricted to the close vicinity of the equivalence point ($c_A^0 \approx c_B^0$).

In fact, only the second derivative of the titration curve:

$$\frac{d^2 c_{AB}}{dc_A^{0\,2}} = -\frac{2c_B^0 K^{-1}}{[(c_A^0 - c_B^0 + K^{-1})^2 - 4c_B^0 K^{-1}]^{3/2}} \tag{2.1-12}$$

shows a direct proportionality to K^{-1}. For $K^{-1} \to 0$ there exists a true singularity; the slope of the titration curve then switches abruptly from one to zero:

$$\frac{dc_{AB}}{dc_A^0} \to \frac{1}{2}\left[1 - \frac{c_A^0 - c_B^0}{|c_A^0 - c_B^0|}\right] \tag{2.1-13}$$

($|c_A^0 - c_B|$ is the absolute amount, which is always a positive quantity, whereas $c_A^0 - c_B^0$ assumes negative values for $c_B^0 > c_A^0$).

It is the differential change of this slope, the curvature of the titration function, which—for large K-values—has to be viewed in comparison with the differential changes brought about by perturbation of a thermodynamic (intensive) parameter. This problem is treated in detail in the next section.

2.2. Relaxation Amplitudes and Time Constants

We shall consider the variation of c_{AB} resulting from a perturbation of the chemical equilibrium by the alteration of an intensive parameter. Here, rather than changing c_B^0 (or a combination of c_A^0 and c_B^0) at constant K, we vary K under fixed conditions of c_A^0 and c_B^0. The quantity, we are interested in, is the differential-quotient $\partial c_{AB}/(\partial \ln K)$ which can be directly detected in a relaxation experiment[5].

Any small perturbation—*e.g.* brought about by an alteration of temperature, pressure or electrical field density—will in general result in a linear relaxation effect. A stepwise shift of the force will cause an exponential temporal response of the concentration variable:

$$\delta_t c_{AB} = \delta_\infty c_{AB}(1 - e^{-t/\tau}) \tag{2.2-1}$$

where $\delta_\infty c_{AB}$ represents the concentration shift after complete equilibration ($t \to \infty$) and τ is a characteristic time constant, the *relaxation time of chemical equilibration.*

For sinusoidal periodic variation, the response can be written in complex notation:

$$\delta_\omega c_{AB} = \frac{\delta_0 c_{AB}}{1 + i\omega\tau} \tag{2.2-2}$$

where $\delta_0 c_{AB}(\omega \to 0)$ again is the concentration shift corresponding to *complete* equilibration. The complex form of eq. (2.2-2) indicates a frequency dependence of the true amplitude (*i.e.* the maximum value of $\delta_\omega c_{AB}$) and a phase relationship between $\delta_\omega c_{AB}$ and $\delta_0 c_{AB}$. Accordingly eq. (2.2-2) can be rewritten as

$$\delta_\omega c_{AB} = \frac{\delta_0 c_{AB}}{\sqrt{1 + \omega^2\tau^2}} e^{-i\varphi} \tag{2.2-3}$$

where $\varphi = \arctan(\omega\tau)$ represents the phase angle, while the square root term describes the frequency-dependent reduction of the amplitude. It should be noted that owing to the periodic variation of force $\delta_0 c_{AB}$ is a periodic function of time: $\delta_0 c_{AB} = a_{AB} e^{i\omega t}$. The amplitude a_{AB} depends on equilibrium parameters only and is determined by the amplitude of the periodically varied force.

If z is an intensive variable, such as temperature, pressure or electrical field density, $\delta_0 c_{AB}$ can be expressed as:

$$\delta_0 c_{AB} = \left(\frac{\delta c_{AB}}{\partial \ln K}\right)_z \left(\frac{\partial \ln K}{\partial z}\right) \delta z = \frac{\Gamma \Delta Z}{RT} \delta z \tag{2.2-4}$$

where δz includes the externally imposed change in intensity (*e.g.* periodic, steplike), while $\Gamma = (\partial c_{AB}/\partial \ln K)_z$ is an amplitude factor, having the dimensions of concentration, and $\Delta Z = RT\ \partial \ln K/\partial z$ defines the extensive reaction quantity complementary to z. For $z = T$ and P, ΔZ is given by $\Delta H/T$ and $-\Delta V$ respectively, ΔH being the enthalpy and ΔV the volume of reaction. The general thermodynamic treatment of relaxation phenomena is briefly outlined in Appendix 1.

Of special interest is the amplitude factor Γ in relation to c_A^0, c_B^0 and K. For the binary complex equilibrium it reads:

$$\Gamma = \frac{c_A c_B}{c_A + c_B + K^{-1}} = \frac{K^{-1}}{2}\left[\frac{1}{\sqrt{1 - 4c_A^0 c_B^0/(c_A^0 + c_B^0 + K^{-1})^2}} - 1\right] \tag{2.2-5}$$

Γ shows a maximum at the equivalence point which parallels the maximum in the logarithmic derivative of the titration function (cf. Fig. 3c, d). For $K^{-1} \ll c_A^0 + c_B^0$ the peak becomes very sharp and its shape represents a sensitive measure of the stability constant.

Although $\delta_\infty c_{AB}$ and $\delta_0 c_{AB}$ are parameters related to the *equilibrium*, their identification usually will require a complete recording of the time or frequency dependence of the concentration shift δc_{AB}. Since the perturbation is brought about by an alteration of the external intensive variable, it may not only result in a shift of the chemical composition, but also in changes of volume (*e.g.* thermal expansion) or of the parameters (*e.g.* extinction coefficients) which are utilized for a detection of the chemical effect. With $c = n/V$ (n = number of moles, V = volume), δc_{AB} can be essentially approximated by two terms: $(\delta c_{AB})_{chem}$ and $-c_{AB}(\delta V/V)$. Only the term $(\delta c_{AB})_{chem}$ refers to the true chemical change, which is characterized by the relaxation time τ. The physical effects of the perturbation (*e.g.* the volume change δV) usually respond much faster. They may actually be assumed to occur "instantaneously" within the limits of resolution. However, all these influences contribute to the final amplitude and hence can be separated only with the help of the characteristic time dependence of the chemical effect. (An example will be shown in Section 2.4). Owing to this fact a dynamical approach

is most appropriate for a correct determination of equilibrium chemical shifts. In addition, the time or frequency dependence offers access to the measurement of the kinetic parameters of equilibration. Such a procedure is straightforward only in the linear domain of expansions, *i. e.* for small perturbations.

At equilibrium the rate of recombination of A and B equals the rate of dissociation of AB:

$$v = k_R c_A c_B = k_D c_{AB} \tag{2.2-6}$$

where v is called the equilibrium exchange rate.

In Appendix 1, it is shown that the relaxation time τ is related to the amplitude factor Γ *via* the exchange rate v. The reciprocal of τ is given by:

$$\tau^{-1} = k_R(c_A + c_B + K^{-1}) \tag{2.2-7}$$

or in explicit form:

$$\tau^{-1} = k_R\sqrt{(c_A^0 + c_B^0 + K^{-1})^2 - 4c_A^0 c_B^0} \tag{2.2-8}$$

For $K^{-1} \ll (c_A^0 + c_B^0)$,—in analogy to Γ—τ reaches a sharp maximum at the equivalence point. Illustrative plots for τ or τ^{-1} are compiled in Figure 2b.

Such simple functional relationships do not exist for Γ, which is a product of the exchange rate and relaxation time, and hence of the two functions c_{AB} and τ (see Appendix 1).

2.3. Relaxation Amplitudes and Time Constants Contrasted with Titration Functions

We are now ready for a more detailed discussion of methods for the determination of stability constants based on the variation of c_{AB} in relation to c_A^0, c_B^0 or K. First we notice that there is, of course, a symmetry for any change of c_{AB} with respect to c_A^0 or c_B^0. Titration techniques usually involve the variation of only one of the concentrations (c_A^0 or c_B^0), while the other is kept at a fixed value. An alternative procedure—better adapted to the symmetry of the functional relations—would be to keep constant the sum of c_A^0 and c_B^0, but to vary their proportion. Both concepts may offer advantages in particular cases and will therefore be treated separately.

For an intuitive description and comparative analysis of the various mathematical expressions it proves useful to substitute the quantity

$$Q \equiv \frac{2\sqrt{c_A^0 c_B^0}}{c_A^0 + c_B^0 + K^{-1}} \equiv \sin\alpha \tag{2.3-1}$$

This substitution is of purely formal nature and has been chosen only for the sake of a uniform mathematical representation.

The angle α thus defined can vary between 0 and (nearly) $\pi/2$. It has its maximum at the equivalence point ($c_A^0 = c_B^0$ or $c_A^0 + K^{-1} = c_B^0$ respectively), where it would reach $\pi/2$ only in the limiting case $K(c_A^0 + c_B^0) \to \infty$. For any finite K-value α will always remain below $\pi/2$.

We now derive expressions for

1) the titration function,
2) its first derivative, *i. e.* the slope,
3) its second derivative or curvature,
4) the relaxation amplitude and
5) the relaxation time,

distinguishing the two cases

a) $c_A^0 + c_B^0 = \text{const.}$
b) $c_B^0 = \text{const.}$

In Table 1 alternative expressions are listed for each of these five quantities, one showing the explicit dependence on the two variables p and q, involving c_A^0, c_B^0 and K for either the constraint a) or b), the other based on the substitution eq. (2.3-1). in the latter case several ways of representation are possible. For uniformity the expressions are given throughout in the form of functions of $\tan(\alpha/2)$.

The presence of a term $[1 - \tan^2(\alpha/2)]^{-1}$ then signifies the appearance of a singularity in the limit of $\alpha \to \pi/2$, (*i. e.* $K \to \infty$). This results in abrupt changes in the values of the various functions if $K(c_A^0 + c_B^0) \gg 1$. The normalized[*] relaxation amplitudes and time constants as functions of the titration variable q_a have here characteristic forms, whereas among the titration functions only the second derivative of T_a or T_b (for $p_a < 1$) shows this behavior. For $K \to \infty$ the normalized curves for Γ, τ and T'' have the appearance of the delta function. Such

Table 1. Binary (1 : 1) complex formation:
Titration function and its various derivatives with respect to overall concentrations and equilibrium parameters. We refer to the complex equilibrium (2.1-1) and to the parameters introduced with eq. (2.1-2).

Two procedures are distinguished.

a) $c_A^0 + c_B^0 = \text{const.}$	b) $c_B^0 = \text{const.}$
K as parameter	K as parameter
Variation of c_A^0 requires a corresponding compensation of c_B^0.	c_A^0 is the variable, common to classical titration procedures.

It is convenient to introduce the following abbreviations:

a)	b)
$p_a \equiv \frac{K^{-1}}{c_A^0 + c_B^0}$	$p_b \equiv \frac{K^{-1}}{c_B^0}$
$q_a \equiv \frac{c_A^0}{c_A^0 + c_B^0}$	$q_b \equiv \frac{c_A^0}{c_B^0}$
$(1 - q_a) \equiv \frac{c_B^0}{c_A^0 + c_B^0}$	
equivalence point:	(apparent) equivalence point:
$q_a = 0.5$, *i.e.* $c_A^0 = c_B^0$	$q_b = 1 + p_b$, *i.e.* $c_A^0 = c_B^0 + K^{-1}$

In these notations the variable Q as defined by eq. (2.3-1) will read:

$Q = \frac{2\sqrt{q_a(1-q_a)}}{1+p_a}$	$Q = \frac{2\sqrt{q_b}}{1+p_b+q_b}$
or for $p \to 0$	
$Q_0 = 2\sqrt{q_a(1-q_a)}$	$Q_0 = \frac{2\sqrt{q_b}}{1+q_b}$

We substitute formally $Q \equiv \sin\alpha$

$$\cos\alpha = \sqrt{1-Q^2}; \quad \tan\alpha = \frac{Q}{\sqrt{1-Q^2}}; \quad \tan\frac{\alpha}{2} = -\frac{1-\sqrt{1-Q^2}}{Q}$$

and obtain the functions compiled below, according to the definitions given.

[*] Cf. Section 2.4.

The range of existence of α is limited due to: $1/(1+p_a) \geq \sin\alpha \geq 0$: (*i.e.* $1/p_a(2+p_a) \geq \tan^2\alpha \geq 0$, or: $1+p_a-\sqrt{p_a(2+p_a)} \geq \tan(\alpha/2) \geq 0$.) α reaches $\pi/2$ only in the limit of $p_a = 0$. The same holds for the case b, where the range of existence of α is given by $1/\sqrt{1+p_b} \geq \sin\alpha \geq 0$.

The parameters for curves 1 to 8 are:

1) p = 0
2) p = 10^{-4}
3) p = 10^{-3}
4) p = 10^{-2}
5) p = 10^{-1}
6) p = 1
7) p = 10
8) p = 100

1. Classical titration function:

a)
Definition:

$$T_a = \frac{c_{AB}}{c_A^0 + c_B^0}$$

Expression I:

$$\frac{1}{2}(1+p_a)\left[1-\sqrt{1-\frac{4q_a(1-q_a)}{(1+p_a)^2}}\right]$$

Expression II:

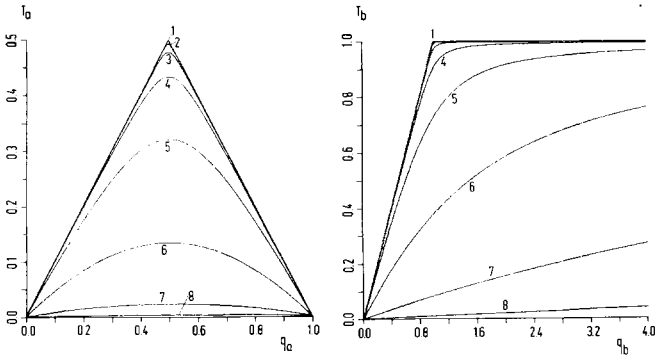
$$(1+p_a)\,\frac{\tan^2\left(\frac{\alpha}{2}\right)}{1+\tan^2\left(\frac{\alpha}{2}\right)}$$

b)

$$T_b = \frac{c_{AB}}{c_B^0}$$

$$\frac{1}{2}(1+p_b+q_b)\left[1-\sqrt{1-\frac{4q_b}{(1+p_b+q_b)^2}}\right]$$

$$(1+p_a+q_b)\,\frac{\tan^2\left(\frac{\alpha}{2}\right)}{1+\tan^2\left(\frac{\alpha}{2}\right)}$$



2. Slope of titration function:

a)
Definition:

$$\frac{dT_a}{dq_a} \equiv T_a'$$

Expression I:

$$\frac{1}{\pm\sqrt{1+p_a(2+p_a)/(1-2q_a)^2}}$$

Expression II:

$$\frac{\pm\sqrt{1-p_a(2+p_a)\tan^2\left(\frac{\alpha}{2}\right)}}{1+p_a}$$

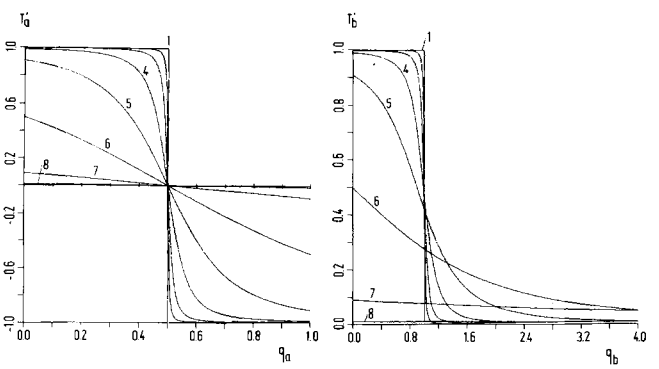
b)

$$\frac{dT_b}{dq_b} \equiv T_b'$$

$$\frac{1}{2}\left[1-\frac{1}{\sqrt{1+4p_b/(p_b+q_b-1)^2}}\right]$$

$$\frac{1-(p_b+q_b-1)\tan^2\left(\frac{\alpha}{2}\right)\Big/\left(1-\tan^2\left(\frac{\alpha}{2}\right)\right)}{1+p_b+q_b}$$

For q_b and $p_b \gg 1$, the classical plot of T_b *vs.* the logarithm of the titration variable will be of advantage. The slope, *i.e.* $\theta_b = dT_b/(d\ln q_b) \approx q_b/p_b/(1+q_b/p_b)^2$ (for q_b and $p_b \gg 1$) will have an extremum at $q_b = p_b$ (standard curve shapes, if plotted *vs.* q_b/p_b).



3. Curvature of titration function:

a)
Definition:

$$\frac{d^2T_a}{dq_a^2} \equiv T_a''$$

Expression I:

$$-\frac{2p_a(2+p_a)}{[p_a(2+p_a)+(1-2q_a)^2]^{3/2}}$$

Expression II:

$$-\frac{2p_a(2+p_a)}{(1+p_a)^3}\left[\frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}\right]^3$$

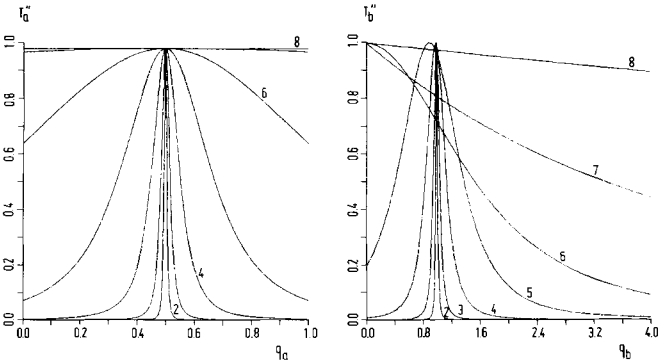
b)

$$\frac{d^2T_b}{dq_b^2} \equiv T_b''$$

$$-\frac{4p_b}{[(1+p_b+q_b)^2-4q_b]^{3/2}}$$

$$-\frac{4p_b}{(1+p_b+q_b)^3}\left[\frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}\right]^3$$

Notes on evaluation:
1) T_a and T_a' will always show extrema at the equivalence point; $q_a = 0.5$.
2) For T_b' an extremum is present only if $p_b < 1$. It will occur at $q_b = 1 - p_b$.
3) The half point: $T_b = 1/2$ will always occur at $q_b = 1/2 + p_b$.



4. Reduced relaxation amplitude factor (Γ according to eq. 2.2-4):

a)
Definition:

$$\Gamma_a = \frac{dT_a}{d\ln p_a} = \frac{\Gamma}{c_A^0 + c_B^0}$$

Expression I:

$$\frac{p_a}{2}\left[\frac{1}{\sqrt{1-4q_a(1-q_a)/(1+p_a)^2}}-1\right]$$

Expression II:

$$p_a\,\frac{\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$$

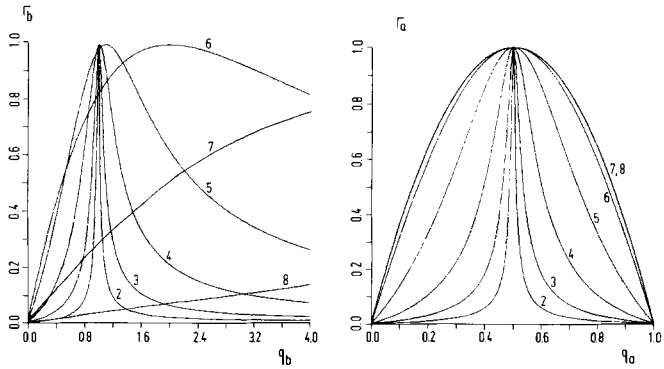
b)

$$\Gamma_b = \frac{dT_b}{d\ln p_b} = \frac{\Gamma}{c_B^0}$$

$$\frac{p_b}{2}\left[\frac{1}{\sqrt{1-4q_b/(1+p_b+q_b)^2}}-1\right]$$

$$p_b\,\frac{\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$$

For p_a and $q_a \gg 1$ there is a close analogy between $\theta_b = dT_b/d\ln q_b$ and $\Gamma_b = dT_b/d\ln p_b$.



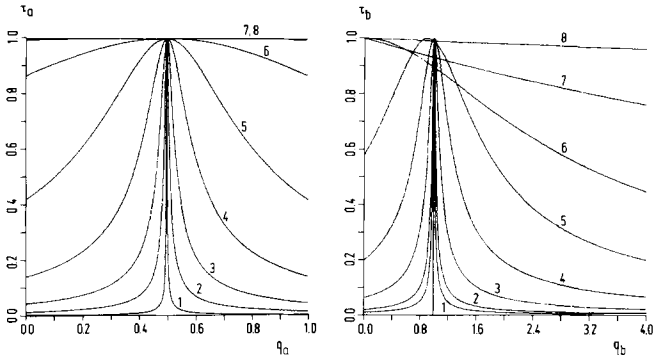
5. Reduced relaxation time (τ according to eq. 2.2-7).

a)	b)
Definition:	
$\tau_a = \tau k_R (c_A^0 + c_B^0)$	$\tau_b = \tau k_R c_B^0$
Expression I:	
$\frac{1}{\sqrt{p_a(2+p_a)+(1-2q_a)^2}}$	$\frac{1}{\sqrt{(p_b+q_b-1)^2+4p_b}}$
Expression II:	
$\frac{1}{1+p_a} \cdot \frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$	$\frac{1}{1+p_b+q_b} \cdot \frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$

One may define a complementary reduced relaxation time as:

$$\tau^* = \tau k_D = \tau_a p_a = \tau_b p_b = \frac{\Gamma_i}{T_i}$$

(T_i being T_a or T_b if $\Gamma_i = \Gamma_a$ or Γ_b, resp.)



Notes on evaluation:

1) Maxima for Γ_a and Γ_b occur always at the equivalence points a) $q_a = 0.5$ and b) $q_b = 1 + p_b$.
2) The same is true for τ_a, while τ_b—due to its relation to T_b—has its maximum at $q_b = 1 - p_b$, *i. e.* present only for $p_b < 1$.
3) Method a) is impracticable for $p_a \gg 1$, while method b) is straightforward to yield p_b from the apparent equivalence point $q_b \approx p_b$. The functions $\theta_b = d\,T_b/d\ln q_b$ and $\Gamma_b = d\,T_b/d\ln p_b$ show equivalent behavior in this situation.
4) Note that for τ the inverse square yields linear plots which can be easily evaluated.

an "end-point"-property is most suitable for the purpose of titration and, in this form, allows a determination of the stability constant K as well.

Graphic *representations* of some key functions used in Table 1 are also given in Figure 4. For practical use numerical tabulations are available. The illustrations in Figure 4 are self-explanatory. They stress the need for an exact calibration of the titration variable q_a (or q_b), and emphasize the importance of relative (rather than absolute) accuracy of calibration in the vicinity of the equivalence point.

If we compare the two procedures: a) $c_A^0 + c_B^0 =$ constant and b) $c_B^0 =$ constant, we notice the advantage of the conservation of symmetry in the former case. Method b) reflects the classical procedure, aiming at a determination of the unknown sample concentration (c_B^0) with the help of a standard A of known concentration c_A^0. This method has later been adapted to yield also the stability constant of the reaction product AB and is straightforward as long as the inverse of the stability constant is larger than or comparable with the sample concentration However it becomes increasingly insensitive for $K^{-1} \ll c_B^0$. Under these circumstances method a) offers advantages. Of course, this method requires a knowledge of c_A^0 as well

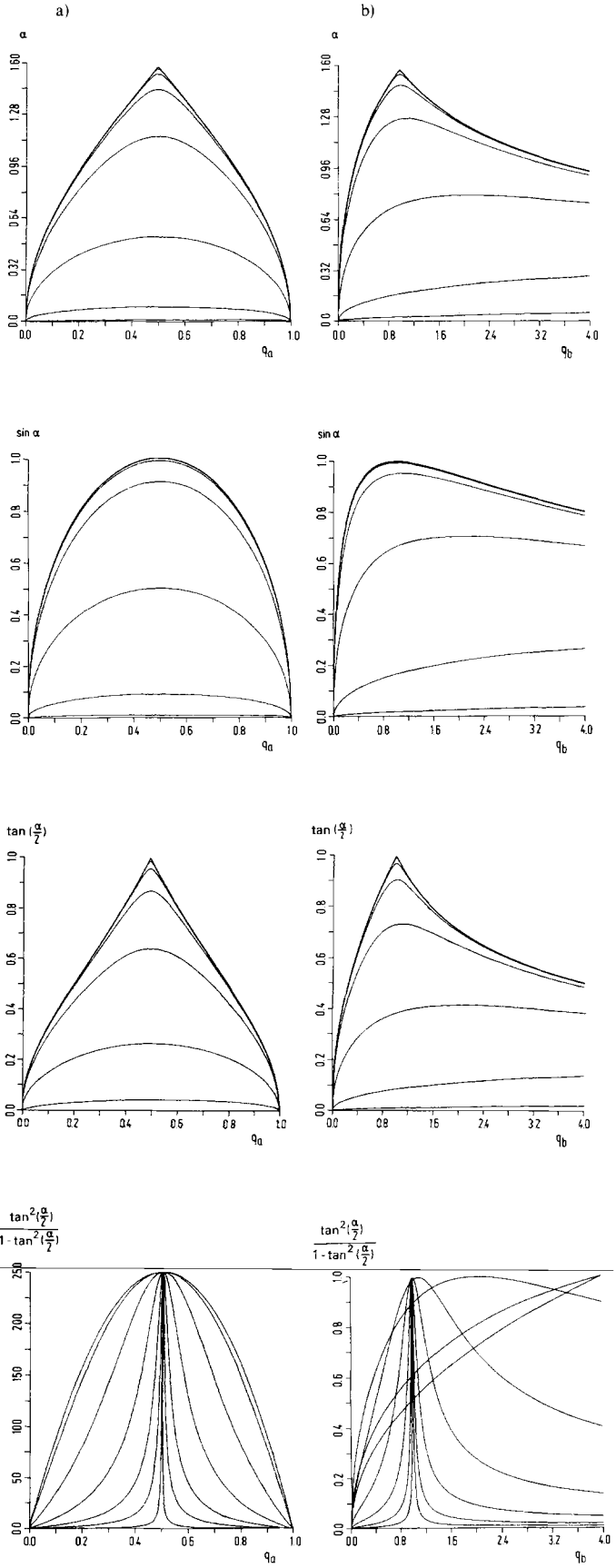


Fig. 4. Some key functions used in Tables 1a and 1b.

as c_B^0, because their sum is to be kept constant. Thus if both concentrations can be adjusted independently it is most natural to have $c_A^0 = c_B^0$ and to use varying fractions of the two solutions. Their combination—apart from possible small non-additive effects showing up only at higher concentrations—does not alter the total number of particles (A *and* B) in any given volume element.

Method a) was introduced by *Job*[6] in complexometry as the *method of continuous variation*. A critical review on related techniques and a survey of the relevant literature can be found in a monograph by *F. J. C. Rossotti* and *H. Rossotti*[7]. The use of this method in relaxation studies is strongly recommended. The symmetry expresses itself most clearly in the trigonometric representation uncovering a unique relationship between relaxation amplitude and time, which is absent in case b). From the expression in Table 1 we see that

$$\tau_a = \frac{1}{1+p_a} + \frac{2\Gamma_a}{p_a(1+p_a)} \tag{2.3-2}$$

or

$$\tau = \frac{1}{k_R(c_A^0 + c_B^0 + K^{-1})} + \frac{2}{k_R(c_A^0 + c_B^0 + K^{-1})K^{-1}\Delta Z}(\Gamma\Delta Z) \tag{2.3-3}$$

The experimental procedure is to vary q_a at constant $(c_A^0 + c_B^0)$ and to plot the measured relaxation time *versus* the respective relaxation amplitude containing the product of Γ_a and ΔH or ΔV (*i.e.* $\Gamma\Delta Z$ in eq. (2.3-3)). The intercept of the straight line (cf. Fig. 5) simply yields the reciprocal of $k_R(c_A^0 + c_B^0 + K^{-1})$ whereas the ratio of intercept and slope is equal to $K^{-1}\Delta Z/2$. Measurement at different fixed values of the sum $(c_A^0 + c_B^0)$ will thus permit a separate detection of all parameters involved. *The elegance of this method lies in the concomitant establishment of k_R, k_D, K and ΔH or ΔV from simple linear plots.*

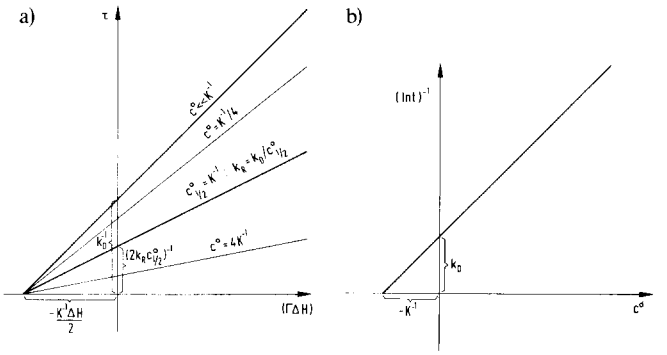


Fig. 5. a) Plot of relaxation time τ *versus* amplitude factor $\Gamma\Delta H$ at constant $c^0 = c_A^0 + c_B^0$.

Both quantities (τ and $\Gamma\Delta H$) can be evaluated from experimental data. At least two series of measurements have to be carried out, each of which refers to a different c^0. Within each series $c^0 = c_A^0 + c_B^0$ is kept constant while the ratio c_A^0/c^0 is varied. From the slopes and intercepts all parameters, such as k_R, k_D, K and ΔH can be determined. If K^{-1} is small or large as compared to c^0, the ordinate intercept yields either $k_R \times c^0$ or $k_R \times K^{-1} \equiv k_D$. Combination with any absolute value for τ at a given ratio c_A^0/c^0 will supplement the other rate constant and hence K, while ΔH follows from the abscissa intercept. $c^0_{1/2}$ refers to the half-value of the slope and is given by $c^0_{1/2} \equiv K^{-1}$.

b) Plot of reciprocal ordinate intercepts $(\mathrm{Int})^{-1}$, obtained from Fig. 5a, as function of the concentration c^0.

The main advantage of dynamic over static titration techniques becomes most evident in studies of multiple-step binding processes. Consider a sequential reaction, typical for the binding of a substrate to an enzyme, which may exist in several conformations:

$$A + B \rightleftharpoons AB_1 \rightleftharpoons AB_2 \tag{2.3-4}$$

Classical titration will yield one "overall binding parameter":

$$\bar{K} = \frac{c_{AB_1} + c_{AB_2}}{c_A \cdot c_B} \tag{2.3-5}$$

Only the dynamical technique can distinguish the two constants referring to the individual reaction steps:

$$K_1 = \frac{c_{AB_1}}{c_A \cdot c_B}; \qquad K_2 = \frac{c_{AB_2}}{c_{AB_1}} \tag{2.3-6}$$

which in the overall constant appear as the combined term.

$$\bar{K} = K_1(1 + K_2) \tag{2.3-7}$$

Two relaxation times (τ_I and τ_{II}) can be measured, both being concentration dependent. In the form of $1/\tau_I + 1/\tau_{II}$ and $1/\tau_I \cdot 1/\tau_{II}$ they can explicitly be expressed in terms of the titration variable $q_a = c_A^0/(c_A^0 + c_B^0)$ or $q_b = c_A^0/c_B^0$, the sum being the trace and the product the determinant of the matrix of rate coefficients. Both functions pass through a sharp maximum, which occurs at $q_a = 0.5$ or $q_b = 1 - p_a$ if (and only if) there is a 1:1 complex formation between A and B. In this way the number of binding sites can be identified. Analysis of the curves yields the four rate constants, which include the individual equilibrium parameters (cf. Table 2).

Table 2. Binary (1:1) complex formation involving additional first order transformations.

Reaction schemes:

1)	2)
$A + B \underset{k_D}{\overset{k_R}{\rightleftharpoons}} AB_1 \underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}} AB_2$	$A_2 + B \underset{k_{12}}{\overset{k_{21}}{\rightleftharpoons}} A_1 + B \underset{k_D}{\overset{k_R}{\rightleftharpoons}} A_1B$

Both reactions yield titration curves formally identical with those discussed in Table 1 and referring to the overall stability constants $\bar{K}$:

1)	2)
$\bar{K} = \frac{c_{AB_1} + c_{AB_2}}{c_A \cdot c_B} = K_1(1 + K_2)$	$\bar{K} = \frac{c_{A_1B}}{c_B(c_{A_1} + c_{A_2})} = \frac{K_1}{1 + K_2}$
$K_1 = \frac{c_{AB_1}}{c_A \cdot c_B} = \frac{k_R}{k_D}$	$K_1 = \frac{c_{A_1B}}{c_{A_1} \cdot c_B} = \frac{k_R}{k_D}$
$K_2 = \frac{c_{AB_2}}{c_{AB_1}} = \frac{k_{12}}{k_{21}}$	$K_2 = \frac{c_{A_2}}{c_{A_1}} = \frac{k_{12}}{k_{21}}$

T_1 and T_2 can be written in explicit form. For the overall concentrations the conservation relations read:

1)	2)
$c_A + c_{AB_1} + c_{AB_2} = c_A^0$	$c_{A_1} + c_{A_1B} + c_{A_2} = c_A^0$
$c_B + c_{AB_1} + c_{AB_2} = c_B^0$	$c_B + c_{A_1B} = c_B^0$

There are two relaxation times associated with each of the reaction schemes. They can be obtained from the original (linearized) rate equations by a normal mode analysis as outlined in Ref. [5]. Sum and product of the

two time constants for each scheme can be expressed in terms of overall concentrations, equilibrium and rate parameters as:

$\tau_I \cdot \tau_{II}$

1)

$$\frac{X}{\sqrt{(c_A^0+c_B^0+\bar{K}^{-1})^2-4c_A^0c_B^0}}$$

2)

$$\frac{X'}{\sqrt{(c_A^0+c_B^0+\bar{K}^{-1})^2-4c_A^0c_B^0}}$$

$\tau_I + \tau_{II}$

1)

$$Y+\frac{Z}{\sqrt{(c_A^0+c_B^0+\bar{K}^{-1})^2-4c_A^0c_B^0}}$$

2)

$$\frac{Y'}{X'}+\frac{Z'-\bar{K}^{-1}\cdot Y'}{X'\sqrt{(c_A^0+c_B^0+\bar{K}^{-1})^2-4c_A^0c_B^0}}$$

with the constants being:

1)

$X=[k_R(k_{12}+k_{21})]^{-1}$

$Y=(k_{12}+k_{21})^{-1}$

$Z=k_R^{-1}+(k_{12}+k_{21})^{-1}K_2\bar{K}^{-1}$

$\bar{K}^{-1}=\frac{k_D}{k_R}\frac{k_{21}}{k_{12}+k_{21}}=k_Dk_{21}\cdot X$

2)

$X'=k_R\cdot k_{21}$

$Y'=k_R\cdot\frac{1+K_2/2}{1+K_2}$

$Z'=k_D+k_{12}+k_{21}$ (for $c_A^0=c_B^0$)

If $c_A^0\neq c_B^0$, a term

$-k_R\frac{K_2/2}{1+K_2}(c_A^0-c_B^0)$

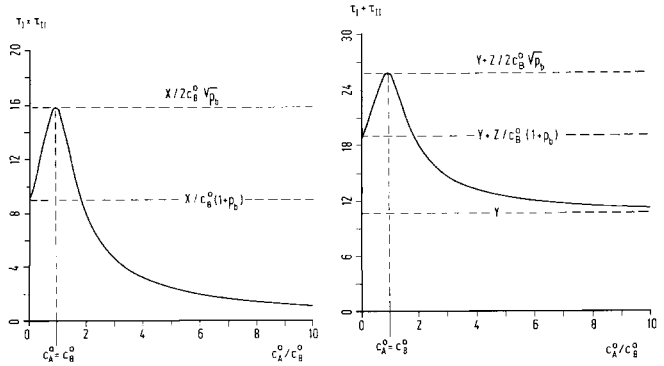
is to be added to Z'.

$\bar{K}^{-1}=\frac{k_D}{k_R}\frac{k_{12}+k_{21}}{k_{21}}=k_D(k_{12}+k_{21})/X'$

For an evaluation one may proceed in the same way as in Table 1, introducing the variables $q_a=c_A^0/c_A^0+c_B^0$ (for $c_A^0+c_B^0=$const.) or $q_b=c_B^0/c_A^0$ (for $c_B^0=$const.) and accordingly $p_a=\bar{K}^{-1}/(c_A^0+c_B^0)$ or $p_b=\bar{K}^{-1}/c_B^0$. The binding parameter p_a then follows immediately from the shape of the $\tau_I\cdot\tau_{II}$-curves. The square root terms can then be calculated and may serve as a variable in reciprocal plots in order to obtain $\tau_I+\tau_{II}$. For case 2) a further concentration factor appears in Z' if $c_A^0\neq c_B^0$. It is suggested that one could apply the condition $c_B^0=$const. only for a determination of $\bar{K}$ using the relation for $\tau_I\cdot\tau_{II}$, but then change to the condition $c_A^0=c_B^0$ (variable) in order to evaluate the sum $\tau_I+\tau_{II}$. Such a difficulty does not arise in case 1). If one of the two steps (in each scheme) is fast with respect to the other, separate expressions for τ_I and τ_{II} can be derived and evaluated accordingly. However, if the first order step is the fast one, the two first order rate constants cannot be discriminated any longer since they enter as a sum, not involving any concentration dependent term.

The concept outlined in this table can be generalized to include a whole sequence of first order transformation steps. The Gaussian method of representing combinations of eigenvalues (such as sum and product in case of two time constants) by the coefficients of the characteristic polynomial leads to a form, which easily yields the single step parameters.

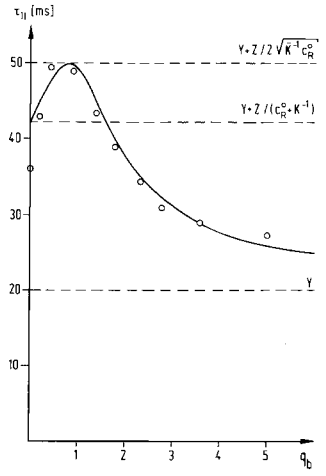
Examples of two step systems are discussed in Sections 2.3 and 4.2. Schematic representations of the curves reflecting the product and sum of the time constants τ_I and τ_{II} are shown for the case 1). The parameters X, Y, and Z are defined in the text at the top of Table 2. The curve shapes are calculated for $\bar{p}_a=\bar{K}^{-1}/c_B^0=10^{-2}$.



Example of an evaluation of measured relaxation times τ [14]. The example refers to the binding of acetylcholine (A) to its receptor (R) (which exists in two conformations) according to the mechanism:

$$A+R\underset{k_D}{\overset{k_R}{\rightleftharpoons}}AR_1\underset{k_{21}}{\overset{k_{12}}{\rightleftharpoons}}AR_2$$

Two relaxation times, associated with this mechanism have been determined. They turned out to be easily separable due to $\tau_I\ll\tau_{II}$. Here, τ_{II} is plotted as a function of $q_b=c_A^0\cdot c_R^0$. As a consequence of the condition $\tau_I\ll\tau_{II}$ the quantity Z is given by $K^{-1}\cdot K_2\cdot Y$ (cf. mechanism 1). Values for k_R and k_D (*i.e.* also for K_1) resulted from the data of τ_I, which refers to the fast binding step. Therefore a complete identification of all four rate constants (and hence of both equilibrium constants) was possible, yielding: $k_R=2.4\ (\pm0.5)\times10^7\ M^{-1}\ s^{-1}$, $k_D=144\ (\pm30)\ s^{-1}$, $k_{12}=43.5\ s^{-1}$ and $k_{21}=6.5\ s^{-1}$ ($K_1=1.7\times10^5\ M^{-1}$, $K_2=6.7$).



This representation can be extended to any further sequences of first order steps, using the Gaussian method of correlating combinations of the different eigenvalues with the coefficients of the characteristic polynomial. For $\bar{K}\gg1$, at least some of the combinations of eigenvalues will show sharp maxima at the equivalence point. *The dynamic titration procedure thus yields a much deeper insight into the binding mechanism than any of the classical complexometric techniques.*

2.4. Evaluation of Data and Some Experimental Examples

The absolute value of a relaxation amplitude depends on the magnitude of the mass action parameter p_a. For *high complex stabilities*, as reflected by small p_a-values, both classical titration and relaxation measurements require a high resolution of the recorded signal. There is, however, an important difference, if we compare the two procedures. *Conventional titration* calls for a *high relative accuracy* in the calibration of concentrations. The desired information is hidden in (small) deviations from a standard curve. Signal amplification does not reduce any relative error, unless some kind of double-differential recording is applied, *e. g.* a direct recording of the second derivative of the titration function. Relaxation amplitudes and times, on the other hand, are related to p_a or K in a more straightforward way. Here *the absolute magnitude* of the signal is of importance. The amplitude vanishes if p_a approaches zero. Therefore, amplification of the signal leads to a true enhancement of resolution, ultimately limited only by the noise introduced by the recording equipment.

Considerable progress in the development of relaxation instruments has been made in recent years. As a consequence,

the dynamic amplitude technique promises to become a powerful new tool in analytical chemistry. The possibility of such applications has been mentioned long ago. In fact, one of the first studies of chemical relaxation effects[8, 9] started from a quantitative estimate of amplitudes and their concentration dependence. The utilization of relaxation amplitudes has until recently been hampered by the inadequate sensitivity of earlier instruments. A combination of the presently-available relaxation techniques with devices for an automatic control of concentration will open a wide range of application in complexometry[*].

The essential information about the stability constant (contained in the parameter p_a) will be obtained from curve *shapes* for T'', Γ and τ as functions of the titration variable q_a rather than from *absolute* values. For an evaluation of data it is, therefore, practical to *normalize* the curves, *i.e.* to divide them by their maximum value. These normalized curves are to be distinguished from the *reduced* terms quoted in Table 1. The latter still contain some unknown factors (p_a or a function thereof), apart from the fact that the reduced form of Γ cannot be detected directly, since relaxation amplitudes contain also ΔH or ΔV. The normalized curves, on the other hand, can be obtained immediately from experimental data (*i.e.* by dividing them by the maximum term). They do not reflect the absolute magnitude of the measured signal. Fitting them with the theoretical curves (cf. Table 1) will allow an assignment of the parameter p_a (or K). Then a further evaluation of the recorded *absolute* signals with respect to rate constants, reaction enthalpies *etc.* can be undertaken.

As an example let us consider a T-jump experiment. Usually, some optical signal is detected which represents a shift in extinction occurring upon perturbation of the equilibrium. For a calibrated perturbation (*i.e.* a T-jump of precisely fixed magnitude and known characteristics of the detection equipment) the amplitude of the relaxation effect can be correlated with δc_{AB}, supposing the difference in the extinction coefficients ($\varepsilon_{AB}-\varepsilon_A-\varepsilon_B$) to be known. The unknown factors of the measured amplitude are Γ or p_a and ΔH. After assignment of p_a from the shape of the normalized curve the absolute number at the maximum can be used to determine ΔH as well. Expressed in terms of δc_{AB} the maximum value is given by:

$$\text{a)}\quad (c_A^0+c_B^0)\frac{p_a}{2}\left[\frac{1+p_a}{\sqrt{p_a(2+p_a)}}-1\right]\frac{\Delta H}{RT}\cdot\frac{\delta T}{T} \tag{2.4-1}$$

$$\text{b)}\quad c_B^0\frac{p_b}{2}\left[\sqrt{1+\frac{1}{p_b}}-1\right]\frac{\Delta H}{RT}\cdot\frac{\delta T}{T} \tag{2.4-2}$$

[a) and b) referring to Table 1].

Both maxima reduce for $p_a\rightarrow 0$ to the same limiting value

$$\frac{1}{2}\sqrt{K^{-1}c_B^0}\;\frac{\Delta H}{RT}\cdot\frac{\delta T}{T} \tag{2.4-3}$$

In a similar way the relaxation times can be analyzed, plotting τ/τ_{max} as a function of q_a, with τ_{max} being

$$\text{a)}\quad [k_R(c_A^0+c_B^0)\sqrt{p_a(2+p_a)}]^{-1} \tag{2.4-4}$$

and

$$\text{b)}\quad [2k_R c_B^0\sqrt{p_b}]^{-1} \tag{2.4-5}$$

With respect to a determination of k_R and k_D, this is just an alternative to plotting $1/\tau^2$ as a function of c^0 (Figure 2b, third diagram from top), which is based on the condition $c_A^0=c_B^0$. For T'', *i.e.* the second derivative of the titration function, such an evaluation using normalized curves is not necessary, since in this case p_a is the only unknown, fixing the shape as well as the maximum value (Table 1). It may nevertheless be of advantage, if T'' is directly detected with the help of a double differential method, and the recorded signals involve any unknown factor. At its maximum T'' is given by:

$$\text{a)}\quad -\frac{2}{\sqrt{p_a(1+p_a)}}\xrightarrow{p_a\rightarrow 0}-2\sqrt{Kc_B^0} \tag{2.4-6}$$

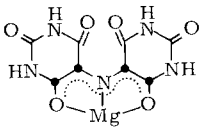
and

$$\text{b)}\quad -\frac{1}{2\sqrt{p_b(1+p_b)^3}}\xrightarrow{p_b\rightarrow 0}-\frac{1}{2}\sqrt{Kc_B^0} \tag{2.4-7}$$

For T_b''—as for τ_b—a maximum is present only if $p_a<1$ and appears at $q_b=1-p_b$.

In conclusion to this section on binary (1:1) complexes some examples of the experimental determination of relaxation amplitudes and time constants and their evaluation for rate and equilibrium parameters are discussed.

The first example[11] deals with the formation of a metal complex between Mg^{2+} and the anion of purpuric acid (murexide) in methanol.



Three independent sources of data, (classical) titration, relaxation amplitudes and time constants, are available for a determination of the stability constant. Oscillograms of the relaxation effects are shown in Figure 6. They demonstrate clearly why a dynamic recording is of advantage. The total change of extinction contains two parts: an instantaneous shift caused by the thermal expansion of the sample, and a chemical relaxation effect occurring with a finite time constant. The chemical effect on which the evaluation of Γ is based would not result directly from any static experiment. A simple static recording of the temperature dependence—due to the superposition of the effects of thermal expansion—could lead to quite erroneous explanations.

The sensitivity of the differential technique is very high. Conventional ratio recording spectrophotometers do not reach any comparable resolution. Titration functions, relaxation amplitudes and time constants are represented in Figures 6c and 6d in the form of normalized plots.

The second case describes a reaction involving two competitive steps, the addition of sulfate and water to 4-pyridinecarbaldehyde, studied by *Schuster et al.*[13].

[*] Only few examples of this technique are known so far; cf. [1, 10—12].

The overall equilibrium constant of complex formation is $\bar{K} = K_1/(1+K_2)$.

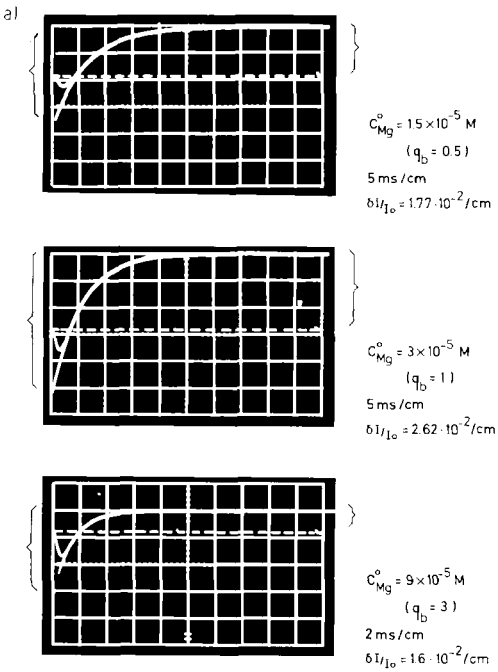
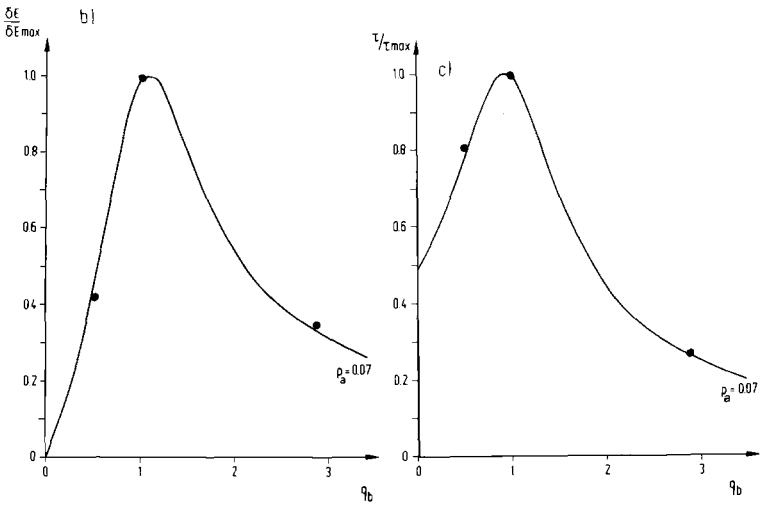


Fig. 6. a) Relaxation curves from *T*-jump experiments (oscillograms) for the system Mg/murexide in methanol;
$c^0_{Mu} = 2.9\times10^{-5}$ M
Note the differences in sensitivity ($\delta I/I_0$). With uniform sensitivities the second oscillogram would show almost twice as large an amplitude. The true amplitudes, resulting from an extrapolation of the dynamic response and indicated by a bracket at the left side of the pictures, differ strikingly from the "static" shifts (indicated by the right hand brackets). The baseline (dashed) indicates the initial position of the temperature jump induced concentration shift.



b) Normalized relaxation amplitudes *versus* titration variable q_b. (Experimental data taken from Ref. [1].)

c) Normalized relaxation times *versus* titration variable q_b. (Experimental data taken from Ref. [1].)

Evaluation of the data with $c^0_{Mu} = 4.2\times10^{-5}$ M yields: $K = 3.5\times10^5$ M^{-1}; $k_R = 8.0\times10^6$ M^{-1} s^{-1}; $k_D = 23$ s^{-1}; $\Delta H = +7.3$ kcal/mol.

The dynamic measurements, however, refer to the sulfate reaction only, since the hydrate is formed (much more) slowly.

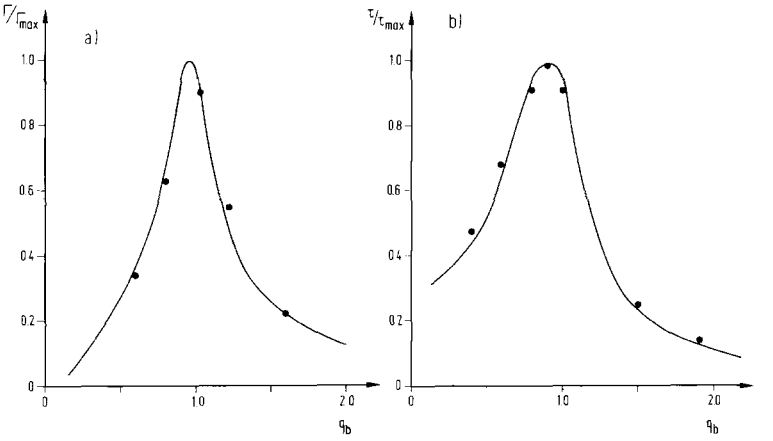
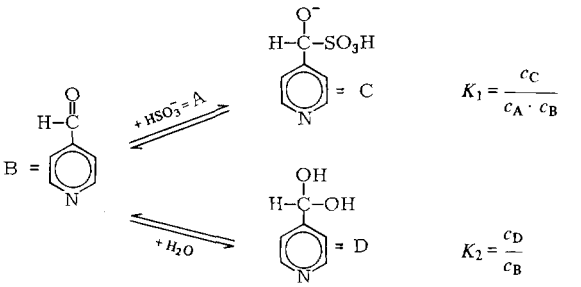


Fig. 7. a) Normalized relaxation amplitude Γ/Γ_{max} as a function of the titration variable $q_b \equiv c^0_A/c^0_B$ for the sulfite/4-pyridinecarbaldehyde system (after [13]). The data are fitted with a curve referring to $K_1 = 6.5\times10^5$ M^{-1} with c^0_B being 1×10^{-3} M (hydrogen sulfite) and pH = 7. Due to the protonation of hydrogen sulfite the maximum does not appear at exactly $q_b = 1$ (cf. Ref. [13]).

b) Normalized relaxation time (τ/τ_{max}) as a function of q_b (data cf. Fig. 7a).

Normalized amplitudes Γ_b (from *T*-jump experiments) as a function of $q_b = c^0_A/c^0_B$ (accounting for the first step only) are shown in Figure 7.



3. Substitution Methods

The applicability of the titration principles described in Section 2 is based essentially on two facts:

There is a measurable shift of properties—such as extinction, fluorescence etc.—occurring upon combination of A *with* B,

and

the stability of the complex AB *is of a magnitude which allows the recording of finite signals.*

What can we do if one of these conditions is not fulfilled? We may use an auxiliary system, *e.g.* an indicator which competes for combination with one of the reaction partners (A or B) and exhibits unique optical (or other) qualities in order to compensate for the absence of detectable changes of the sample. The stability of such a competitor has to be similar to that of the complex under investigation.

In enzyme chemistry an analogous case is that of competitive inhibition. Straightforward expressions are obtained if substrate and inhibitor are in large excess of the enzyme (Figure 8). Such simplifying assumptions, however, will not be made in the following treatment.

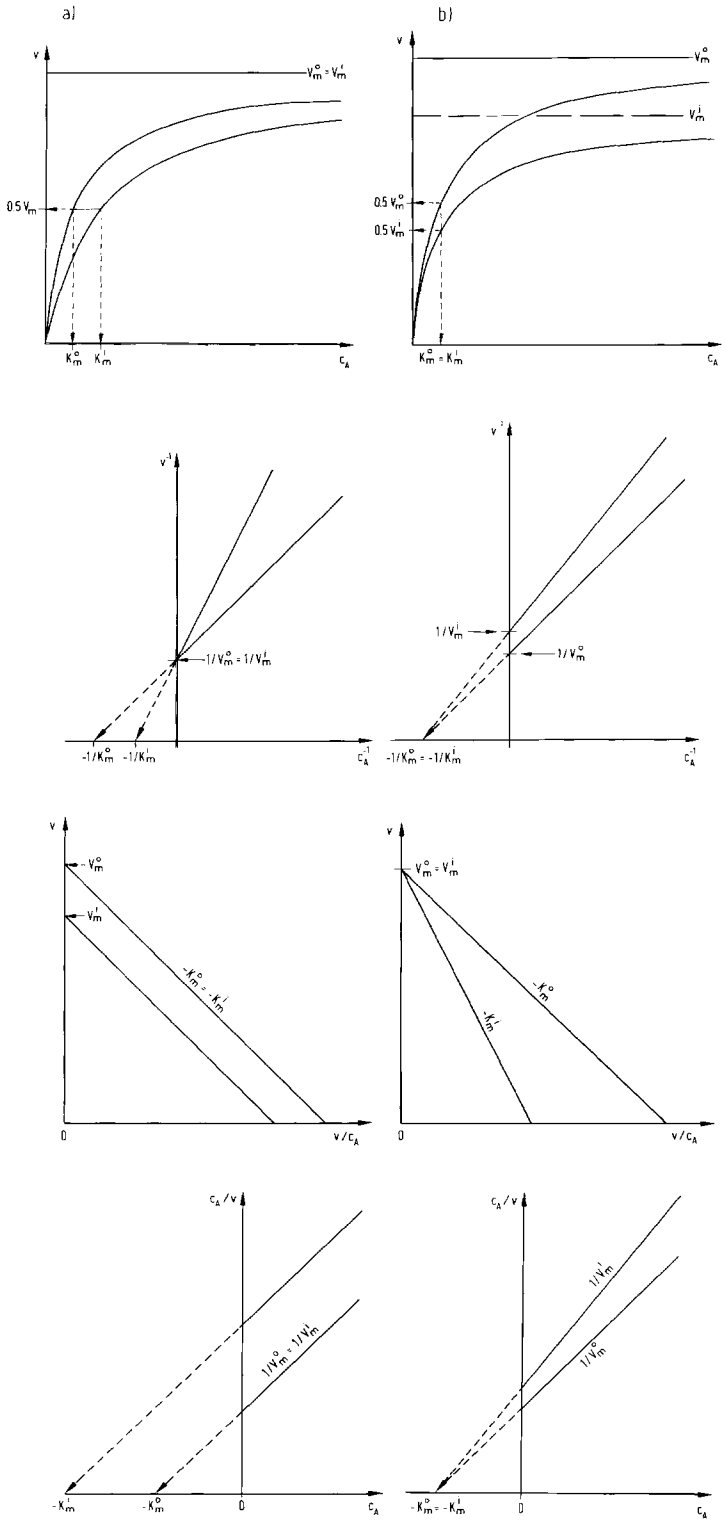


Fig. 8: Simple linear plots—analogous to those shown in Figure 2—for coupled binding processes: a) competitive inhibition, b) non-competitive inhibition. (Data from *Dixon and Webb*[3].)

The plots are based on the relation (cf. Figure 2a):

$$v = V_m^i c_A/(c_A + K_m^i)$$

where V_m^i and K_m^i have the following meaning:

a) competitive	b) non-competitive
$V_m^i = V_m^0$	$V_m^i = V_m^0/(1 + K_i c_i)$
$K_m^i = K_m^0(1 + K_i c_i)$	$K_m^i = K_m^0$

K_i being the stability constant of the enzyme-inhibitor complex, c_i the inhibitor concentration. V_m^0 and K_M^0 are the maximum velocity and Michaelis constant, respectively in absence of the inhibitor, and c_A is the substrate concentration.

Let us introduce the auxiliary system as an indicator I, which undergoes complex formation with one of the reactants, say B:

$$I + B \rightleftharpoons IB$$

in competition with

$$A + B \rightleftharpoons AB$$

A complete description of the dynamic properties requires two coupled differential equations, the solutions of which refer to certain normal modes of reaction. With respect to applications in complexometry it is sufficient to consider the overall-equilibration.

Two limiting cases are of special interest:

1. The stability of both complexes AB and IB is so high that free B is not present to any detectable extent. The reaction equation then can be written:

$$AB + I \rightleftharpoons A + IB$$

2. The auxiliary system is used as a true indicator without essentially influencing the sample equilibrium. This means I and IB are present at relatively low concentrations—still allowing optical or any other kind of detection—while the amount of B is similar to that of A and AB.

3.1. Complete Exchange of a Ligand B

The first mentioned case represents a true one-step reaction.

$$AB + I \underset{k_{-S}}{\overset{k_S}{\rightleftharpoons}} A + IB$$

We define the equilibrium and rate parameters as:

$$\frac{c_A \cdot c_{IB}}{c_{AB} \cdot c_I} = K = \frac{k_S}{k_{-S}} \tag{3.1-1}$$

Furthermore we have the conservation conditions:

$$\begin{aligned} c_A + c_{AB} &= c_A^0 \\ c_I + c_{IB} &= c_I^0 \\ c_{IB} + c_{AB} &= c_B^0 \end{aligned} \tag{3.1-2}$$

(Note that c_B is assumed to be negligibly small.)

From these equations we can calculate the explicit expressions for all individual concentrations at equilibrium, *e.g.*

$$c_{IB} = \frac{c_A^0 - c_B^0 + K(c_B^0 + c_I^0)}{2(K-1)}\left[1 - \sqrt{1 - \frac{4K(K-1)c_B^0 c_I^0}{[c_A^0 - c_B^0 + K(c_I^0 + c_B^0)]^2}}\right] \tag{3.1-3}$$

Several ways of performing the experiments are possible. For instance:

- We may start with a given amount of I (in its uncomplexed form) and add aliquots of A and B, such that always $c_A^0 = c_B^0$, or:
- We fix the concentration of IB (*i.e.* $c_I^0 = c_B^0$) and add varying amounts of (uncomplexed) A.

Mathematically, we do not have to distinguish between these procedures explicitly because we can deduce one from the other taking into account the symmetry of the substitution process in which the symbols of I and A can be interchanged. Using the *conditions* (3.1-2) we can derive c_{AB} from expression (3.1-3) for c_{IB}. The various cases then refer to either c_{IB} or c_{AB} under the secondary requirement $c_A^0 = c_B^0$. The resulting formulae are always symmetrical with respect to c_I^0 and c_B^0, *i.e.* we could alter one and keep the other constant or—in analogy to the method a) in Table 1—fix the sum of c_I^0 and c_B^0 and vary their proportions.

It is therefore sufficient to quote one example only. Let us choose the conditions

$$c_I^0 = \text{const.}; \quad c_A^0 = c_B^0 = \text{variable}$$

Hence we define the titration variable $q_b \equiv c_B^0/c_I^0$ and the titration function $T_b \equiv c_{IB}/c_I^0$. The reciprocal of the (dimensionless) equilibrium constant will be called $p_b (= K^{-1})$ in analogy to the nomenclature in Table 1. We obtain

$$T_b = \frac{1+q_b}{2(1-p_b)}\left[1 - \sqrt{1 - \frac{4(1-p_b)q_b}{(1+q_b)^2}}\right] \tag{3.1-4}$$

This titration function is similar to the one already described. For $p_b \to 0$ it approaches the limiting linear form:

$$T_b = \frac{(1+q_b) \pm (1-q_b)}{2} \quad \text{or} \quad T_b = \begin{cases} q_b & \text{for } q_b < 1 \\ 1 & \text{for } q_b > 1 \end{cases} \tag{3.1-5}$$

T_b changes abruptly at $q_b = 1$. For $p_b = 1$ it simply reads

$$T_b = \frac{q_b}{1+q_b} \tag{3.1-6}$$

while for $p_b \gg 1$ again a limiting form with respect to a generalized variable will result:

$$T_b \to \frac{q_b}{2p_b}\left[\sqrt{1 + \frac{4p_b}{q_b}} - 1\right] \tag{3.1-7}$$

The point of half transition ($T_b = 0.5$) will always be found for $q_b = (1 + p_b)/2$.

From this it follows that the choice of the particular titration procedure depends on the magnitude of p_b and upon the purpose of the titration experiment. If it is the concentration of a sample (c_I^0 or c_A^0) which is to be measured one fixes the concentration of the weaker and varies the concentration of the stronger complex. In this case, corresponding to $p_b \ll 1$, one reaches a sharp end-point, indicated by a (quasi) singularity in the curvature of the titration function T_b (more precisely the transition is singular only in the limiting case $p_b \to 0$). If, on the other hand, the object is a determination of K or p_b it may be advisable to titrate with the weaker complexing agent and to calibrate precisely the excess of c_A^0 over c_B^0 necessary to reach the half-point [where $q_b = (1 + p_b)/2$]. The added substance, of course, should not be identical with the indicator, since its concentration may have to be varied over several orders of magnitude.

Note that—owing to the symmetry of the substitution reaction—one could equally as well designate a complementary titration function T_{-b} based on c_{AB} rather than c_{IB}. With $T_{-b} = c_{AB}/c_I^0$ we have $T_{-b} = q_b - T_b$ and $T'_{-b} = -T'_b$, $T''_{-b} = -T''_b$. Furthermore, utilizing the symmetry of T_b with respect to c_I^0 and c_B^0, one may also introduce $T_b = c_{IB}/c_B^0$, so that $T_{-b} = c_{AB}/c_B^0 = 1 - T_b$. This definition is to be preferred if $c_A^0 = c_B^0$ is kept constant while c_I^0 is the variable.

Often one is not free to choose the ideal substance. The most frequently encountered problem in titration is the *solubility* limit. The alternative "method of continuous variation", in which the sum of c_I^0 and c_B^0 (or c_A^0) is fixed, then offers advantages. Again the essential information about the equilibrium constant may result from small variations of q_a in the neighborhood of the equivalence point ($q_a = 0.5$).

Expressions for the titration function, its first and second derivative, as well as for relaxation amplitudes and time constants under the requirement $c_I^0 + c_B^0 = \text{const.}$ and $c_A^0 = c_B^0$ are compiled in Table 3. Again, owing to the symmetry of the substitution scheme, the symbols I and A are convertible. For reasons of comparative representation, the introduction of trigonometric functions proves to be especially useful. In this treatment a *formal* complication arises owing to the fact that the term $\sqrt{(1-p_a)}$ appears in all expressions. Since p_a can be larger than one those terms may become imaginary. We therefore have to distinguish the following cases:

$p_a < 1$
$p_a = 1$
$p_a > 1$

For $p_a < 1$, $\sin\alpha$ can be introduced in the same straightforward way as before. For $p_a > 1$ we have to remember that $-i\sin(ix) \equiv \sinh x [\sinh x = (e^x - e^{-x})/2]$. Here all trigonometric functions have to be replaced by the corresponding hyperbolic ones.

Table 3 shows that there is only a *formal* correspondence between the expressions for $p_a < 1$ and $p_a > 1$. Although the form of the expressions is (nearly) conserved if we substitute hyperbolic terms for the trigonometric ones, the functional relationships with respect to q_a and p_a vary considerably. For $p_a < 1$ the angle α can vary between 0 and $\pi/2$ (reaching $\pi/2$ only in the limiting case $p_a \to 0$), while for $p_a > 1$, α can assume any value, *i.e.* any multiple of $\pi/2$ with the limit ∞ for $p_a \to \infty$. Hence for $p_a \to 0$, $\tan(\alpha/2)$ steeply approaches unity if α gets close to $\pi/4$, yielding sharp maxima wherever the term $1/(1 - \tan^2(\alpha/2))$ is involved. On the other hand,

Table 3. Substitution reactions $I + AB \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} IB + A$ at constant $(c_I^0 + c_{AB}^0)$. Titration function and its derivatives, relaxation amplitude and time constants. The equilibrium constant K is defined according to eq. 3.1-1), and the conservation conditions (3.1-2) hold. Furthermore, the procedure requires $c_A^0 = c_B^0 \equiv c_{AB}^0$ and $c_I^0 + c_{AB}^0 = \text{const.}$, *i.e.* a positive variation of c_{AB}^0 is compensated by an equivalent negative variation of c_I^0.

It is useful to define the dimensionless parameters in analogy to Table 1:

$$p_a = K^{-1}; \quad q_a = \frac{c_{AB}^0}{c_I^0 + c_{AB}^0}; \quad 1 - q_a = \frac{c_I^0}{c_I^0 + c_{AB}^0}$$

The reduced quantities are given as:

1) Titration function: $T_a = \dfrac{c_{IB}}{c_I^0 + c_{AB}^0}$

2) Slope of titration function: $T'_a = \dfrac{dT_a}{dq_a}$

3) Curvature of titration function: $T''_a = \dfrac{d^2 T_a}{dq_a^2}$

4) Relaxation amplitude factor: $\Gamma_a = \frac{\Gamma}{c_I^0 + c_{AB}^0}$

5) Relaxation time $\tau_a = \tau k_S (c_I^0 + c_{AB}^0)$

$\tau_{-a} = \tau k_{-S} (c_I^0 + c_{AB}^0) \equiv p_a \tau_a$

One may also derive complementary titration functions:

$$T_{-a} = \frac{c_{AB}}{c_I^0 + c_{AB}^0} = q_a - T_a; \quad T'_{-a} = -T'_a; \quad T''_{-a} = -T''_a$$

Explicit expressions for reduced quantities:

1) $T_a = \frac{1}{2(1-p_a)} [1 - \sqrt{1 - 4(1-p_a) q_a (1-q_a)}]$

2) $T'_a = \frac{1 - 2q_a}{\sqrt{1 - 4(1-p_a) q_a (1-q_a)}}$

3) $T''_a = -\frac{2p_a}{[1 - 4(1-p_a) q_a (1-q_a)]^{3/2}}$

4) $\Gamma_a = \frac{p_a [1 - \sqrt{1 - 4(1-p_a) q_a (1-q_a)}]^2}{4(1-p_a)^2 \sqrt{1 - 4(1-p_a) q_a (1-q_a)}}$

5) $\tau_a = \sqrt{1 - 4(1-p_a) q_a (1-q_a)}$

In analogy to Table 1 the explicit relations can be represented by formal substitution of suitable trigonometric or hyperbolic functions, in which form their interrelations become more easily seen. However, three cases have to be distinguished.

$p_a < 1$ $\qquad$ $p_a = 1$ $\qquad$ $p_a > 1$

Formal Definitions

$\sin\alpha \equiv 2\sqrt{(1-p_a) q_a (1-q_a)}$ $\qquad$ — $\qquad$ $\sinh\alpha \equiv 2\sqrt{(p_a - 1) q_a (1-q_a)}$

Range of Existence of α

$0 \le \sin\alpha \le \sqrt{1-p_a}$ $\qquad$ $0 \le \sinh\alpha \le \sqrt{p_a - 1}$

$0 \le \tan\alpha \le \sqrt{\frac{1-p_a}{p_a}}$ $\qquad$ $0 \le \tanh\alpha \le \sqrt{\frac{p_a - 1}{p_a}}$

$0 \le \tan\frac{\alpha}{2} \le \frac{\sqrt{1-p_a}}{1+\sqrt{p_a}} = \frac{1-\sqrt{p_a}}{\sqrt{1-p_a}}$ $\qquad$ $0 \le \tanh\frac{\alpha}{2} \le \frac{\sqrt{p_a - 1}}{1+\sqrt{p_a}} = \frac{\sqrt{p_a - 1}}{\sqrt{p_a - 1}}$

Reduced Functions

$T_a = \frac{1}{1-p_a} \cdot \frac{\tan^2\left(\frac{\alpha}{2}\right)}{1+\tan^2\left(\frac{\alpha}{2}\right)}$ $\qquad$ $T_a = q_a(1-q_a)$ $\qquad$ $T_a = \frac{1}{p_a - 1} \cdot \frac{\tanh^2\left(\frac{\alpha}{2}\right)}{1-\tanh^2\left(\frac{\alpha}{2}\right)}$

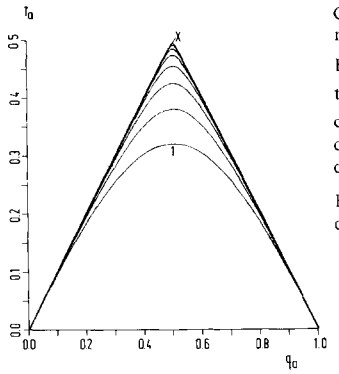
$T'_a = \sqrt{1 - \frac{p_a}{1-p_a} \tan^2\alpha}$ $\qquad$ $T'_a = 1 - 2q_a$ $\qquad$ $T'_a = \sqrt{1 - \frac{p_a}{p_a - 1} \tanh^2\alpha}$

$T''_a = -2p_a \left[\frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}\right]^3$ $\qquad$ $T''_a = -2$ $\qquad$ $T''_a = -2p_a \left[\frac{1+\tanh^2\left(\frac{\alpha}{2}\right)}{1-\tanh^2\left(\frac{\alpha}{2}\right)}\right]^3$

$\Gamma_a = \frac{p_a}{(1-p_a)^2} \cdot \frac{\tan^4\left(\frac{\alpha}{2}\right)}{1-\tan^4\left(\frac{\alpha}{2}\right)}$ $\qquad$ $\Gamma_a = T_a^2 = [q_a(1-q_a)]^2$ $\qquad$ $\Gamma_a = \frac{p_a}{(1-p_a)^2} \cdot \frac{\tanh^4\left(\frac{\alpha}{2}\right)}{1-\tanh^4\left(\frac{\alpha}{2}\right)}$

$\tau_a = \frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$ $\qquad$ $\tau_a = 1$ $\qquad$ $\tau_a = \frac{1+\tanh^2\left(\frac{\alpha}{2}\right)}{1-\tanh^2\left(\frac{\alpha}{2}\right)}$

As compared to Table 1 the very pronounced dependences should be emphasized. It appears most clearly in T'_a. The dissymmetry for $p_a < 1$ and $p_a > 1$, expressed by a transition from trigonometric to hyperbolic functions is most obvious for Γ_a and τ_a. The trigonometric forms show much sharper transitions, especially for small p_a-values. For τ_a the dependences are inverted at $p_a = 0$.



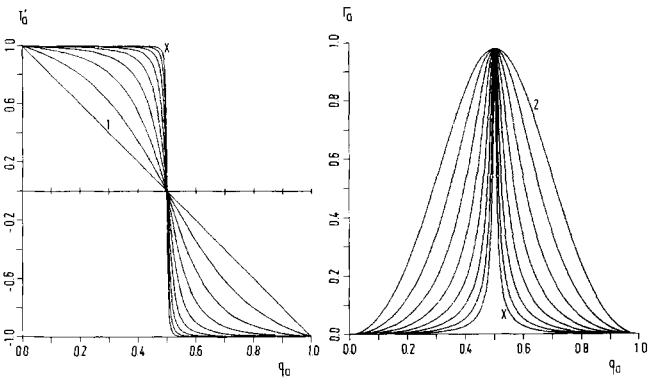
Graphic representation of the five mentioned functions:

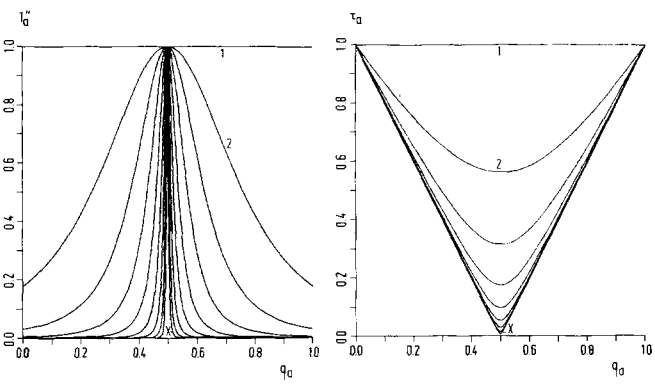
For the case: $p_a \le 1$.

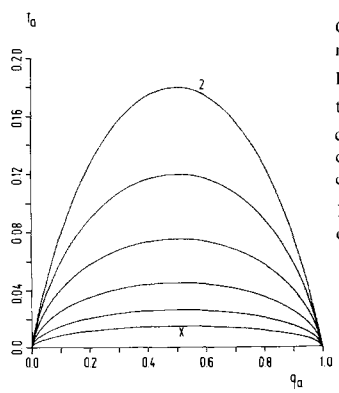
the parameters are

curve 1: $p_a = 1$
curve 2: $p_a = 10^{-0.5}$
curve x: $p_a = 10^{-1}$

For the curves between 2 and x p_a changes by the factor $10^{-0.5}$.







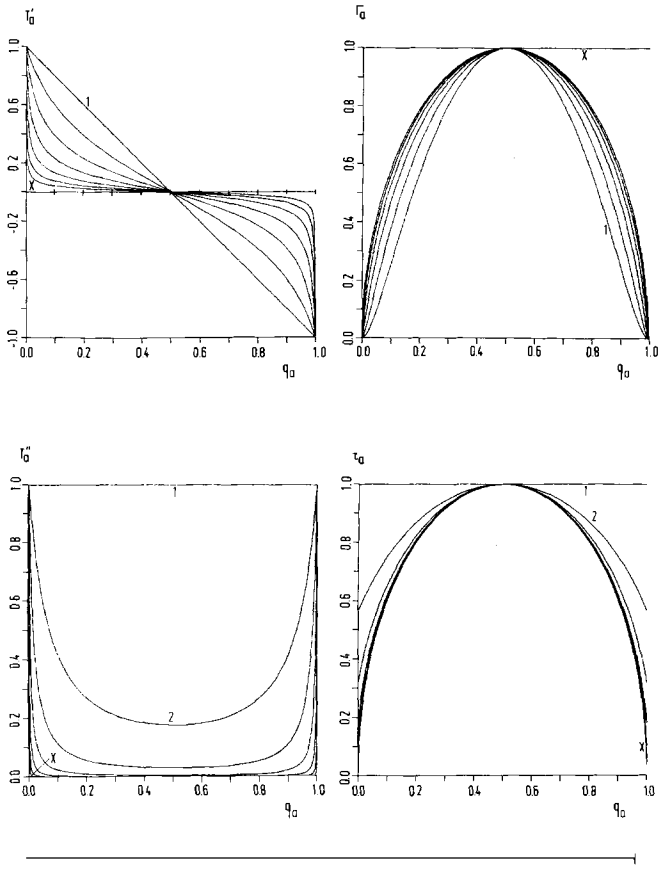
Graphical representation of the five mentioned functions.

For the case: $p_a \ge 1$.

the parameters are

curve 1: $p_a = 1$
curve 2: $p_a = 10^{0.5}$
curve x: $p_a = 10^{3}$.

For the curves between 2 and x p_a changes by the factor $10^{0.5}$.



tanh α for large p_a approaches unity asymptotically, allowing only rather flat extrema around the equivalence point.

This abstract description may be illustrated by the following example: We start with a solution of I at the concentration c_I^0. Adding aliquots of AB and replacing equivalent amounts of I will keep $c_I^0 + c_B^0$ constant, while $c_A^0 = c_B^0$. For large p_a the equilibrium distribution is such that only relatively little B is transferred from AB to I. This minor exchange starts quite early and does not alter substantially if one comes close to the equivalence point, since c_I^0 decreases steadily while c_A^0 increases. However, a quite different situation is met for small p_a values. Here almost all B available converts into IB upon addition of AB until the equivalence point is reached, where the relative proportion of IB starts abruptly to decrease, since all I has been converted to IB and only AB will accumulate. Correspondingly the curvature of the titration function shows a sharp peak at $q_a = 0.5$ in contrast to the former case (cf. the graphical representation in Table 3.)

If we compare the expressions for T_a'', Γ_a and τ_a in Table 3 with those in Table 1 we notice the even sharper q_a-dependence of Γ_a relative to T_a'' and τ_a since $\tan^2(\alpha/2)$ in Γ_a is replaced by $\tan^4(\alpha/2)$, while τ_a and T_a'' formally remain unchanged (note, however, the difference in the definition of α). As a consequence the relation between relaxation amplitude and time constant now assumes a different form. It is most obvious for the complementary relaxation time τ_{-a} (cf. Table 3), reading explicitly:

$$\tau_{-a} = p_a + 2(1-p_a)\sqrt{\Gamma_a \tau_{-a}} \tag{3.1-8}$$

The quantities available from experiments are the relaxation time τ and the amplitude factor $\Gamma\Delta H$. A plot of τ *versus* the square root of the products of τ and $\Gamma\Delta H$ at constant $c_I^0 + c_{AB}^0$ should give a straight line with an intercept at: $[k_S(c_I^0 + c_{AB}^0)]^{-1}$ and a slope of

$$\frac{2(1-p_a)}{c_I^0 + c_{AB}^0}\sqrt{\frac{1}{k_S p_a \Delta H}} \tag{3.1-9}$$

This relation is not quite as useful for a separate determination of equilibrium parameters as is the corresponding one for association-dissociation reactions [see eq. (2.3-3)], though the intercept in this case yields directly the rate constant k_S.

3.2. Coupled Reaction System: Sample-Indicator

The second limiting case to be discussed in this section is the use of an auxiliary system as indicator in the presence of finite concentrations of free B-particles ($c_I^0 \ll c_A^0, c_B^0$). The two stability constants:

$$K_A = \frac{c_{AB}}{c_A \cdot c_B} \quad \text{and} \quad K_I = \frac{c_{IB}}{c_I \cdot c_B} \tag{3.2-1}$$

now have to be distinguished explicitly.

Let us assume that any shift of extinction (or other detectable parameters) can be solely attributed to the indicator, so that—in analogy to our previous treatment outlined in Section 2.1—we have for the extinction ratios:

$$\frac{E - E_0}{E_\infty - E_0} \equiv \eta = \frac{c_{IB}}{c_I^0} \quad \text{or} \quad \frac{E_\infty - E}{E_\infty - E_0} \equiv (1-\eta) = \frac{c_I}{c_I^0} \tag{3.2-2}$$

The amount of uncomplexed B is then uniquely defined by the extinction ratio if K_I is known:

$$c_B = \frac{\eta}{1-\eta} K_I^{-1} \tag{3.2-3}$$

Any derivation of an explicit expression for c_{IB}, based on the conservation conditions

$$c_I^0 = c_I + c_{IB}; \quad c_A^0 = c_A + c_{AB}; \quad c_B^0 = c_B + c_{AB} + c_{IB} \tag{3.2-4}$$

would involve the solution of a cubic equation. However, with the help of relation (3.2-3) we can easily deduce an implicit form, correlating the extinction ratios with the overall concentrations, which for known K_I provides the value for the unknown K_A:

$$\frac{\eta}{1-\eta} + K_I(c_A^0 - c_B^0 + \eta c_I^0) = \frac{K_I^2}{K_A}\left(c_B^0 \frac{1-\eta}{\eta} - c_I^0(1-\eta)\right) - \frac{K_I}{K_A} \tag{3.2-5}$$

A straightforward procedure of substitution titration is to start with a given amount of I ($c_I^0 = \text{const}$) and add A and B in stoichiometric aliquots ($c_A^0 = c_B^0$). Assuming that the indicator concentration is small compared with K_I^{-1}, $c_I^0 \ll K_I^{-1}$, eq. (3.2-5) will reduce to the very convenient form

$$\frac{\eta}{1-\eta} = \frac{K_I^2}{K_A}\frac{1-\eta}{\eta} c_B^0 - \frac{K_I}{K_A} \tag{3.2-6}$$

A plot of the extinction ratio $\eta/(1-\eta)$ *versus* its reciprocal multiplied by c_B^0 will yield a straight line, having the following features:

slope: K_I^2/K_A
abscissa intercept: K_I^{-1} (3.2-7)
ordinate intercept: $-K_I/K_A$

An experimental example[11] is shown in Figure 9. Both K_A and K_I can be determined by this simplified procedure of substitution titration, which is somewhat analogous to the Hildebrand-Benesi method and represents an especially advantageous technique of complexometry.

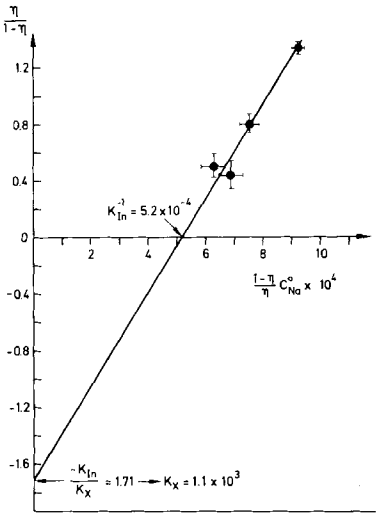


Fig. 9. Substitution titration method according to eq. (3.2-6) as applied to the complexation of dinactin (–) with Na^+ in methanol (data from Ref. [15b]). The obtained value for K is 1.1×10^3 M^{-1}.

It should be emphasized that the general principle of an indicator—a chemical tool of enormous practical importance—is based on the existence of relations such as (3.2-3), or (2.1-10) and (3.2-6). These show how a substance (I), whose physical properties allow the determination of its binding state with respect to a particular reaction partner, can be used in order to characterize the binding states of *any* other compound (A) with which it has this reaction partner (B) in common. Since the partner (B) is the link between the two equilibria, the detection of its concentration [*e.g.* with the help of the extinction ratio (2.2-3)] permits a decoupling of both mass action relations and hence reduces the problem of determining the binding state of the unknown compound (A) to an evaluation of simple mass balance equations (such as, *e.g.* $c_B^0 = c_B + c_{IB} + c_{AB}$).

In this respect an ideal indicator and an ideal buffer are complementary to each other. Both lead to an assignment of the coupling factor, the concentration of the common reaction partner B. The indicator, present at relatively low concentrations, does not fix c_B, but allows its measurement (eq. 3.2-3). The buffer, on the other hand, fixes c_B by its presence at very high concentration compared with that of any of the competitors.

The procedure just outlined applies equally well to an *evaluation of relaxation amplitudes.* Relaxation measurements have to be carried out in the absence and in the presence of the sample AB:

The corresponding implicit expressions are:

$$\delta c_{IB} = \Gamma_I(\delta \ln K_I) \tag{3.2-8}$$

$$\delta c_{IB}^{\pm} = \Gamma_I^{\pm}\left(\delta \ln K_I - \frac{\Gamma_A}{c_B}\delta \ln K_A\right) \tag{3.2-9}$$

where Γ_I, Γ_A and $\Gamma_I^{\pm}$ are defined as:

$$\Gamma_I = \frac{c_I \cdot c_B}{K_I^{-1} + c_B + c_I}; \quad \Gamma_A = \frac{c_A \cdot c_B}{K_A^{-1} + c_B + c_A} \tag{3.2-10}$$

$$\Gamma_I^{\pm} = \frac{c_I \cdot c_B}{K_I^{-1} + c_B + c_I\left(1 - \frac{\Gamma_A}{c_B}\right)} \tag{3.2-11}$$

Thus the A-system influences the amplitude δc_{IB} in two ways. One appears to be a buffering effect and hence shows up in $\Gamma_I^{\pm}$; the other reflects the finite shift of the AB-equilibrium due to a finite $\delta \ln K_A$ which, *via* the concentration change of B, is coupled with the indicator equilibrium. The buffering action is of especial importance, whenever A, AB, I and IB are in large excess of free B. This very case was treated in the first part of this section. Here we are concerned with the other case, where the indicator is present at small concentration, in particular $c_I \ll K_I^{-1} + c_B$ (c_B being controlled by the AB-system). Γ_I and $\Gamma_I^{\pm}$ then become identical, because the c_I-term is negligible, and the difference amplitude $\Delta(\delta c_{IB}) = \delta c_{IB}^{\pm} - \delta c_{IB}$ is simply given by:

$$\Delta(\delta c_{IB}) = -\frac{\Gamma_I \Gamma_A}{c_B}\delta \ln K_A \tag{3.2-12}$$

Γ_I is taken to be known, since it can be either calculated from K_I or detected independently in absence of the AB-system.

Γ_A/c_B for small c_I^0 is identical with the expression obtained for an uncoupled system:

$$\Gamma_A/c_B = \frac{c_A}{c_A + c_B + K_A^{-1}} = \frac{1}{2}\left[1 - \frac{1}{\sqrt{1 + \frac{4K_A^{-1} \cdot c_A^0}{(K_A^{-1} + c_B^0 - c_A^0)^2}}}\right] \tag{3.2-13}$$

or with the convenient assumption $c_A^0 = c_B^0$,

$$\Gamma_A/c_B = \frac{1}{2}\left[1 - \frac{1}{\sqrt{1 + 4K_A \cdot c_A^0}}\right] \tag{3.2-14}$$

This expression, of course, cannot be directly recorded. The quantity yielded by the experiment, according to eq. (3.2-12), is

$$f_{exp} = \frac{\Gamma_A}{c_B}\delta \ln K_A \tag{3.2-15}$$

where $\delta \ln K_A$ is given by $(\Delta H_A/RT)(\delta T/T)$ in case of a T-jump. There is a simple trick for evaluating the measured quantity f_{exp} (if one does not want to leave it completely to a computer).

We guess a value for $\delta \ln K_A$ (*e.g.* for ΔH_A) and then consider the factor

$$\frac{f_{exp}}{(\delta \ln K_A)_{guessed}} = f^* = \frac{1}{2}\left[1 - \frac{1}{\sqrt{1+4K_A \cdot c_A^0}}\right] \qquad (3.2\text{-}16)$$

which can be rearranged to:

$$\phi = (1-2f^*)^{-2} - 1 = 4K_A c_A^0 \qquad (3.2\text{-}17)$$

A plot of ϕ *versus* c_A^0 should yield a straight line with a slope of $4K_A$, if (and only if) we have guessed the correct value for $\delta \ln K_A$.

What happens if our guess was not correct is illustrated in Fig. 10. For excessively large values of $(\delta \ln K_A)_{guessed}$ all curves bend downwards, whereas for small values they bend upwards. Hence we have a *converging* method for iterative guesses which leads finally to the correct number for $\delta \ln K_A$ (i.e. ΔH_A or ΔV_A *etc.*) and also for K_A itself, resulting from the slope of the interpolated straight line.

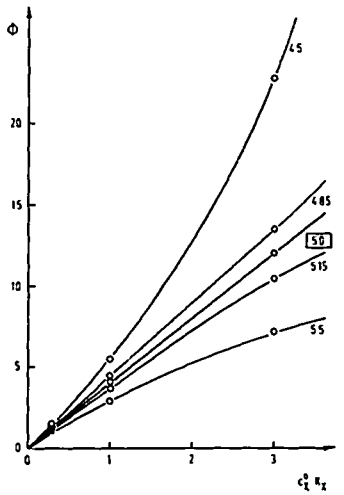
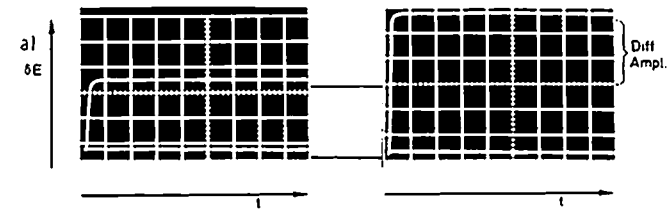


Fig. 10. Evaluation of stability constants and reaction enthalpies from relaxation amplitude-differences, using the substitution method described in the text. The function ϕ which is based on the experimental data, but contains also a guessed value for ΔH, is plotted *versus* the concentration c_X^0 (here given in reduced units: $c_X^0 K_X$). The numbers at the curves refer to the guessed ΔH values [kcal/mol].

The curves converge into a straight line for the correct ΔH value of 5.0 kcal/mol. The slope of this line yields $4K_X$.

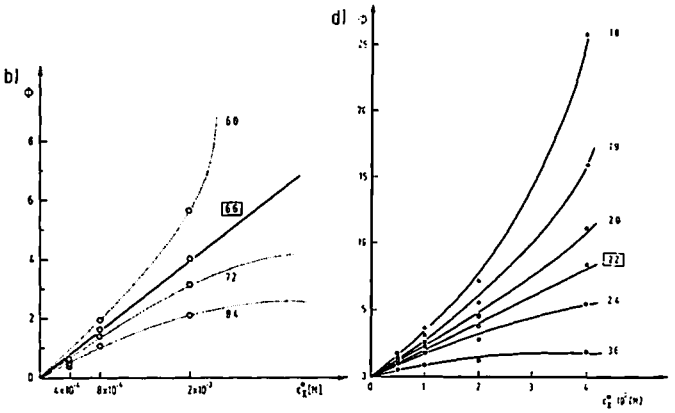
The example in Figure 10 shows how sensitive this method is with respect to a determination of ΔH. For the conventional van't Hoff plots one has to scan through a quite substantial temperature range in order to obtain comparably precise values for ΔH. Many compounds—especially enzymes which may undergo conformational changes or even denaturation—do not tolerate large temperature variations. The relaxation procedure described here works with a relatively small temperature shift δT (*e.g.* ≈ 5 to 10°C) around a suitable reference state.

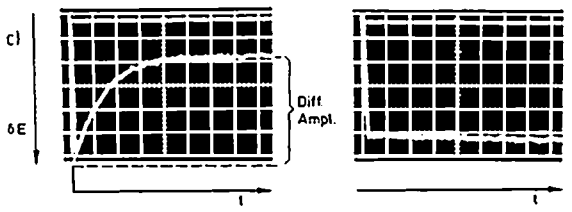
How convenient both substitution methods are, may be seen from Figures 11a—d, where some experimental data resulting from studies of alkali metal complexes with antibiotics[11] and related substances[15a] are presented. Further applications are to be found in a joint paper with *P. B. Chock* and *F. Eggers*[15b].



With monactin:
$4 \cdot 10^{-5}$ M murexide
$2 \cdot 10^{-3}$ M monactin
$2 \cdot 10^{-3}$ M sodium (total)
$\delta E = 1.5 \times 10^{-3}$/large division
time base: 10 ms/large division

Without monactin:
4×10^{-5} M murexide
1.3×10^{-3} M sodium (total)
$\delta E = 1.5 \times 10^{-3}$/large division
time base: 10 ms/large division





With antamanide:
4×10^{-5} M murexide
1×10^{-3} M antamanide
1×10^{-3} M sodium (total)
$\delta E = 3.5 \times 10^{-4}$/large division
(compensated to 6.03×10^{-3})
$\tau = 2.3$ ms

Without antamanide:
4×10^{-5} M murexide
0.75×10^{-3} M sodium (total)
$\delta E = 3.7 \times 10^{-4}$/large division
(compensated to 6.34×10^{-3})

(Note, that the sensitivities of measurements for δE in both cases are somewhat different. The initial (fast) extinction changes are almost identical in both cases.)

Fig. 11. Experimental data exemplifying the amplitude substitution method.

a) and c) relaxation oscillograms of the Na^+-monactin [1] and Na^+-antamanide [15a] systems in methanol under the specified conditions. The amplitudes in the presence and in the absence of monactin or antamanide, respectively, are measured under exactly equal concentrations of free sodium ions and indicator (murexide).

b) and d) show the evaluation according to the method described in Fig. 10. The resulting values are at $T = 293$ °K.

Na^+-monactin: $K = 5 \times 10^2\ M^{-1}$ $\Delta H = -6.6$ kcal/mol
Na^+-antamanide: $K = 5 \times 10^2\ M^{-1}$ $\Delta H = -2.2$ kcal/mol

4. Multiple Step Systems

The theoretical considerations as well as the practical procedures discussed above lead to some generalizations. We have already mentioned that it is not the aim of this paper to deal with general theoretical aspects of the dynamics of

complex reaction systems near equilibrium. The linear algebra required for the solution of this problem is well known[5, 16]. In the present paper we want to discuss primarily the application of dynamical methods to analytical chemistry. The desired information about the properties of an individual complex reaction system can only result from a detailed analysis of the particular mechanism involved.

Three cases of more general interest for complexometry will be treated in this section.

1. Two reaction partners are specified which form a complex:

$$A + B \rightleftharpoons AB$$

Each of the two partners is further involved in a series of binding steps with auxiliary systems. We may, for instance, consider a typical problem of complexometric titration. A metal ion (or general electrophile) in buffered solution is titrated with a ligand which exists in various protonated forms. The buffer also binds to the metal ion, in various proportions, and simultaneously controls the pH of the system.

2. A center A binds a certain number of ligands B:

$$A + B \rightleftharpoons AB;\ AB + B \rightleftharpoons AB_2;\ldots;AB_{n-1} + B \rightleftharpoons AB_n$$

Under such particular conditions a sequential binding process can be characterized by one equilibrium parameter, as follows:

2a) The intrinsic binding constant for each step is degenerate:

$$K_1 = K;\quad K_2 = 2K;\ldots;K_n = nK$$

An example is provided by an allosteric enzyme which consists of several identical subunits, each of which can independently bind a substrate.

2b) The intermediates (AB_i for $1 \leq i < n$) have a low stability and hence are present at a very low concentration. The overall process can then treated as if it were one single step:

$$A + nB \rightleftharpoons AB_n$$

2c) The individual steps differ so strongly in their binding constants that for any given concentration range of B, one complex is always present in large excess. If the mid-points of those transitions can be reached at finite concentrations of uncomplexed B, we have just a series of separate steps of binary complex formation *e.g.*

$$AB_{k-1} + B \rightleftharpoons AB_k$$

as have been discussed in Section 2.

If, alternatively, the stability of all steps is so high that the concentrations of free ligand particles B is small compared with the complex concentrations, the particular reaction may be written as a disproportionation:

$$AB_{k-1} + AB_{k+1} \rightleftharpoons 2AB_k$$

3. The complex-forming agent A is assumed to be involved in several competitive 1 : 1 association reactions with different ligands X, Y, Z. Significant examples are the ternary systems: {sample, buffer, indicator} or {sample 1, competing sample 2, indicator}.

In fact, most other cases of general multiple complex formations may be reduced to any one of these principal mechanisms.

4.1. Complexometric Titration

This Section heading resembles the title of *Gerold Schwarzenbach*'s famous monograph[17], in which the prototype of a multiple step complexation reaction was considered. Adopting *Schwarzenbach*'s notation we call the metal ion $M^{+\nu}$, the ligand used for titration $Y^{-\mu}$, and the auxiliary complex partner L. The latter may be the buffer providing constant pH, which must naturally be in sufficient excess. All changes associated with the ML- and HY-equilibria have to occur rapidly in comparison with the complexation reaction M + Y under study. Examples outlined by *Schwarzenbach* include various di- and trivalent metal ions, the complex partner ethylenediaminetetraacetic acid, and the auxiliary buffer system NH_3. One may determine the concentration of MY spectroscopically if Y shows detectable optical or electrical properties. Otherwise an additional system may be added as indicator, which has to be present at appropriately low concentration, in order not to interfere with any of the conservation relations. The indicator, furthermore, has to react rapidly in comparison with the sample. If these conditions are not fulfilled, the indicator must be treated as an additional reaction partner, as set out in Section 4.2 or 4.3.

Taking into account the two chains of equilibria

$$M + L \rightleftharpoons ML,\ldots,\ ML_{n-1} + L \rightleftharpoons ML_n \tag{4.1-1}$$

and

$$Y + H \rightleftharpoons YH,\ldots,\ YH_{m-1} + H \rightleftharpoons YH_m \tag{4.1-2}$$

we define the apparent concentrations:

$$\begin{aligned} c'_M &= c_M + c_{ML} + \cdots + c_{ML_n} \\ &= c_M(1 + K_1 c_L + K_2 c_L^2 + \cdots + K_n c_L^n) \equiv \beta_L c_M \end{aligned} \tag{4.1-3}$$

where β_L is a constant at fixed c_L^0 (for a large excess of L).

Likewise

$$\begin{aligned} c'_Y &= c_Y + c_{YH} + \cdots + c_{YH_m} \\ &= c_Y(1 + K_1 c_H + K_2 c_H^2 + \cdots + K_m c_H^m) \equiv \alpha_H c_Y \end{aligned} \tag{4.1-4}$$

with α_H being a constant at given pH (*i.e.* in a buffered solution). Then for the complex formation between M and Y we have:

$$K_{MY}^{App} = \frac{c_{MY}}{c'_M \cdot c'_Y} = \frac{c_{MY}}{c_M \cdot c_Y} \cdot \frac{1}{\alpha_H \beta_L} = \frac{K_{MY}}{\alpha_H \beta_L} \tag{4.1-5}$$

The conservation relations

$$c_M^0 = c_{MY} + c'_M \text{ und } c_Y^0 = c_{MY} + c'_Y \tag{4.1-6}$$

contain the missing link for an explicit solution in terms of the titration function, which—as was described in Section 2—follows from a quadratic equation:

$$\frac{c_{MY}}{(c_M^0 - c_{MY})(c_Y^0 - c_{MY})} = \frac{K_{MY}}{\alpha_H \beta_L} \qquad (4.1\text{-}7)$$

The solution has precisely the form of T_b introduced in Table 1. The constant $K = K_{MY}/\alpha_H\beta_L$ is now—with the help of α_H and β_L—an adjustable quantity. In a similar way all the other expressions, such as T_b'', Γ_b and τ_b can be derived from the solution of eq. (4.1-7). Details are to be found in Section 2.1 to 2.3. Applications of the titration function T_b were discussed by *Schwarzenbach*[17].

4.2. Sequential Complex Formation and Ligand Exchange

Three limiting cases have been distinguished in the introduction to Section 4. The first two are: 2a) *degeneracy* of intrinsic binding parameters for homotropic sites, and 2b) *all-or-none* binding at multiple sites—possibly mediated by concerted conformational changes. These are typical for multi-subunit protein molecules. The classical titration procedures, such as the well-known methods of *Bjerrum*[18], *Scatchard*[19] and others (as detailed in the monograph by *Edsall* and *Wyman*[4]) easily yield the number of binding sites per molecule (for a survey of plots cf. Figure 12). In a similar way the relaxation

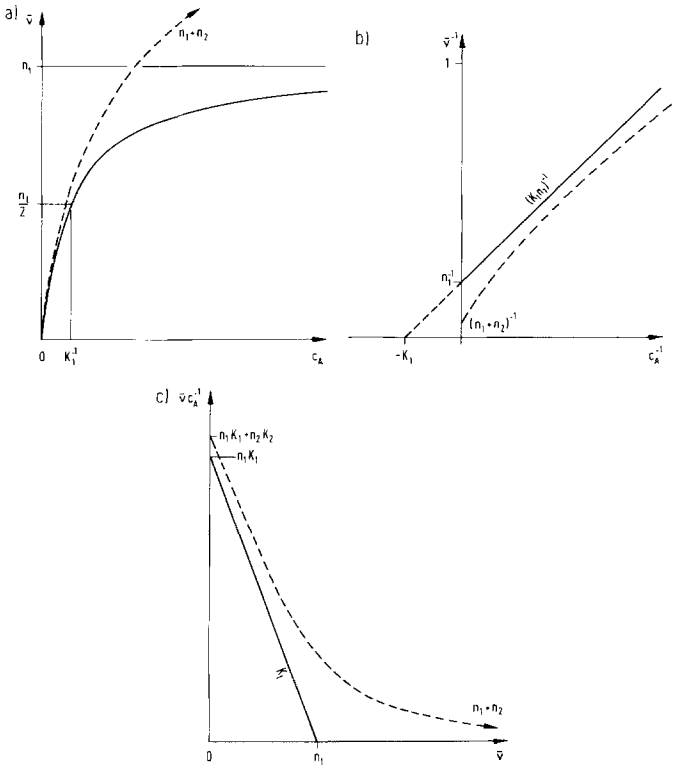


Figure 12. Conventional plots of binding functions in the presence of several groups of equivalent binding sites. The full line refers to appearance of only one group of n_1 equivalent sites, while the broken line indicates the presence of two groups with n_1 and n_2 sites, respectively, having binding constants K_1 and K_2 ($<K_1$). Data taken from *Edsall* and *Wyman* [4]. a) correspond to the Michaelis-Menten plot and b) to the Linewaver-Burk plot (see Fig. 2). c) is named after *Scatchard* [19].
For a) the following relation holds $\bar{\nu} = \sum n_i c_A/(K_i^{-1} + c_A)$; n_i = number of equivalent binding sites of sort i, K_i = respective binding constant and c_A = (free) ligand concentration. In the case b) the relations are: $1/\bar{\nu} = [(1/n_1) + (1/K_1 n_1 c_A)]f_{12}$ with

$$f_{12} = \frac{n_1 K_1 (1 + K_2 c_A)}{n_1 K_1 + n_2 K_2 + (n_1 + n_2) K_1 K_2 c_A}, \quad (f_{12} = 1 \text{ for } K_2 = 0)$$

and for c) $\bar{\nu}/c_A = K_1[(n_1/f_{12}) - \bar{\nu}]$.

Table 4. Relations for general ligand exchange

$$AB_{n-1} + AB_{n+1} \rightleftharpoons 2AB_n$$

$$p = \frac{c_{n-1}\, c_{n+1}}{c_n^2}; \quad 4p < 1\ [*]$$

a)	b)
c_A^0 = const., c_B^0 = variable	c_B^0 = const., c_A^0 = variable
$q_a \equiv \frac{c_B^0}{c_A^0}$	$q_b \equiv \frac{c_A^0}{c_B^0}$
T_a, Γ_a, τ_a related to const. c_A^0	T_b, Γ_b, τ_b related to const. c_B^0
$\sin\alpha \equiv \sqrt{(1-4p_a)[1-(q_a-n)^2]}$	$\sin\alpha \equiv \sqrt{(1-4p_b)\left[1-\left(\frac{1}{q_b}-n\right)^2\right]}$
Range:	Range:
$n-1 \le q_a \le n+1$	$n-1 \le \frac{1}{q_b} \le n+1$
$0 \le \sin\alpha \le \sqrt{1-4p_a}$	$0 \le \sin\alpha \le \sqrt{1-4p_b}$
or $0 \le \tan\frac{\alpha}{2} \le \frac{1-2\sqrt{p_a}}{\sqrt{1-4p_a}}$	or $0 \le \tan\frac{\alpha}{2} \le \frac{1-2\sqrt{p_b}}{\sqrt{1-4p_b}}$

a)
$$\begin{cases} T_a = \dfrac{1}{1-4p_a}\left\{1-\sqrt{1-(1-4p_a)[1-(q_a-n)^2]}\right\} \\ T_a = \dfrac{1}{1-4p_a}\cdot\dfrac{2\tan^2\left(\frac{\alpha}{2}\right)}{1+\tan^2\left(\frac{\alpha}{2}\right)} \end{cases}$$

$$T_a' = -\frac{q_a - n}{\sqrt{1-(1-4p_a)[1-(q_a-n)^2]}}$$

$$T_a'' = -4p_a\left[\frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}\right]^3$$

$$\Gamma_a = p_a T_a^2 \tau_a = \frac{4p_a}{(1-4p_a)^2}\cdot\frac{\tan^4\left(\frac{\alpha}{2}\right)}{1-\tan^4\left(\frac{\alpha}{2}\right)}$$

$$\tau_a = 1-(1-4p_b)[1-(q_a-n)^2]^{-1/2} \qquad \tau_a = \frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$$

b)
$$\begin{cases} T_b = \dfrac{q_b}{1-4p_b}\left\{1-\sqrt{1-(1-4p_b)\left[1-\left(\frac{1}{q_b}-n\right)^2\right]}\right\} \\ \dfrac{T_b}{q_b} = \dfrac{1}{1-4p_b}\cdot\dfrac{2\tan^2\left(\frac{\alpha}{2}\right)}{1+\tan^2\left(\frac{\alpha}{2}\right)} \end{cases}$$

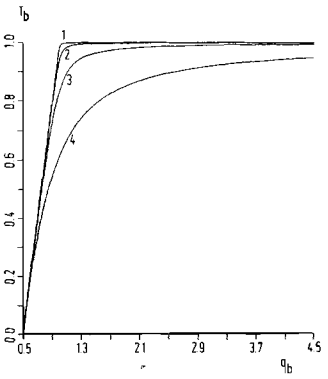
$$q_b T_b' = -\left[\frac{\left(\frac{1}{q_b}-n\right)}{\sqrt{1-(1-4p_b)\left[1-\left(\frac{1}{q_b}-n\right)^2\right]}} - T_b\right]$$

[*] For $4p_a > 1$, substitution of hyperbolic functions analogous to Table 3

$$q_b^3 T_b'' = -4 p_b \left[\frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)} \right]^3$$

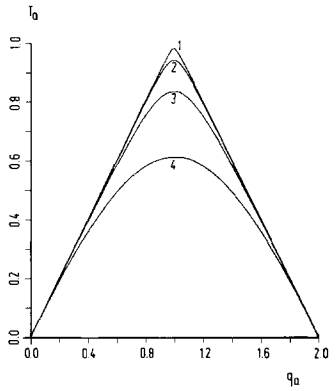
$$\frac{\Gamma_b}{q_b} = \frac{p_b (T_b/q_b)^2}{\sqrt{1-(1-4p_b)\left[1-\left(\frac{1}{q_b}-n\right)^2\right]}} = \frac{4p_b}{(1-4p_b)^2} \frac{\tan\psi\left(\frac{\alpha}{2}\right)}{\left(1-\tan^4\left(\frac{\alpha}{2}\right)\right)}$$

$$\tau_b q_b = \frac{1+\tan^2\left(\frac{\alpha}{2}\right)}{1-\tan^2\left(\frac{\alpha}{2}\right)}$$



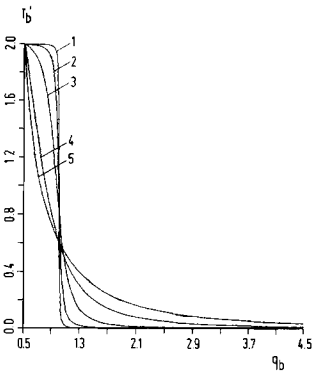
For the case n = 1 the parameters are:

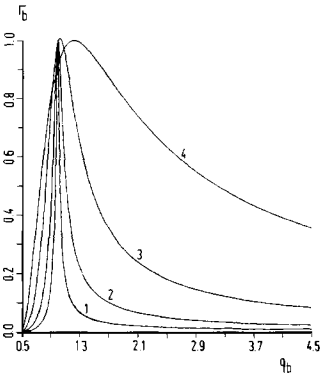
curve 1: $p_b = 1 \times 10^{-4}$
2: $p_b = 1 \times 10^{-3}$
3: $p_b = 1 \times 10^{-2}$
4: $p_b = 1 \times 10^{-1}$
5: $p_b = 2.5 \times 10^{-1}$

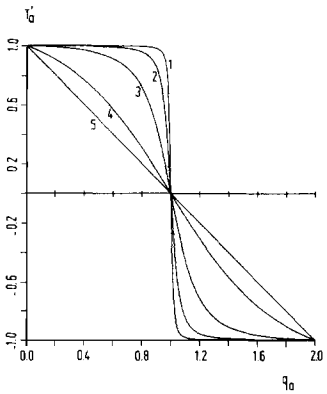


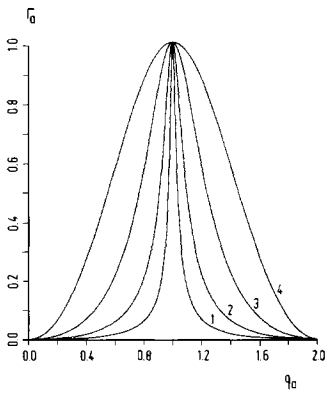
For the case n = 1 the parameters are:

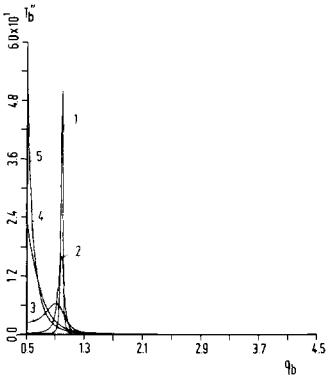
curve 1: $p_a = 1 \times 10^{-4}$
2: $p_a = 1 \times 10^{-3}$
3: $p_a = 1 \times 10^{-2}$
4: $p_a = 1 \times 10^{-1}$
5: $p_a = 2.5 \times 10^{-1}$

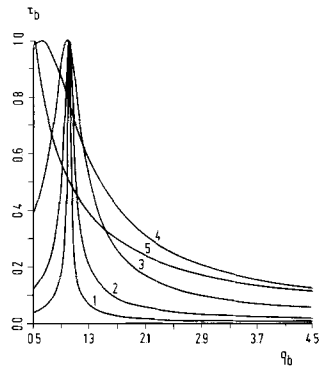


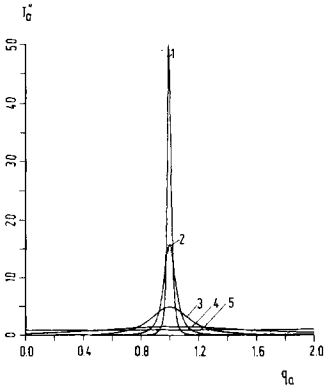


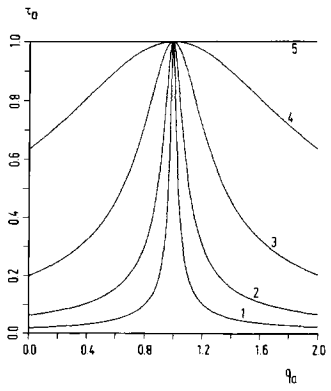


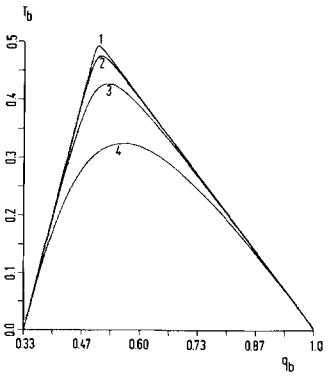






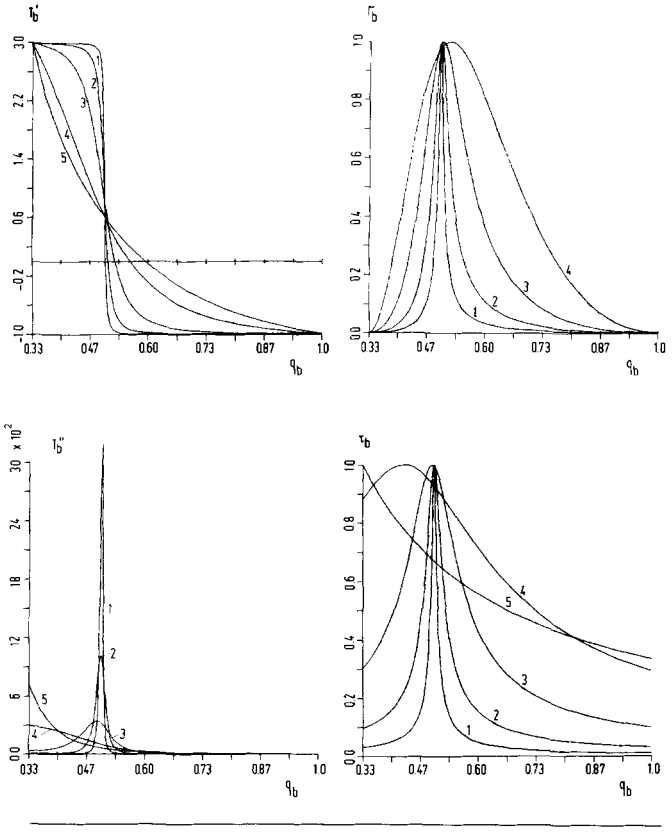






For the case n = 2 the parameters are:

curve 1: $p_b = 1 \times 10^{-4}$
2: $p_b = 1 \times 10^{-3}$
3: $p_b = 1 \times 10^{-2}$
4: $p_b = 1 \times 10^{-1}$
5: $p_b = 2.5 \times 10^{-1}$



parameters can be evaluated, using the principles outlined in Table 1. For n equivalent sites per molecule the term c_B^0 has simply to be replaced by $n c_B^0$, shifting the maxima for Γ_a, Γ_b, τ_a, T_a'' to the equivalence points:

a) $c_A^0 + n c_B^0 = 0.5$

and

b) $c_A^0 = n c_B^0 + K^{-1}$

and for τ_b and T_b'' to $c_A^0 = n c_B^0 - K^{-1}$.

Any deviation from the standard curve shapes, *e.g.* dissymmetries, will indicate the presence of nonequivalent binding sites. There will be as many relaxation times as groups of nonequivalent sites. If they are independent of each other, the evaluation is straightforward (cf. Table 4). An example of an enzyme with (at least) two independent nonequivalent groups, each containing 6 degenerate sites, is provided by glutamic dehydrogenase[20]).

The more complex relations for the relaxation parameters of systems with nonequivalent and interacting sites—including some common models for allosteric enzymes[21, 22]—will be discussed in a forthcoming paper[23].

True cooperativity is mainly confined to macromolecular species, such as proteins, nucleic acids or membrane vesicles. In fact, for most other sequential binding processes involving polyfunctional entities of lower molecular weight just the opposite is true. One might call their behavior "negatively cooperative". It is the first ligand which, in general, is most strongly bound, while with increasing number of ligands one finds a gradual decrease of binding strength. Exceptions to this rule usually involve a more complex mechanism. For instance, the two phenolic protons in phenolphthalein have identical pK's (*i.e.* dissociate in the same pH range) as a consequence of the superimposed quinone-lactone transformation.

If the binding constants of individual groups differ sufficiently one may treat each step separately as outlined in Section 2. Difficulties appear if all binding constants are high, so that all sites are (almost) saturated, which means that their concentrations are in large excess of the free ligand concentration. The essential process at any given stage then has to be formulated as a ligand exchange reaction:

$$AB_{n-1} + AB_{n+1} \underset{k_{-n}}{\overset{k_n}{\rightleftharpoons}} 2\,AB_n \qquad (4.2\text{-}1)$$

The explicit expressions of all functions (T_b and its higher derivatives, Γ_b and τ_b) with respect to the titration variable are very similar to those given in Section 2, and especially in Table 2, although minor modifications show up due to the n-fold appearance of B in AB_n.

The equilibrium constant is defined as

$$K = \frac{c_{n-1} \cdot c_{n+1}}{c_n^2} = \frac{k_{-n}}{k_n} \qquad (4.2\text{-}2)$$

The indices n−1, n and n+1 refer to the species AB_{n-1}, AB_n and AB_{n+1}, respectively. The conservation conditions read:

(4.2-3)

$$c_A^0 \approx c_{n-1} + c_n + c_{n+1}; \qquad 2c_{n+1} = c_A^0 + c_B^0 - n c_A^0 - c_n$$

$$c_B^0 \approx (n-1)c_{n-1} + n c_n + (n+1)c_{n+1}; \quad 2c_{n-1} = c_A^0 - c_B^0 + n c_A^0 - c_n$$

The explicit expression for c_n can then be obtained as the solution of a quadratic equation

$$c_n = \frac{c_A^0}{1-4K}\left\{1 - \sqrt{1-(1-4K)(1-[(c_A^0/c_B^0)-n]^2)}\right\} \qquad (4.2\text{-}4)$$

The most convenient and simple procedure is to maintain the overall concentration of the complex forming agent c_A^0 and to vary c_B^0, which has to be present in about n-fold excess of c_A^0. The constancy of the c_A^0 factor in the prebracket-term leads to very symmetrical relations for $T_a \equiv c_n/c_A^0$, $\Gamma_a = \Gamma/c_A^0$ and $\tau_a = \tau k_n c_A^0$ [analogous to case a) quoted in Tables 1 and 3] which are easy to handle. However, mathematical convenience is not always identical with practical applicability. If the complexes are very strong, and the strength decreases with increasing n, it may be preferable to add aliquots of A to the B-sample, where c_B^0 = const. The highest stages AB_n will then be populated immediately, as long as B is still in (more than) n-fold excess. But as soon as c_A^0 becomes larger than c_B^0/n, there will be a competition for the ligands according to the scheme (4.2-1). This competition will shift steadily to lower n-values with increasing c_A^0. Here we refer to the fixed concentration c_B^0 defining: $T_b \equiv c_n/c_B^0$, $\Gamma_{nb} = \Gamma_n/c_B^0$ *etc.*

The results for both treatments are compiled in Table 4. Their correspondence with the expressions listed in Tables 1 and 3 is most obvious if the trigonometric form of representation is chosen.

Amplitude recording (*i.e.* Γ or T'') offers exciting new opportunities for complexometry, especially for sequential ligand

binding. Using the titration variable q_a in the range from (below) 1/n to (above) 1 means scanning through a number of well defined sharp peaks, each being characteristic of one of the n steps of ligand binding. The search for a method yielding singularities pays off particularly where a series of ligand binding processes shows up in a narrow range of concentration variation, and where ordinary binding curves just exhibit a more or less broad transition.

To illustrate the usefulness of the dynamic techniques let us consider two examples of multiple step titration.

The first case is that of complex formation involving the substitution of solvent by two ligands in the inner coordination sphere of a metal ion.

$$M + 2L \rightleftarrows ML + L \rightleftarrows ML_2 \qquad (4.2\text{-}5)$$

If the individual stability constants are so high that at the lowest detectable level of ligand concentration both complexes are already formed, it is advisable to apply method b), *i.e.* to fix c_L^0 and titrate with the metal ion. If Γ or T_b' is recorded for $c_M^0 \approx c_L^0/2$, a maximum appears, which is due to the formation of ML_2. This maximum vanishes when c_M^0 becomes larger than $c_L^0/2$, but soon a second peak shows up caused by the—now dominating—exchange reaction (4.2-1) which, of course, is only present if the binding strength for the first ligand is higher than that for the second one. Figure 13 illustrates

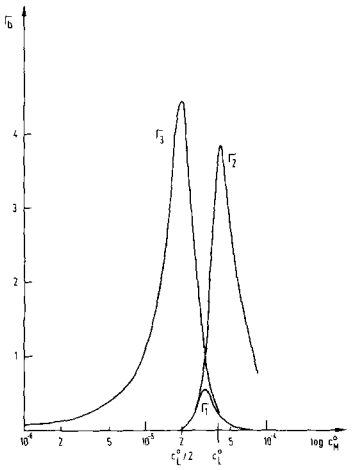


Fig. 13. Reduced amplitude factor for a two step dissociation process according to eq. (4.2-5). The two sharp maxima are responsible for the two processes:

1) $L + ML \rightleftarrows ML_2$
2) $ML_2 + M \rightleftarrows 2ML$

The parameters for the scheme

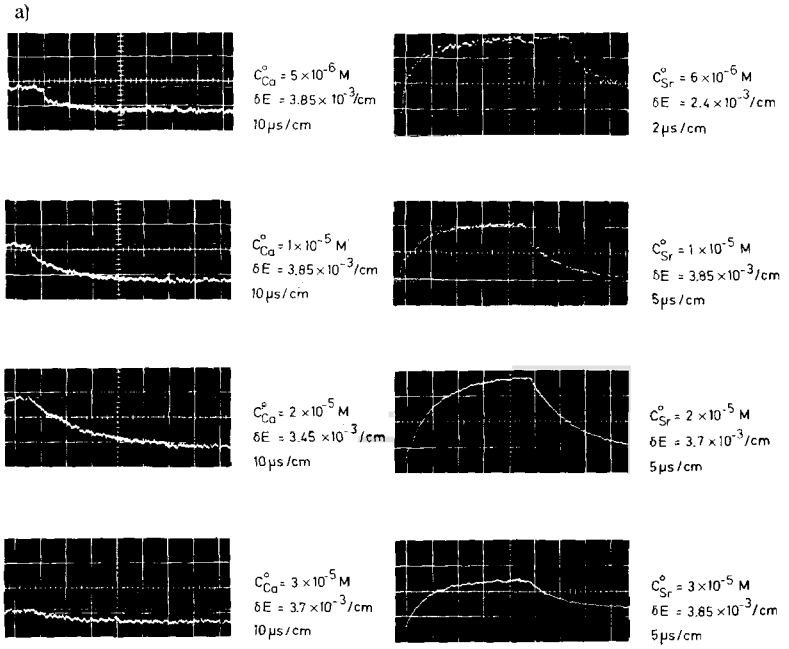
$$M + 2L \underset{}{\overset{K_1}{\rightleftharpoons}} ML + L \overset{K_2}{\rightleftharpoons} ML_2$$

$$ML_2 + M \underset{K_3}{\rightleftharpoons} 2ML \underset{K_4}{\rightleftharpoons} 2M + 2L$$

are:

$K_1 = 10^8\ M^{-1}$
$K_2 = 10^6\ M^{-1}$
$c_L^0 = 4 \times 10^{-5}\ M$

this type of behavior for Γ_b. The sensitivity expressed by the sharpness of peaks is striking. Experimental recordings of this kind have been obtained with the murexide-complexes of Ca^{2+} and Sr^{2+} in methanol[11]. Both relaxation amplitudes and time constants could be determined by electric field-pulse and temperature-jump measurements. Examples of oscillograms and their interpretation are shown in Figure 14.



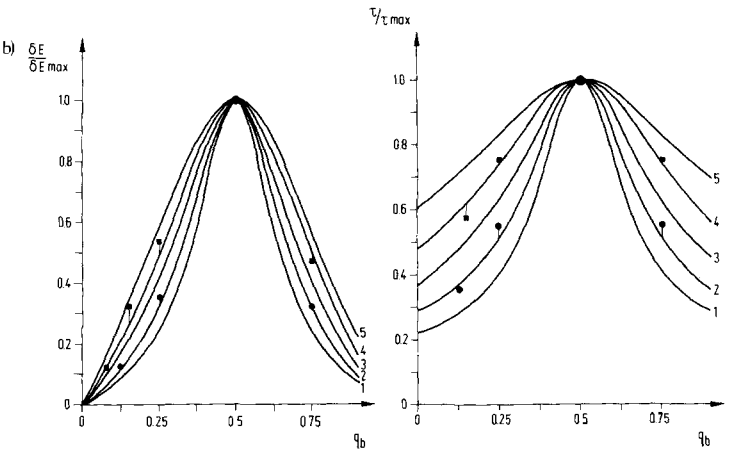


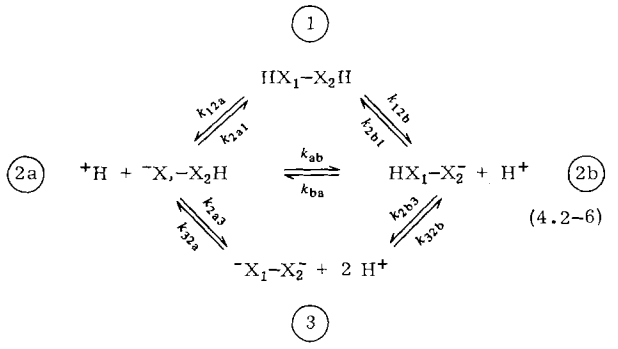
Fig. 14. Relaxation curves from electric field pulse measurements for the systems Ca-murexide and Sr-murexide in methanol. The data refer to the step $ML + L \rightleftarrows ML_2$. The maxima of Γ and τ occur at $c_M^0 = \frac{1}{2} c_L^0$. A second (slower) relaxation effect occurring at higher concentrations of M refers to the step $ML_2 + M \rightleftarrows 2ML$.

a) Oscillograms.

b) Normalized plots for $\Gamma(E)$ and τ. The evaluation of the data yields for Ca: $K_2 = 5\times10^5\ M^{-1}$ and for Sr: $K_2 = 1.5\times10^5\ M^{-1}$. c_M^0 refers to the total concentration of the metal ion. c_L^0 for both series was fixed at 4×10^{-5} M. 1–5 refers to: 1) 1.0×10^6, 2) 5.6×10^5, 3) 3.1×10^5, 4) 1.8×10^5, and 5) 1.0×10^5.

Only if saturation of M with L occurs in distinct concentration ranges of L, with $c_L^0 \gg c_M^0$ for both steps, may one scan through those ranges at constant c_M^0 and monitor the signals characteristic of the individual steps of complex formation according to scheme (4.2-5). Evaluation in this case would simply follow the procedure of Section 2.

The second example is concerned with the titration of a dibasic acid. So far only little reference has been made in this paper to pH-titration, since straightforward procedures using suitable buffers throughout the pH-scale are usually



(4.2-6)

available. The case of polybasic acids, however, involves a problem, which has not yet found a completely satisfactory solution. It is the problem of the so-called "microscopic" dissociation constants[4]. What is meant by these constants, can immediately be seen from the reaction scheme (4.2-6).

The two pK-values resulting from titration refer to the overall equilibra (1)–(2a)–(2b) and (3)–(2a)–(2b).

$$\frac{c_{HX_1-X_2H}}{c_H \cdot (c_{X_1-X_2H} + c_{HX_1-X_2})} = K_1 \text{; and } \frac{c_{X_1-X_2H} + c_{HX_1-X_2}}{c_H \cdot c_{X_1-X_2}} = K_2 \qquad (4.2\text{-}7)$$

These pK-values may differ by orders of magnitude, but this fact does not necessarily imply that the intrinsic pK's of the individual groups X_1 and X_2 are greatly dissimilar. Strongly differing pK-values are also found for identical groups X_1 and X_2, and are due to neighboring group effects attributed to a change of the state of ionization. In order to have access to the true or "microscopic" constants, one needs to know—in addition to pK_1 and pK_2—the constant of the isomerization equilibrium (2a)⇌(2b). A straightforward assignment would require an experimental identification of the two states (2a) and (2b), *e.g.* by spectroscopy. Usually, this is very difficult and often involves certain more or less valid assumptions concerning spectral or other analogies with similar (*e.g.* methylated) compounds. Because of the rapid interconversion between states (2a) and (2b), it is impossible to quench the exchange and titrate one of the states separately using a specific reaction.

With the help of the dynamic method, we can in principle identify the isomerization step in the relaxation spectrum, In other words: there is a time constant in the spectrum which in the right pH range refers directly to the first-order conversion (2a)⇌(2b). Unfortunately, first-order steps yield concentration-independent time constants and amplitudes[5], and there is no straightforward way (other than by using analogies), either of evaluating the measured relaxation time in terms of both rate constants, or of splitting the relaxation amplitude into the unknown quantities: equilibrium constant, reaction enthalpy or volume and recording parameter (such as difference of extinction coefficients for the state (2a) and (2b)). Thus here again is an interpretation only possible under simplifying assumptions.

One way out of the difficulty could be to record carefully the whole relaxation spectrum and evaluate the concentration dependences of time constants and amplitudes. The reaction scheme under appropriate pH-conditions may be reduced to one of the triangles (low pH: (1)–(2a)–(2b); high pH: (2a)–(2b)–(3)). However, this method also has its difficulties, since protolytic reactions are generally diffusion-controlled, *i.e.* fast and not readily discernible in their rate (so that steps (1)–(2a), and (1)–(2b), or (2a)–(3) and (2b)–(3) cannot directly be discriminated).

A more elegant solution of the problem is offered by a little trick. Starting from situations where the states (2a) and (2b) predominate, one adds a specific reaction partner which interacts with only one of the states a or b (for example, for $HS-R-NH_2$ a specific SH-reagent). This interaction, of course, must *not* be an irreversible one, nor should it be slow as compared with the first-order reaction. In other words, the auxiliary system must not remove one of the states, but rather equilibrate quickly and hence couple with the isomerization a⇌b. For such a system, the relations derived in Table 4b apply. The evaluation of data requires nothing but the knowledge of measurable quantities (*e.g.* two relaxation times and the weighed-in concentrations of the sample as well as that of the auxiliary system). In fact, the addition of sulfite to 4-pyridinecarbaldehyde, discussed earlier, belongs to this category of reactions. In Section 2.4 we were only concerned with the—fast and hence separately occurring—second-order step. The terms for the slow first-order hydration reaction in presence of sulfite now in fact contain concentration dependent factors so that all rate and equilibrium parameters could be assigned. Although these slow hydration processes can be studied by other means, the example demonstrates a very useful application—especially for biochemistry.

4.3. Ternary Systems

In relaxation studies a sample has to fulfill two requirements: firstly, it has to respond to the enforced change of an intensive parameter (T, P, E), and secondly, it must provide a suitable signal for recording the shift of equilibrium. The extent of perturbation depends on the magnitude of the reaction parameters, such as enthalpy (ΔH) or volume of reaction (ΔV). If those parameters for a given sample are too small one may still enforce an equilibrium perturbation *via* an auxiliary system which possesses typical buffer properties and is more sensitive to the external force. This principle may be of special importance in the application of strong electric fields in perturbation methods. A measurable dissociation field effect is present only if both reaction partners carry excess charges. Metal complexes with neutral ligands do not fulfill this condition. However, "secondary" field effects can be induced with the help of competing charged ligands which buffer the concentration of free metal ions and hence influence their interaction with the neutral reaction partner.

Binary equilibria have already been discussed in detail in Section 3, but under certain circumstances there may be a demand for two auxiliary systems, a buffer *and* an indicator. A generalization of this procedure is therefore of common interest and will be given explicitly for two kinds of ternary systems. An example in Appendix 2, furthermore, will demonstrate how to generalize the treatment for any number of reaction partners—metal ions or ligands—by iteration.

4.3.1. Sample, Buffer, Indicator

Let three different types of ligands, X, Y and Z, compete for the same metal ion M. Intentionally it is not yet specified, which of the three substances represents the sample, the buffer or the indicator, in order to keep the treatment as general as possible. Later on, of course, it is necessary to identify the properties of each of the three compounds, since they fulfill their particular role only under selected conditions of concentration. For the corresponding equilibria:

$$\begin{array}{l} M+X \rightleftharpoons MX \\ M+Y \rightleftharpoons MY \\ M+Z \rightleftharpoons MZ \end{array} \qquad (4.3\text{-}1)$$

the following mass action relations hold:

$$\frac{c_{MX}}{c_M c_X} = K_X; \quad \frac{c_{MY}}{c_M c_Y} = K_Y; \quad \frac{c_{MZ}}{c_M c_Z} = K_Z \qquad (4.3\text{-}2)$$

to which are attributed the amplitude factors:

$$\Gamma_X = \frac{c_M c_X}{K_X^{-1} + c_M + c_X}; \Gamma_Y = \frac{c_M c_Y}{K_Y^{-1} + c_M + c_Y}; \Gamma_Z = \frac{c_M c_Z}{K_Z^{-1} + c_M + c_Z} \qquad (4.3\text{-}3)$$

Assuming that only one system, the indicator, shows detectable changes upon complex formation, its concentration shift is the quantity monitored. In absence of X and Y this shift is given by:

$$\delta c_{MZ} = \Gamma_Z \delta \ln K_Z \qquad (4.3\text{-}4)$$

In Section 3.2 it has been shown that the presence of the X-system will modify the recorded signal to:

$$\delta c_{MZ}^{\pm} = \Gamma_Z^{\pm} \left(\delta \ln K_Z - \frac{\Gamma_X}{c_M} \delta \ln K_X \right) \qquad (4.3\text{-}5)$$

where

$$\Gamma_Z^{\pm} = \frac{c_M c_Z}{K_Z^{-1} + c_M + c_Z(1-\Gamma_X/c_M)} = \Gamma_Z \frac{1}{1-\Gamma_Z \Gamma_X / c_M^2} \qquad (4.3\text{-}6)$$

If the Y-system is also included, an expression symmetrical with respect to the parameters of X and Y is obtained:

$$\delta c_{MZ}^{\pm\pm} = \frac{\Gamma_Z}{1-\Gamma_Z \Gamma_{XY}/c_M^2} \left\{ \delta \ln K_Z - \frac{\Gamma_X/c_M(1-\Gamma_Y/c_M)}{1-\Gamma_X\Gamma_Y/c_M^2} \delta \ln K_X - \frac{\Gamma_Y/c_M(1-\Gamma_X/c_M)}{1-\Gamma_X\Gamma_Y/c_M^2} \delta \ln K_Y \right\} \qquad (4.3\text{-}7)$$

with

$$\Gamma_{XY} = \frac{\Gamma_X + \Gamma_Y - 2\Gamma_X\Gamma_Y/c_M}{1-\Gamma_X\Gamma_Y/c_M^2} \qquad (4.3\text{-}8)$$

Since the indicator Z is the only substance contributing a finite signal for detection, c_M is given by $K_Z^{-1} \cdot \eta/(1-\eta)$, where $\eta/(1-\eta)$ is the extinction ratio $(E-E_0)/(E_\infty - E)$ introduced in Section 2.1. For a perturbation brought about by a T-jump, we have:

$$\delta c_{MZ}^{\pm\pm} = \frac{\Gamma_Z}{1-\Gamma_Z\Gamma_{XY}/c_M^2} \left\{ \Delta H_Z - \frac{(\Delta H_X \Gamma_X + \Delta H_Y \Gamma_Y)/c_M - (\Delta H_X + \Delta H_Y)\Gamma_X\Gamma_Y/c_M^2}{1-\Gamma_X\Gamma_Y/c_M^2} \right\} \frac{\delta T}{RT^2} \qquad (4.3\text{-}9)$$

So far no particular discrimination between X and Y has been made. We see that even if one of the reaction enthalpies happens to be zero, the influence of a secondary shift still allows both systems to contribute to the amplitude. Complete buffering of M by the X- as well as by the Y-system means:

$$c_X, c_{MX}, c_Y, c_{MY} \gg c_M \qquad (4.3\text{-}10)$$

or explicitly

$$c_X \gg c_M + K_X^{-1}; \quad c_Y \gg c_M + K_Y^{-1} \qquad (4.3\text{-}11)$$

$$\Gamma_X \simeq \Gamma_Y \simeq c_M; \quad \Gamma_{XY} \simeq 1 \qquad (4.3\text{-}12)$$

The response depends on the relative strength of the two buffering effects, represented by the magnitude of the ratio

$$\frac{c_i}{c_M + K_i^{-1}} \gg 1 \qquad (4.3\text{-}13)$$

where i refers either to X or Y. If one buffer (i) is much stronger than the other, eq. (4.3-7) simplifies to:

$$\delta c_{MZ}^{\pm\pm} = \frac{c_M c_Z}{c_M + K_Z^{-1}} (\delta \ln K_Z + \delta \ln K_i) \qquad (4.3\text{-}14)$$

The properties of the competitor of i cannot then be recorded any more. If, on the other hand, X and Y exhibit identical buffering behavior, then—independent of their absolute strengths—they both contribute to the amplitude:

$$\delta c_{MZ}^{\pm\pm} = \frac{c_M c_Z}{c_M + K_Z^{-1}} (\delta \ln K_Z + \frac{1}{2} \delta \ln K_X + \frac{1}{2} \delta \ln K_Y) \qquad (4.3\text{-}15)$$

The trick of obtaining finite sample signals consists of selecting a buffer with a complex stability comparable with that of the sample. If only one of the two competitors X or Y acted as a strong buffer, its equilibrium constant could not be determined from the relaxation signal. The fact that the signal shows up only in the presence of *both* X *and* Y characterizes the overall reaction as a substitution process.

The possibility of inducing "secondary" shifts opens a new and very general applicability of the relaxation techniques to the determination of stability constants. For instance, it can be used for a study of the interaction of alkali ions with electrically neutral antibiotics acting as ion-carriers. In this very case a "secondary" field effect is to be produced with the help of electrically active ionophores, such as nigericin or monensin.

4.3.2. Indirect Monitoring of Concentration

While general competition involving more than three partners is of only minor practical relevance, another binary system may play a more important role in titration: two substrates A and B compete for the same binding site P (*e.g.* at an enzyme), but one of them, say B, can also react

with a competitor of P, which may be an indicator (I) changing its absorption spectrum upon binding with B. An alternative but formally similar situation is found if B does not complex with the indicator, but transfers some particle, for instance a proton, an electron or a metal ion to I. A titration procedure based on this kind of reaction may be of great value since quite often neither the protein nor the substrate is discernible by suitable optical properties. On the other hand, one may be able to find a substance which at the same time binds to the protein *and* to some indicator as well. Many proteins lose a metal ion upon association with a substrate. Ca^{2+}, for instance, is released upon binding of acetylcholine to its receptor[14]. None of the three components (Ca^{2+}, acetylcholine or the receptor) offers optical shifts convenient for detection. However, Ca^{2+} may couple to an indicator such as murexide and thereby yield information about its competition with acetylcholine (see Table 2 and Fig. 4). There are many similar cases in protein chemistry and also in complexometry, so that more details about this problem are desirable.

For simplicity the protein is denoted by P, the indicator by I, and the two competitors by A and B respectively.

The binding equilibria and their corresponding (simplified) mass action relations are:

$$\left.\begin{array}{ll} A+P\rightleftharpoons AP & K_A=\dfrac{c_{AP}}{c_A\cdot c_P} \\ B+P\rightleftharpoons BP & K_B=\dfrac{c_{BP}}{c_B\cdot c_P} \\ B+I\rightleftharpoons BI & K_I=\dfrac{c_{BI}}{c_B\cdot c_I} \end{array}\right\}$$

or

$$B+I'\rightleftharpoons B'+I \qquad K_I=\frac{c_{B'}\cdot c_I}{c_{I'}\cdot c_B}$$

The overall composition is conserved:

$$c_P^0=c_P+c_{AP}+c_{BP} \qquad c_B^0=c_B+c_{BP}+c_{BI}$$
$$c_A^0=c_A+c_{AP} \qquad c_I^0=c_I+c_{BI}$$

or $c_I^0=c_I+c_{I'}$ and $c_I=c_{B'}$, if the sum $c_{I'}+c_{B'}$ also equals c_I^0.

Note that with respect to the symbols including a "prime", whatever it means (*e.g.* a proton or electron) the conservation law must be fulfilled as well. The above equations then only hold as long as no other acceptor for the "prime" is present and the "prime" itself cannot exist as a free particle (at least not to any extent comparable to c_I and c_B).

In the scheme above, the two brackets indicate how the competitions for P and for B are related to one another.

The indicator species I and IB, or I and I′ respectively, are the only ones which contribute to the measurable absorption. Hence c_B is directly given by the extinction quotient:

$$c_B=K_I^{-1}\frac{\eta}{1-\eta} \qquad \text{or} \qquad c_B=K_I^{-1}\cdot c_I^0\frac{\eta^2}{1-\eta}$$

with

$$c_{IB}=\eta\, c_I^0 \quad \text{and} \quad c_I=(1-\eta)c_I^0 \text{ (cf. Section 3.2)}$$

or

$$c_I=\eta\, c_I^0 \quad \text{and} \quad c_{I'}=(1-\eta)c_I^0$$

Further progress requires a suitable combination of the different terms, leading to a correlation between the *measurable* extinction ratios or their differential shifts, the overall concentrations (to be chosen suitably) and the stability constants which are to be determined. Appendix 3 contains a compilation of the formulae obtained. The relaxation amplitudes are written in an implicit form. The general relations are of fairly complicated structure and must therefore be analyzed in detail in order to be applied optimally.

The existence of two overlapping competing systems restricts severely the choice of conditions. K_A and K_B should not differ too much, and the indicator must be in a concentration range where the shifts of c_B can be monitored most sensitively. Furthermore, c_A, c_B, and c_P have to be adjusted with special reference to K_A^{-1} and K_B^{-1}.

The expression for the amplitude $(\delta c_{BI})_{III}$ is given in Appendix 3. The simplest way of measuring K_A would be to record the corresponding relaxation time τ_{III} at an excess of c_A^0. The linear plot—as in the examples shown in Figure 2b—will yield the two rate constants, the ratio of which defines K_A. The equation of $(\delta c_{BI})_{III}$ indicates where finite signals can be recorded.

In general, the application of secondary indication demands thorough understanding of the theoretical basis, rather than a schematic realization of a recipe.

5. General Comments on Application

The chemist's interest in titration is naturally more of a practical than of a fundamental theoretical nature. It is therefore appropriate, in conclusion, to give a brief critical review on the practical merits of the different kinds of titration principles. No attempt is made to provide anything like a complete description of the various procedures or of the necessary properties of complexing agents, indicators, buffers *etc.*, which can be found in the literature (*e.g.* in the excellent monographs by *F.* and *H. Rossotti*[17] and by *Schwarzenbach*[17]).

A good titration curve is characterized by its sharpness of transition signifying a well defined end-point. In the extreme limit such an end-point is a true discontinuity. In real cases, within a critical concentration range around the equivalence point the addition of a minute amount of standard solution changes the concentration of unreacted sample—or any function thereof—by orders of magnitude. Wherever one can arrange for such a situation—assuming the aim is quantitative analysis—the conventional method of titration is unbeatable. If, on the other hand, the object is a determination of the complex stability constant rather than of the sample concentration, an extreme sharpness of transition does not offer any advantage. On the contrary, the transition should here occur more smoothly, since it is the deviation from discontinuous change which contains all the information about K. As the titration curve becomes broader the mid-point of the change monitored will shift along the concentration axis, until for $Kc_B^0 \ll 1$ its position becomes a direct measure of K^{-1}. If T_b is then plotted *versus* the logarithm of the standard concentra-

tion (c_A^0) the inflection point occurs at exactly $\log c_A^0 = -\log K$. In this limit the curve assumes again a standard shape (cf. Fig. 3). The classical plots of enzyme chemistry—including the applications of steady state kinetics—usually refer to those circumstances (cf. Figures 2, 8 and 12). Obviously, the requirement for such a situation, $c_{standard} \gg c_{sample}$, can be fulfilled only for complexes which are not too strong. Most detection methods cease to be sufficiently sensitive for concentrations below 10^{-4} to 10^{-6} M. This is certainly true for polarimetry (ORD and CD), spectrophotometry—supposing even strongly absorbing substances—and for conductometry in aqueous media. Fluorimetry[*], insofar as it is applicable, may permit some further extension to lower concentrations ($<10^{-6}$ M), and with regard to a *selective* recording of very small concentrations polarography and other electrochemical techniques deserve particular attention. Nevertheless, if one wants to use these methods for the titration of very strong complexes, it is necessary to provide auxiliary systems and to proceed according to the rules of the substitution scheme.

The dynamic titration techniques apply to all situations in which the more conventional static procedures have been used thus far. The information they yield is in fact more directly related to the equilibrium (and kinetic) parameters and is much more detailed, if multiple step processes are involved. In such cases dynamic analysis may offer solutions to problems which were not accessible by classical methods (cf. Table 2, Figs. 7 and 11).

For binary complex formation with $K^{-1} \gg c_{sample}$ the logarithmic derivatives $\partial T_b/\partial \ln K$ and $\partial T_b/\partial \ln c_{standard}$ are very similar. In this case, it is the position of the maximum on the $c_{standard}$ axis (Fig. 3) which yields the information about the stability constant K, otherwise hidden in the uniform curve shape. For $K^{-1} \ll c_{sample}$, the situation is quite different. Actually the concentration dependence of the amplitude and, even more, of the time constants then resembles closely the second derivative of T_b with respect to $c_{standard}$. In a way, the use of higher derivatives of T_b may be considered as a mobilization of all the information which the end-point can provide about stability constants. We therefore have to concentrate on those relations which signify the approach of a singularity. In trigonometric representation, these are especially the functions which contain the term $1-\tan^n(\alpha/2)$ in the denominator, n being an integer ≥ 1. They correlate an equilibrium parameter with some distance on the concentration axis, *e.g.* the half-width of the bell-shaped curves for T'' and Γ or τ, or a distance between two peaks for Γ', (Γ' being the derivative of Γ with respect to the concentration variable). The sharper the end-point, the smaller these distances and therefore the higher the demands for signal amplification, signal/noise resolution and calibration of concentrations. For multiple-step schemes, differential recording offers considerable advantages. It is solely the sharpness of the peaks occurring in the functions Γ, Γ', τ or T'' which leads to the discrimination of several closely superimposed reaction steps, otherwise appearing as a continuum in the titration function.

In this context we should focus our attention on the differential concentration shift δc itself. Since total concentrations are known only within certain limits of accuracy, this difference should be calibrated in the most direct way. For this purpose—whatever the particular relaxation or observation technique is—two identical cells should be filled with the *same* standard solution, so that no differences can arise owing to dissimilar compositions. Small, exactly calibrated equal amounts of standard are now added to both cells, but the perturbation of equilibrium is applied only to one cell. The differential response to such a dissymmetry of perturbation is monitored as a function of the amount of standard added. Procedures of this kind are well known in the field of polarography[24]. Usually it is not necessary to know the *absolute* values of concentrations; if the relative variations of the concentration are exactly calibrated, one may reconstruct the equivalence point uniquely from the curve shapes (*i.e.* their maxima and points of inflection).

The dissymetry of perturbation in the two cells may also refer to the concentration change δc^0 rather than to the change in the intensive variable δz. Only for the direct determination of the relaxation amplitude is the alteration of z ($= T$, P or E) (as was mentioned just before) applied to just one of the cells. If the second derivative of the titration function is to be measured, one keeps both solutions at a fixed finite difference of c_A^0 while adding the same (small) amounts of standard solution concomitantly to both cells. With this technique a differential recording of relaxation amplitudes is possible as well. The external perturbation (*e.g.* a T-jump) may then be applied simultaneously to *both* cells, which, however, are not congruent with respect to their standard content.

The two latter approaches differ in one important aspect. The determination of the curvature of the titration function T'' requires the recording of a second order differential shift $\delta^2 c_A^0$, while the differential recording of amplitudes (*i.e.* Γ') involves only a first order difference in the concentration variable. The shift of the intensive parameter δz is independent of δc_A^0 and can be adjusted in order to yield the largest possible signals. This shows that one of the decisive limiting factors, *i.e.* δc_A^0, influences the two procedures in a quite different manner. For large K-values minute additions of c_A^0 have to be made since all observable changes appear in the close vicinity of the equivalence point. Hence the absolute magnitude of δc_A^0 becomes the limiting factor of accuracy, imposing quite different error limits on both methods.

These considerations lead to the essential question:

Which method is best for which problem?

On the basis of the preceding discussion we can say that for a determination of equilibrium constants the dynamic amplitude techniques are clearly superior, especially when the system has high stability constants, *i.e.* small p-values or sharp endpoints. This advantage holds for all kinds of reactions, *i.e.* binary (1:1) complex formation, substitution or—especially—any of the multiple-step transformations. Moreover, the relaxation amplitudes include additional information on derivatives of the equilibrium constants, such as ΔH or ΔV, and on rate parameters.

On the other hand, relaxational titration requires quite sophisticated techniques for dynamic recording, usually not available as standard laboratory equipment. One may think also of using a static method, *e.g.* a difference recording of the titration function in two cells held at slightly different

[*] A comprehensive review of fluorimetric techniques for both titration and relaxation studies has appeared (*T. Jovin* [12]).

temperatures. However, as was shown in section 2.4 the inevitable corrections for physical effects such as thermal expansion are of a magnitude similar to that of the expected chemical effects, and have to be carried out by suitable calibration.

Among the different *relaxation* techniques we may come to special preferences in order to achieve the optimal response of the system upon variation of T, P or E. In absence of a direct response, a suitable buffer may aid in providing a sufficiently large perturbation of equilibrium.

The very pronounced curve shapes of T'', Γ and τ demand a careful selection of the optimal concentration range in which the differential studies are to be carried out. Otherwise one may not obtain any finite signal at all. In relaxation measurements, both the amplitude as well as the time range have to be taken into consideration. For binary complex formation *Brubacher*[25] has proposed a plot of reduced amplitudes *versus* reduced time constants, under particular constraints concerning c_A^0 and c_B^0, in order to find out the optimal conditions. The representation by trigonometric functions, chosen in this article, serves the same purpose. The various plots shown in previous sections are in this respect self-explanatory. They also show where the method of continuous variation, in which the sum of overall sample and standard concentrations is kept constant, is to be preferred. The interrelations between several functions (T_a, Γ_a, τ_a, T_a' *etc.*) become especially simple in symmetrical cases and suggest applications hitherto unexplored, such as Γ *versus* τ plots (Fig. 5) in which the parameters to be determined can be directly read off from the slopes and the intercepts of a family of lines. This procedure can be especially well adapted to microtitration.

There is no limitation as to the kind of problems to be studied by any of the methods discussed in this article. Dynamic amplitude titration has proven to be of great advantage in complexometric investigations, yet acid-base, electron donor-acceptor and—in particular—enzyme-substrate interactions may equally well be objects of study.

Finding the optimal approach to each problem means mastering the art of titration.

We are greatly indebted to Miss Ursula Wisniewski and Dipl.-Phys. Gerhard Kessling for writing the computer programs and providing graphical representations of the calculated functions.

We wish to thank also Prof. Peter Schuster, Prof. Eberhard Neumann, and Dr. Heinz Winkler for providing us with yet unpublished experimental data. Dr. Paul Woolley was kind enough to revise the English manuscript.

Appendix 1. Outline of the Thermodynamic Treatment of Chemical Relaxation Phenomena[*]

The concentration variable is represented by the extent of reaction ξ, which correlates the stoichiometric changes of reactants and reaction products: $d\xi = dn_i/\nu_i$. n_i is the mole number and ν_i the stoichiometric coefficient of compound i (being positive for reaction products and negative for reactants). If related to a reference value of n_i, ξ is identical for all participants of a given reaction, *e.g.* $dn_{AB} = -dn_A = -dn_B$. Complementenary to ξ is the affinity A, defined by

$$A = -(\partial G/\partial \xi)_z$$

where G denotes Gibbs' free energy. Referring to general intensive variables z (T, P *etc.*) the total equilibrium shift can be expressed as

$$\delta\xi = \left(\frac{\partial \xi}{\partial z}\right)_A \delta z = -\frac{(\partial A/\partial z)_\xi}{(\partial A/\partial \xi)_z}\,\delta z$$

Maintenance of equilibrium during the variation of ξ with respect to z is indicated by the subscript A, which in particular means $A = \text{const.} = 0$. The term $\partial A/\partial z)$ corresponds to the Δ-term, *e.g.* for $z = T$: $\Delta H/T$ or for $z = P$: $-\Delta V$. The reciprocal of $-(\partial A/\partial \xi)_z$ yields the amplitude factor Γ_z divided by RT. This factor—appearing also in the relaxation time τ—is dependent on the variables z kept constant during the variation of ξ, *e.g.* $\Gamma_{T,P}$ and $\tau_{T,P}$ if the process refers to sufficiently slow equilibration under atmospheric pressure and thermostatic control. For solutions, however, we may well omit these subscripts since the factors discriminating differing external conditions—Γ_{SV}, Γ_{TP} *etc.*—are negligibly small. In ionic solutions which are highly diluted or where the ionic strength is kept constant, activity coefficients do not have to be taken into account explicitly. Then Γ simply reduces to the form

$$\Gamma^* = \frac{1}{\sum_i \frac{\nu_i^2}{c_i}}$$

which is valid for any kind of reaction order. The sum has to include all reactants and products involved in the equilibration process. It is positive since ν_i enters as a square term. If activity coefficients contribute measurably to the change of affinity A with respect to the extent of reaction ξ, Γ is to be replaced by

$$\Gamma = \frac{\Gamma^*}{1 + \Gamma^*(\partial \Sigma \nu_i \ln f_i/\partial \xi)_z}$$

Γ^* being identical with the expression quoted above.

Relaxation time τ and amplitude factor Γ are correlated *via* the exchange velocity v, which for a general reaction process

$$\nu_1 A_1 + \nu_2 A_2 \ldots \nu_k A_k \underset{\overleftarrow{k}}{\overrightarrow{k}} \nu_{k+1} A_{k+1} + \cdots \nu_n A_n$$

reads

$$v = \overrightarrow{k} \prod_{i=1}^{k} c_{A_i}^{\nu_i} = \overleftarrow{k} \prod_{i=k+1}^{n} c_{A_i}^{\nu_i}$$

For a non-diffusion-controlled process k contains the essential part of the equilibrial activity coefficients $\prod f_i^{\nu_i}$.

τ, Γ and v are related to each other by

$$\tau = \Gamma/v$$

As was pointed out by *Katchalsky* [26], there is a formal similarity between electrical and chemical networks. The linearized rate equation—as a relation between a chemical flux (turnover rate) and force (affinity)— defines the chemical analogue of a resistance R_{Chem}, and the dependence of a temporal derivative of the force on the flux allows the introduction of a "chemical capacitance" C_{Chem}. The comparison yields

$$R_{Chem} C_{Chem} = \tau$$

$$R_{Chem} = \frac{RT}{v}$$

$$C_{Chem} = \frac{\Gamma}{RT}$$

Both "resistance" and "capacitance" in a chemical "circuit" have a quite obvious physical meaning [27].

Appendix 2. Generalization for Multiple Ligand Competition

a) Ligands L_1, $L_2 \ldots$ + complexing partners M

Given a number of ligands 1, 2, ..., n, which can competitively interact with a common complexing partner (or binding site) in forming such a 1 : 1 complex.

[*] Cf. also [5] and [16].

The common complexing partner may be denoted by M (usually being some metal ion) and the ligands by $L_1 \ldots L_n$: The mass action relations are written as:

$$\begin{aligned} M + L_1 &\rightleftharpoons ML_1 \quad K_1 = \frac{c_{M_1}}{c_M \cdot c_1} \\ M + L_2 &\rightleftharpoons ML_2 \quad K_2 = \frac{c_{M_2}}{c_M \cdot c_2} \\ &\vdots \\ M + L_n &\rightleftharpoons ML_n \quad K_n = \frac{c_{M_n}}{c_M \cdot c_n} \end{aligned} \tag{1}$$

where the concentrations c_i or c_{M_i} refer to the corresponding ligand L_i or metal complex ML_i, respectively. The conservation conditions for any perturbation are:

$$\delta c_i = -\delta c_{M_i} \tag{2}$$

for $i = 1,2,\ldots n$

and $$\delta c_M = -\sum_{k=1}^{n} \delta c_{M_k} \tag{3}$$

Expansion of any of the mass action relations yields:

$$\delta c_{M_i} = \Gamma_i \delta \ln K_i - \gamma_i \sum_{k \neq i} \delta c_{M_k} \tag{4}$$

with the usual definitions:

$$\Gamma_i = \frac{1}{\frac{1}{c_M} + \frac{1}{c_i} + \frac{1}{c_{M_i}}} = \frac{c_i c_M}{c_M + c_i + K_i^{-1}} \tag{5}$$

and

$$\gamma_i \equiv \frac{\Gamma_i}{c_M} = \frac{c_i}{c_M + c_i + K_i^{-1}} \tag{6}$$

The sum $\sum_{k \neq i}$ is taken over all partners k = 1 to n except for k = i. An explicit expression for $\sum_{k \neq i} \delta c_{M_k}$ can be derived by iteration. According to eq. (4) one may write:

$$\begin{aligned} \delta c_{M_1} &= \Gamma_1 \delta \ln K_1 - \gamma_1 \delta c_{M_2} - \gamma_1 \sum_{k \neq 1,2} \delta c_{M_k} \\ \delta c_{M_2} &= \Gamma_2 \delta \ln K_2 - \gamma_2 \delta c_{M_1} - \gamma_2 \sum_{k \neq 1,2} \delta c_{M_k} \end{aligned} \tag{7}$$

Combination results in:

$$\delta c_{M_1} + \delta c_{M_2} = \bar{\Gamma}_{12} \delta \ln \bar{K}_{12} - \bar{\gamma}_{12} \sum_{k \neq 1,2} \delta c_{M_k} \tag{8}$$

with

$$\bar{\Gamma}_{12} \delta \ln \bar{K}_{12} \equiv \frac{\Gamma_1(1-\gamma_2)\delta \ln K_1 + \Gamma_2(1-\gamma_1)\delta \ln K_2}{1 - \gamma_1 \gamma_2} \tag{9}$$

and

$$\frac{\bar{\Gamma}_n}{c_M} \equiv \bar{\gamma}_{12} \equiv \frac{\gamma_1(1-\gamma_2) + \gamma_2(1-\gamma_1)}{1 - \gamma_1 \gamma_2} \tag{10}$$

The sum $\sum_{k \neq 1,2}$ now contains all terms δc_{M_k} for k from 3 to n (*i.e.* all, except k = 1 and k = 2). A corresponding expression would hold for any two partners i and j. The same procedure can be iterated for inclusion of any further partner suggesting a general expression:

$$\sum_{k=1}^{m} \delta c_{M_k} = \bar{\Gamma}_{1\ldots m} \delta \ln \bar{K}_{1\ldots m} - \bar{\gamma}_{1\ldots m} \sum_{k=m+1}^{n} \delta c_{M_k} \tag{11}$$

with

$$\bar{\Gamma}_{1\ldots m} \delta \ln \bar{K}_{1\ldots m} = \frac{\bar{\Gamma}_{1\ldots m-1}(1-\gamma_m)\delta \ln \bar{K}_{1\ldots m-1} + \Gamma_m(1-\bar{\gamma}_{1\ldots m-1})\delta \ln \bar{K}_{1\ldots m-1}}{1 - \bar{\gamma}_{1\ldots m-1}\gamma_m} \tag{12}$$

and

$$\frac{\bar{\Gamma}_{1\ldots m}}{c_M} \bar{\gamma}_{1\ldots m} = \frac{\bar{\gamma}_{1\ldots m-1}(1-\gamma_m) + \gamma_m(1-\bar{\gamma}_{1\ldots m-1})}{1 - \bar{\gamma}_{1\ldots m-1}\gamma_m} \tag{13}$$

The validity of this form can be shown by complete induction, which in this case is a simple extension of the procedure applied above for k = 1 and 2. Starting from eq. (11) with a split sum term:

$$\sum_{k=1}^{m} \delta c_{M_k} = \bar{\Gamma}_{1\ldots m} \delta \ln \bar{K}_{1\ldots m} - \bar{\gamma}_{1\ldots m} \delta c_{M_{m+1}} - \bar{\gamma}_{1\ldots m} \sum_{k=m+2}^{n} \delta c_{M_k} \tag{14}$$

and adding eq. (4), written as:

$$\delta c_{M_{m+1}} = \Gamma_{m+1} \delta \ln K_{m+1} - \gamma_{m+1} \sum_{k=1}^{m} \delta c_{M_k} - \gamma_{m+1} \sum_{k=m+2}^{n} \delta c_{M_k} \tag{15}$$

leads to the general form of eq. (11) for m + 1.

Finally one has to derive an explicit form for eq. (4), valid for any complexing agent. Substituting the sum term in eq. (4) according to eq. (11), by:

$$\sum_{k \neq i} \delta c_{M_k} = \bar{\Gamma}_{k \neq i} \delta \ln \bar{K}_{k \neq i} - \bar{\gamma}_{k \neq i} \delta c_{M_i} \tag{16}$$

where the index $k \neq i$ means (n − 1)-fold iteration from k = 1 to n, except for k = i (*e.g.* i = n, iteration 1 to n − 1. Note that the way of numbering is arbitrary).

The explicit form of eq. (4) then reads:

$$\delta c_{M_i} = \frac{\Gamma_i}{1 - \bar{\gamma}_{k \neq i}\gamma_i} (\delta \ln K_i - \bar{\gamma}_{k \neq i} \delta \ln \bar{K}_{k \neq i}) \tag{17}$$

in which the ternary system treated in the text reflects only a special example, where the combination term with the index $k \neq i$ involves the contributions of the buffer and the sample, while i represents the indicator.

Explicit expressions for c_i can be obtained if we combine the respective mass action and conservation relation for each ligand.

$$c_i + c_{M_i} = c_i^0 \tag{18}$$

$$\frac{c_{M_i}}{c_i} = K_i c_M \quad \frac{c_i^0 - c_i}{c_i} = K_i c_M \tag{19}$$

$$c_i = \frac{c_i^0}{1 + K_i c_M} \tag{20}$$

$$c_{M_i} = c_i^0 \frac{K_i c_M}{1 + K_i c_M} \tag{21}$$

If c_M can be determined uniquely (*e.g. via* an extinction ratio) a complete representation in weighed-in concentrations, and measurable parameters is possible.

Three possible ways of evaluation result:

1) All but one K_i values are known (natural system)

2) Successive addition of ligand 1...n (practical for not higher than ternary systems)

3a) Time constants differ sufficiently so that successively all steps can be determined (dynamic analysis)

3b) Binding constants differ markedly so that by addition of M one may scan through all binding ranges (often identical with 3a).

b) Ligand L + macromolecule P with several binding sites

The same general concept can be applied to the case of general ligand binding by a macromolecular reactant P, usually being a protein. The titration procedure was discussed by *Edsall* and *Wyman*[4]. The common ligand L is bound at different sites, 1,2...n, each characterized by a specific affinity, expressed in terms of binding constants, $K_1 \ldots K_n$:

$$K_1 = \frac{c_{PL_1}}{c_L \cdot c_{P_1}}; \quad \ldots \quad K_n = \frac{c_{PL_n}}{c_L \cdot c_{P_n}} \tag{22}$$

As is seen, the common ligand L now plays the same role as the metal ion M in the first example, whereas the various binding sites 1...n at P resemble the former ligands. The mass action and conservation relations hence are of completely analogous form. In Ref. [4] an equation for the degree of binding, was given

$$\bar{\nu} = \frac{\sum_{k=1}^{n} c_{PL_k}}{\sum_{k=1}^{n} c_{PL_k} + \sum_{k=1}^{n} c_{P_k}} \tag{23}$$

which in our (slightly differing) terminology reads:

$$\bar{\nu} = \frac{\sum_{k=1}^{n} \frac{K_k c_L}{1 + K_k c_L}}{n} = \frac{\bar{K}_{1\ldots n} c_L}{1 + \bar{K}_{1\ldots n} c_L} \tag{24}$$

n may or may not include groups of m-fold degeneracy, *i.e.* m-sites having identical binding constants. $\bar{K}_{1-n}$ is defined as above:

$$\bar{K}_{1\ldots n} = \frac{\sum_{k=1}^{n} c_{PL_k}}{c_L \sum_{k=1}^{n} c_{P_k}} \tag{25}$$

and related to individual binding constants by the iteration formula:

$$\bar{K}_{1\ldots i+1} = \frac{\sum_{k=1}^{i} c_{P_k}}{\sum_{k=1}^{i+1} c_{P_k}} \bar{K}_{1\ldots i} + \frac{c_{P_{i+1}}}{\sum_{k=1}^{i+1} c_{P_k}} K_{i+1} \tag{26}$$

The general amplitude relationship, derived in the first part of this appendix holds analogously for the perturbation of $\bar{\nu}$:

$$\delta\nu = \frac{\bar{\Gamma} \ln \bar{K}_{1\ldots n}}{\sum_{k=1}^{n} c_{PL_k} + \sum_{k=1}^{n} c_{P_k}} \tag{27}$$

As *Edsall* and *Wyman* point out, these equations include "endless possible sets of n's and K's, and it would be hopeless to attempt any general discussion of all these possibilities". It should be emphasized, however, that especially in such cases of multiple binding processes, the relaxation amplitude techniques offer new possibilities of obtaining individual, rather than only overall or average binding parameters. Several examples are given in the text, and a more detailed analysis applying to allosteric proteins will be given in a forthcoming paper [23].

Appendix 3. Secondary Indication

a) Indication by Complex Formation

The general correlation between extinction ratios, overall concentrations and equilibrium parameters is

$$\left\{\frac{c_A^0}{K_B^{-1} + K_I^{-1}\frac{\eta}{1-\eta} - c_P^0/U}\right\} + \{u\} = -\frac{K_B}{K_A} \tag{1}$$

with

$$u = K_I \frac{1-\eta}{\eta}(c_B^0 - \eta c_I^0) - 1 \tag{2}$$

or explicitly:

$$\left\{c_A^0 - c_P^0 + \left(c_B^0 - \eta c_I^0 - K_I^{-1}\frac{\eta}{1-\eta}\right)\left(1 + K_B^{-1} K_I \frac{1-\eta}{\eta}\right)\right\}$$
$$= -\frac{K_B}{K_A}\left\{K_I^{-1}\frac{\eta}{1-\eta} - \frac{c_P^0}{K_I \frac{1-\eta}{\eta}(c_B^0 - \eta c_I^0) - 1}\right\} - K_A^{-1} \tag{3}$$

which reduces for $K_B^{-1} \ll K_I^{-1}$, K_A^{-1} to

$$\left\{c_A^0 + c_B^0 - c_P^0 - \eta c_I^0 - K_I^{-1}\frac{\eta}{1-\eta}\right\} + K_I^{-1} =$$
$$= -\frac{K_B}{K_A}\left\{K_I^{-1}\frac{\eta}{1-\eta} - \frac{c_P^0}{K_I \frac{1-\eta}{\eta}(c_B^0 - \eta c_I^0) - 1}\right\} \tag{4}$$

or for K_A^{-1}, $K_B^{-1} \ll K_I^{-1}$

$$\left\{K_I \frac{1-\eta}{\eta}(c_B^0 - \eta c_I^0 + c_A^0 - c_P^0)\right\} = \frac{K_B}{K_A}\left\{\frac{c_P^0}{c_B^0 - \eta c_I^0 - K_I^{-1}\frac{\eta}{1-\eta}}\right\} + 1 - \frac{K_B}{K_A} \tag{5}$$

The brackets in each equation denote which combinations of terms have to be plotted against each other. Further simplifications are obtained for $c_B^0 = c_P^0$ and for $c_I^0 \ll c_A^0$, c_B^0, or $c_B^0 K_I \gg 1$.

Overall amplitude:

$$(\delta c_{BI})_{tot.} = \frac{\Gamma_I}{1 - \gamma_I\gamma_B - \gamma_A\gamma_B'}\left[(1 - \gamma_A\gamma_B')\delta \ln K_I - \gamma_B \delta \ln K_B + \gamma_A\gamma_B \delta \ln K_A\right] \tag{6}$$

with

$$\gamma_I \equiv \frac{\Gamma_I}{c_B} = \frac{c_I}{c_I + c_B + K^{-1}}; \quad \gamma_B \equiv \frac{\Gamma_B}{c_B} = \frac{c_P}{c_P + c_B + K_B^{-1}}$$
$$\gamma_B' \equiv \frac{\Gamma_B}{c_P} = \frac{c_B}{c_P + c_B + K_B^{-1}}; \quad \gamma_A \equiv \frac{\Gamma_A}{c_P} = \frac{c_A}{c_P + c_A + K_A^{-1}} \tag{7}$$

The implicit terms can be expressed by overall-concentrations and extinction ratios according to:

$$c_{BI} = \eta c_I^0; \quad c_I = (1-\eta)c_I^0; \quad c_B = K_I^{-1}\frac{\eta}{1-\eta}; \tag{8}$$

$$c_P = K_B^{-1} u; \quad u \text{ according to eq. (2)} \tag{9}$$

$$c_A = c_A^0 - c_P^0 + u\left\{K_B^{-1} + K_I^{-1}\frac{\eta}{1-\eta}\right\} \tag{10}$$

Amplitude differences can be determined, as was pointed out in Section 4. Under identical conditions with respect to c_I^0, c_P and c_B the amplitudes are measured in presence and absence of the A-system.

If the equilibration of the A-system is the slowest step, *i.e.* if reactant and competitor B equilibrate sufficiently fast, the lowest time constant τ_{III} provides information about K_A. In systems

$$A + P \underset{k_{43}}{\overset{k_{34}}{\rightleftharpoons}} AP$$

this (reciprocal) time constant reads:

$$\tau_{III}^{-1} = k_{34}\{c_A + c_P + K_A^{-1}\} f_{ABI} \tag{11}$$

with

$$f_{ABI} = \frac{1 - \gamma_I\gamma_B - \gamma_A\gamma_B'}{1 - \gamma_I\gamma_B} \to 0 \quad \text{for} \quad K_B c_B \to 0 \tag{12}$$

This time constant is associated with a relaxation amplitude

$$(\delta c_{BI})_{III} = \Gamma_A \frac{\gamma_I\gamma_B}{1 - \gamma_I\gamma_B - \gamma_A\gamma_B'}\left\{\delta \ln K_A - \frac{\gamma_B'}{1 - \gamma_I\gamma_B}(\delta \ln K_B - \gamma_I \delta \ln K_I)\right\} \tag{13}$$

b) Indication *via* exchange reactions

The same sample and competitor binding equilibria as in a) are supposed. Indication, however, is effected by an exchange process

$$B + I' \rightleftharpoons B' + I \tag{14}$$

All expressions of case a) apply, if the extinction ratio $K_I^{-1}\,\eta/1-\eta$ is replaced by

$$K_I^{-1} \cdot c_I^0 \eta^2/(1-\eta)$$

using the definitions given in the text.

The amplitude factor of the indicator equilibrium is defined as

$$\Gamma_I = \frac{1}{\frac{1}{c_I} + \frac{1}{c_{B'}} + \frac{1}{c_{I'}} + \frac{1}{c_B}} = \frac{c_{B'} c_I}{c_{B'} + c_I + K_I(c_B + c_I)} \tag{15}$$

and

$$\gamma_I = \frac{\Gamma_I}{c_B} = \frac{K_I c_{I'}}{c_{B'} + c_I + K_I(c_B + c_I)} \tag{16}$$

Received: October 28, 1974 [A 154 IE]
German version: Angew. Chem. 91, 20 (1979)

The original manuscript was dedicated to *Gerold Schwarzenbach* on the occasion of his 70th birthday. Owing to various unforeseen circumstances simultaneous publication of the German and English versions has been delayed.

[1] *R. Winkler*, Doctoral Thesis, Wien—Göttingen 1969.
[2] *H. A. Benesi, J. H. Hildebrand*, J. Am. Chem. Soc. *71*, 2703 (1949).
[3] *M. Dixon, E. C. Webb:* Enzymes, 2nd Edit., Longmans, London 1965.
[4] *J. T. Edsall, J. Wyman:* Biophysical Chemistry, Vol. I. Academic Press, New York 1958.
[5] *M. Eigen, L. DeMaeyer*, Tech. Org. Chem. *VIIIb*, 895 (1963); see also *G. G. Hammes* in: Techniques of Chemistry. Vol. VI/2. Wiley, New York 1974, p. 63.
[6] *P. Job*, Ann. Chim. Paris *9*, 113 (1928).
[7] *F. J. C. Rossotti, H. Rossotti:* The Determination of Stability Constants, McGraw-Hill, New York 1961.
[8] *M. Eigen, G. Kurtze, K. Tamm*, Z. Elektrochem. Ber. Bunsenges. Phys. Chem. *57*, 103 (1953).
[9] *M. Eigen, K. Tamm*, Z. Electrochem. Ber. Bunsenges. Phys. Chem. *66*, 107 (1962).
[10] *G. Czerlinski*, Theor. Exp. Biophys. *2*, 69 (1969).
[11] *D. Thusius* in *C. Sadron:* Dynamic Aspect of Conformational Changes in Biological Macromolecules. Reidel, Dordrecht 1973, p. 271.
[12] *T. M. Jovin* in *R. Chen, H. Edelhoch:* Biochemical Fluorescence: Concepts, Dekker, New York 1975, p. 305.
[13] *G. Beier, S. Basu, P. Schuster*, to be published; cf. also *G. Beier*, Doctoral Thesis, Vienna 1975.
[14] *H. W. Chang, E. Neumann*, Proc. Nat. Acad. Sci. U.S. *73*, 3364 (1976).
[15] a) *W. Burgermeister, Th. Wieland, R. Winkler*, Eur. J. Biochem. *44*, 305 (1974); b) *P. B. Chock, F. Eggers, M. Eigen, R. Winkler*, Biophys. Chem. *6*, 239 (1977).
[16] *J. Meixner*, Kolloid-Z. *134*, 3 (1953).
[17] *G. Schwarzenbach, H. Flaschka:* Die komplexometrische Titration. 5th Edit., Enke Verlag, Stuttgart (1965).
[18] *J. Bjerrum*, Chem. Rev. *50*, 381 (1950).
[19] *G. Scatchard*, Am. Acad. Sci. *51*, 660 (1949); cf. also Ref. [4].
[20] *H. Sund, K. Markau, R. Koberstein*, Biol. Macromol. Ser. 7: "Subunits in Biological Systems", Vol. C. Marcel Dekker, New York 1975.
[21] *J. Mond, J. Wyman, J. P. Changeux*, J. Mol. Biol. *12*, 88 (1965).
[22] *D. E. Koshland, G. Nemethy, D. Filmer*, Biochemistry *5*, 365 (1966).
[23] *M. Eigen, G. Ilgenfritz*, to be published.
[24] *H. V. Malmstadt*, Anal. Chem. *26*, 1348 (1954); *27*, 1757 (1955); *P. Delahay, ibid. 20*, 1212 (1948).
[25] *L. Brubacher*, personal communication.
[26] *G. Oster, A. Perelson, A. Katchalsky*, Q. Rev. Biophys. *6*, 1 (1973).
[27] *M. Eigen* in *F. O. Schmitt et al.:* Neurosciences, Third Study Program, The MIT Press, Cambridge, Mass. 1973, p. XIX.

Plastics as Optical Materials

By Helmut Dislich[*]

The principal material used in optics is glass. Plastics can only gain acceptance in optics if they have properties not encountered with glass or if a desired article can be produced more rationally from a plastic. An example of the first case is provided by UV light guides consisting of a quartz glass core surrounded by a plastic cladding; there is no glass with a sufficiently low refractive index. Examples of the second case are viewfinder optics for cameras and lenses for sunglasses and industrial safety spectacles.

1. Introduction

"Plastics in optics"—when considering this topic it is inadvisable to start from the annual production of 1000 tons because even the potentially interested reader is likely to feel his interest wane at the thought of such unusually low production figures. The turnover of high-value products made possible by new plastics and plastics technologies would appear to attract much more attention. In many cases the user is unconscious of the application of plastics, unless he notices it by way of the price which may be very low (example: high quality viewfinder optics) or very high (example: spectacles worn after removal of a cataract or UV fiber optics). In the former case, use of plastics is dictated by the market, in the second case by the optical and other properties of the plastics.

The most comprehensive report about the use of plastics for optical purposes appeared in 1945[1]. At that time, however, many of the plastics of interest nowadays were unknown. Widely acclaimed surveys were subsequently authored by *Schreyer*[2–4]. Optical properties are listed in Landolt-Börnstein[5, 6]. An exceptional wealth of detail is given in a review by *Torbin* and *Daminov*[7].

In the present article, the optical properties of plastics will be correlated with their chemical structure wherever possible. Rather exotic plastics hardly known outside the realm of optics sometimes prove particularly interesting. Mass produced plastics—in optics, these include poly(methyl methacrylate) or polycarbonate—are of interest with regard to the possibilities of working them. Combinations of plastics with glasses were frequently the logical consequence of studies on the optical scope of plastics.

Any consideration of optics compels us to look at glass, because glass was, and still is, the classical material of optics, and any plastics making an inroad into this field will be measured against glasses. In view of the well established position of glass, serious consideration must be given to the question of the motivation for the intense work being done on plastics for optical purposes, particularly by an author in a glass-house who, as the saying goes, may not throw stones with impunity. There are two simple answers:

1) A desired article can be produced more rationally from plastics;

[*] Dr. H. Dislich
JENAer Glaswerk Schott & Gen., Mainz
Postfach 2480, D-6500 Mainz (Germany)

2) some plastics have—urgently required—properties not shown by glasses.

2. Glasses and Plastics

In this article, glass is taken to mean a fused inorganic product, and plastic an organic high polymer, produced, for example, by polymerization, polycondensation, or polyaddition of low-molecular starting materials. We shall restrict our attention to glass-clear, preferably more recent plastics.

2.1. Comparison of Optical Properties

Essential properties always employed as initial selection criteria are the spectral transmittance, the refractive index n_d, and the Abbe number

$$\nu_d = \frac{n_d - 1}{n_F - n_C}$$

n_F, n_C = refractive indices for the F and C lines, respectively.

2.1.1. Transmittance

In the case of glasses the ranges of high transmittance extend from the ultraviolet region (silica glass) *via* the visible (many optical glasses often having very high transmittance owing to extremely high homogeneity and purity) to the infrared region (chalcogenide glasses)[8].

The transmittance ranges are somewhat more limited in the case of plastics. Apart from the good transmittance in the visible range, the UV transmittance of poly(methyl methacrylate), methylpolysiloxanes, and perfluorinated polymers deserves mention; some perfluorinated polymers, *e.g.* the copolymer of tetrafluoroethylene and hexafluoropropylene (Teflon FEP®), are also transparent to IR up to about 6 μm (Figs. 1 and 2).

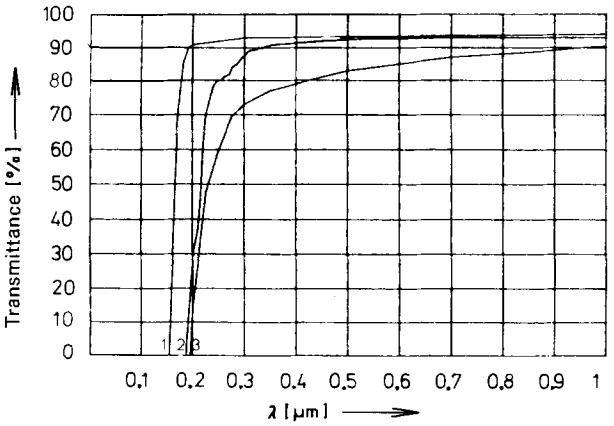


Fig. 1. Spectral transmittance of (1) silica glass (Suprasil W), 1.0 mm; (2) methylpolysiloxane (Glass Resin 650), 1.04 mm; (3) polytetrafluoroethylene-hexafluoropropylene copolymer (Teflon FEP®), 0.02 mm.

A monomethyl polysiloxane ("Glass Resin 650") produced mainly from methyltrialkoxysilane[9], can be designated as

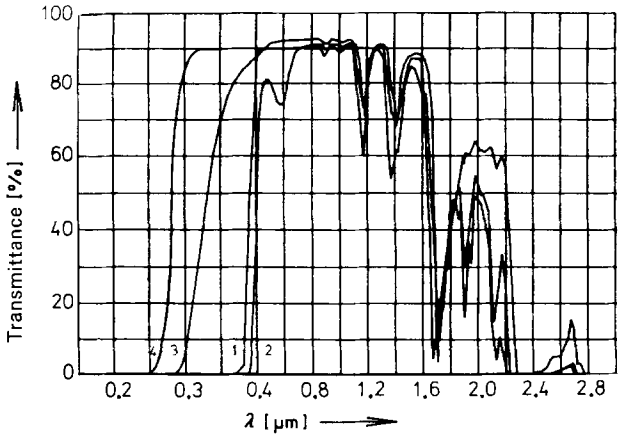
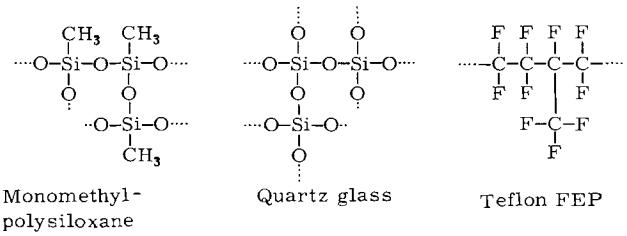


Fig. 2. Spectral transmittance of (1) poly(methyl methacrylate) (Plexiglass® 201 with UV absorber), 3 mm; (2) poly[*p*-(*p*-hydroxy-α,α-dimethylbenzyl)-phenyl hydrogen carbonate] (Makrolon, Lexan®), 3 mm; (3) poly(diethylene glycol diallyl biscarbonate) (CR39), 3 mm; (4) poly(methyl methacrylate) (pure), 3 mm.

"monomethylated quartz glass", which is suggestive of its high transmittance resembling that of quartz glass.



As a result of their high IR transmittance, fluorinated polymers can be used as embedding agents in IR spectroscopy. FEP®, which is glass-clear as thin films, owes its special position as a largely non-crystalline, and hence non-scattering, perfluorinated polymer (in contrast to polytetrafluoroethylene) to the branching arising from copolymerization, which inhibits crystallization.

The reflection losses of plastics having higher refractive indices, such as polystyrene or polycarbonate, can be reduced by coating with a layer of material having a lower refractive index such as MgF_2 and their transmittance consequently enhanced[10], as is common practice with glasses.

2.1.2. The $n_d - \nu_d$ Diagram

The "optical position" of transparent plastics and glasses[11] is normally represented in a $n_d - \nu_d$ diagram. Figure 3 shows some examples.

The plastics region overlaps with the glass region but appears more extensive at the bottom. The extremely low refractive indices of Teflon FEP® (point 19) and methylpolysiloxane (point 5) permit their use as optical coatings for silica glass fibers and rods[12, 13]; no alternative glass is foreseen.

Correlation of the "optical position" with the chemical structure of polymers leads to simple relationships with which new plastics always comply. Directed syntheses of tailormade products would be readily feasible. In practice, however, one

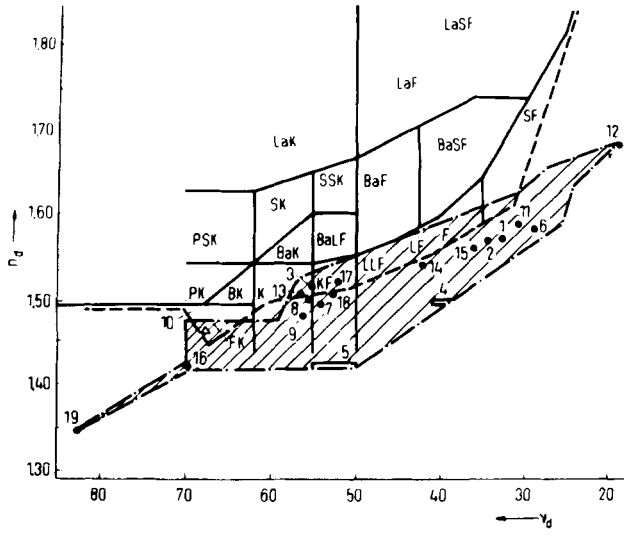


Fig. 3. Glass region and plastics region in the $n_d - \nu_d$ diagram. ---: present limit of the glass region; ·····: present limit of the region of transparent plastics. △ quartz glass, ● plastics 1—19. 1 = styrene-acrylonitrile copolymer, 2 = poly(*o*-diallyl phthalate), 3 = poly(methyl α-chloroacrylate), 4 = methylphenylpolysiloxane, 5 = methylpolysiloxane, 6 = poly[*p*-(*p*-hydroxy-α,α-dimethylbenzyl)phenyl hydrogencarbonate], 7 = poly(methyl methacrylate), 8 = poly(diethylene glycol diallyl biscarbonate), 9 = cellulose acetate, 10 = cellulose propionate, 11 = polystyrene, 12 = poly-*N*-vinylcarbazole, 13 = poly(cyclohexyl methacrylate), 14 = poly(vinyl chloride), 15 = epoxy resin (Araldite Cy 206), 16 = poly(2,2,2-trifluoroisopropyl methacrylate), 17 = methyl methacrylate-α-methylstyrene copolymer, 18 = methyl methacrylate-acrylonitrile copolymer, 19 = tetrafluoroethylene-hexafluoropropylene copolymer.

searches through known materials, applying possible corrections by copolymerization.

Highly aromatic plastics, such as polystyrene, poly(aryl carbonates), or even poly-*N*-vinylcarbazole, have high refractive indices and low Abbe numbers; fluorinated, and especially perfluorinated, plastics have low refractive indices and high Abbe numbers.

By means of the Lorentz-Lorenz equation[2, 11]

$$R_M = \frac{n^2-1}{n^2+2}\frac{M}{d}$$

R_M = molar refractivity, M = molecular weight, d = density, n = refractive index

it is possible to estimate the limits of plastics, including hypothetical polymers: as far as can be seen nowadays no polymers will become available with refractive indices much in excess of $n_d = 1.73$ or below $n_d = 1.33$. Plastics fail to reach the center of the glass region. Thus the terms of competition between optical glasses and transparent plastics are defined, as are the limitations of their combinations.

2.1.3. Effects of Thermal and Mechanical Properties of Plastics on Optical Properties

The lower specific gravity of plastics (≈1.0 to 1.5) often gives them an advantage over glasses (≈2.2 to >3). The coefficient of linear thermal expansion of plastics is roughly ten times greater than for glasses; this is a disadvantage since the optical properties become strongly temperature dependent. The refractive index of a plastic decreases with increasing temperature[14]. The drawback of being less hard or less resistant to wear is less serious because it can be at least partly overcome by mechanical protection or coating.

The greater impact resistance of plastics can be of advantage since the danger of fracture is reduced. Their low thermal conductivity can lead to deformation on fast changes in temperature.

The effects of these properties are accurately known[4]; it may therefore be predicted whether the required tolerances can be met for any given application.

The main plastics used are polymers and copolymers of methyl methacrylate, styrene, diethylene glycol diallyl biscarbonate, and acrylonitrile, as well as polycarbonate, cellulose acetate, and cellulose acetobutyrate. Polymethylpentene TPX should also be mentioned in passing. Let us turn our attention specifically to poly(methyl methacrylate) (PMMA) and polystyrene among this relatively sparse selection. Their optical positions (see Fig. 3) are sufficiently different to lead to achromatism in an optical system. PMMA then corresponds to the crown glasses and polystyrene to the flint glasses.

2.2. Comparison of Production Techniques

2.2.1. Glasses

According to the ASTM definition, glass is "an amorphous inorganic usually transparent or translucent substance formed by cooling and solidifying a molten mass without crystallization", and has been prepared in this way for some 4000 years. The ingredients of glass, frequently oxides, are mixed and heated until they melt (usually above 1000°C), reactions between the components leading to formation of the glass melt. On cooling, the melt solidifies to a glass without crystallizing. This cooling can be carried out in a mold. The optical component (lens, prism, disk, *etc.*) is then fashioned from the casting by grinding and polishing.

2.2.2. Plastics

The starting materials are monomers which are transformed into polymers by polymerization, polycondensation, or polyaddition. These reactions take place at relatively low temperatures. It is of considerable importance that conversion into the polymeric state can occur in the mold (casting process) and so immediately lead to the finished component. As an example we can consider the polymerization of diethylene glycol diallyl biscarbonate to give spectacle lenses as described in Section 3.1.2. This "one-step process" is by no means highly rationalized because polymerization must be performed slowly and under careful control in order to ensure formation of a homogeneous optical component of reproducible geometry. The mold, which is usually rather complicated, is blocked during this time.

The relatively short treatment given to plastic optical components produced by injection molding or similar processes should not disguise the fact that this is actually the largest market. Several reports have already been published on this topic. Combined Optical Industries Ltd. in England were pioneers in this field.

Whenever possible the polymer is converted into granules and shaping is by standard injection molding processes. Thus

lenses and prisms for the viewfinder optics of a camera are molded from poly(methyl methacrylate), as are reflectors, Fresnel lenses, and many other similar objects. Without doubt this is still the most rational method for the production of large numbers of objects.

Injection molding of lenses requires a high, but nowadays attainable, degree of precision; the accuracy obtainable with ground and polished glass lenses is greater. The material used for the injection mold and the quality of its surface play an important role along with other parameters. A recent development is the use of glass molds[17].

Injection pressing, stamping, and extrusion are included in this section as broadly similar processes starting from a polymeric material. For example, pressing and stamping techniques are used to manufacture thick-walled lenses of large diameter, reflector optics, traffic signals, mirrors, and aspherical optics.

Apart from injection molding, machining of plastic blocks is used for the production of large Fresnel lenses which can hardly be manufactured from glass.

Adhesive layers of epoxy resins, consisting of resin and curing agent (amine or anhydride), are often used to join two halves of a component. Alkylpolysiloxanes are used mainly as layers on substrates. The starting material is often methyltrialkoxysilane, which is hydrolyzed by atmospheric moisture, according to

$$CH_3Si(OR)_3 + 3\,H_2O \rightarrow CH_3Si(OH)_3 + 3\,ROH$$

With increasing temperature, methylsiloxanes are formed by polycondensation.

The method of choice for manufacturing a given product depends upon the technical possibilities and requirements, and also on the manufacturing runs involved[15].

2.2.3. Synthesis of Glasses by Polycondensation

While the production techniques for glasses and plastics do show a certain resemblance (thermoplastic processing), this does not appear to apply to the synthesis of glasses and of plastics. It therefore appeared most challenging to synthesize a glass by one of the principles used in the synthesis of plastics, *i.e.* by polycondensation.

An analogy was seen in the synthesis of a silica glass[18] according to

$$Si(OR)_4 + 4\,H_2O \rightarrow [Si(OH)_4] + 4\,ROH$$

$$[Si(OH)_4] \xrightarrow{-2\,H_2O} SiO_2$$

which proceeds *via* polyorgano(hydroxy)siloxanes.

In fact, numerous oxide glasses—and also crystals—containing many elements from various positions in the periodic table can be synthesized without having to go through the molten phase if the highly reactive and invariably hydrolyzable alkoxides of several elements are allowed to react with one another in alcohol. Hydrolysis and polycondensation ultimately lead to the pure multicomponent oxide, *i.e.* a glass[19]. This reaction is illustrated for the known glass Duran 50 in Figure 4[20].

$$m\,Si(OR)_4 + n\,B(OH)_3 + p\,Al(OR)_3 + q\,NaOR + r\,KOR \rightarrow$$

$$[(Si_mB_nAl_pNa_qK_r)(OR)_{4m+3p+q+r}(OH)_{3n}] \xrightarrow{H_2O}$$

$$[(Si_mB_nAl_pNa_qK_r)(OH)_{4m+3p+q+r+3n}] \xrightarrow{\Delta,\ -H_2O}$$

$$[Si_mB_nAl_pNa_qK_rO_{(4m+3p+q+r+3n)/2}]$$

Fig. 4. Synthesis of a borosilicate glass Duran 50 by polycondensation (schematic).

This approach can be exploited for the production of thin oxide layers by a dipping process[21].

3. Plastics for Optical Applications

Glass still reigns supreme in the field of optics, and will continue to do so. Nevertheless, there are narrow yet interesting areas which plastics have already conquered and will conquer in the future. Information supplementing that in [1–7] will be found in[22–24]. In the following, examples will be given in which plastics are chosen because of their optical properties such as transmittance or refractive index, because of more rational production methods, or even because of their non-optical properties such as specific gravity, impact resistance, ease of coloring.

Once again the reader is reminded that poly(methyl methacrylate) plays a dominant role among plastics, and has even been described as "organic glass". However, all this is so well known (see, *e.g.* [25]) that it will only be mentioned in passing.

3.1. Spectacle Lenses

3.1.1. Thermoplastics

Most people have had close contact with lenses made of plastics such as poly(methyl methacrylate), cellulose acetate, or polycarbonate in sunglasses and safety spectacles. Rational production and impact resistance are of advantage. A disadvantage of thermoplastics is their sensitivity to scratching and wiping. Attempts have been made in the last five years to reduce the sensitivity to wiping by aftertreatment. One approach employed vacuum condensation with inorganic materials[26]—often glass—and another involved dip coating, preferentially with methylpolysiloxanes. Many of these developments were apparently promoted by the Glass Resin 650 of Owens Illinois[9], and led to specific formulations by various companies (Degussa, Toray, Daicel, Resart, Röhm, *etc.*).

Du Pont's Abcite® layers employ a copolymer of partly hydrolyzed vinyl acetate and tetrafluoroethylene which is crosslinked with a silicic ester. Curing is performed thermally or with hard radiation[27]. The search for new markets for large transparent plastic sheets as a substitute for glass, *e.g.* in buses as is promoted by present legislation in the USA, has had a stimulating effect on this very active field.

The prospects[28] of producing integral spectacles—frame and lenses injection-molded as a single unit—are very interesting, in order to meet the needs of those countries where normal medical care will remain impossible for years to come owing to the lack of any infrastructure. A lens which roughly satisfies requirements is said to be far better than no aid at all.

3.1.2. Duroplastics

The properties of poly(diethylene glycol diallyl biscarbonate) are ideal for spectacle lenses—whether correcting or non-correcting. Apart from its very good optical quality, it has the best wiping properties of all the transparent plastics produced as bulk solids. Its optical data (see 8 in Fig. 3) lie in the glass region and thus permit true competition between glass and plastic. The refractive index $n_d = 1.499$ can be modified as desired by copolymerization. The specific weight of 1.32 is roughly half that of glasses, which is of great advantage in lenses of high focal power; it shatters far less readily than the usual glasses.

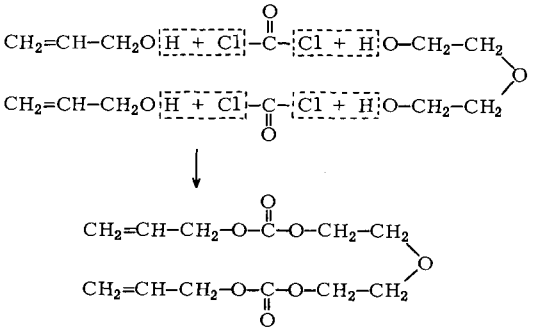
The material developed by Pittsburgh Plate Glass[29] in the 1940's (CR 39, from "Columbia Resin 39") has long been accepted on the market and certainly promoted by legislation in the USA. On the other hand, the spectacle glass industry has taken up the challenge and marketed silicate glasses hardened by ion exchange which comply with legal requirements, as defined in a ball-impact test.

Of greater significance is the negative cosmetic effect in the case of plastics. Lenses produced from the lower refractive index material CR39 must have a greater curvature then those made of more refractive glass. Highly refractive but lighter glass, which has recently become available by replacement of the heavy element lead by titanium[30], will probably lower the market potential of CR39 in some areas[31].

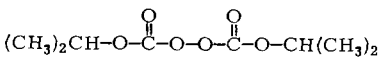
Moreover, trends in fashion play a role in the spectacle market. Thus allyl carbonate (there are many trade names corresponding to the multitude of manufacturers) is coming to the fore because of numerous possibilities of bulk and surface coloring by diffusion processes. A diffusion technique is also used to produce a continuously changing transmission from the bottom to the top of the lens (graded spectacles). Glass is an excellent substance for making photochromic lenses whose transmission adjusts to the brightness of incident light.

Despite all improvements to CR39 (*e.g.* condensed SiO_2 coating), glass remains far more resistant to scratching, and lower weight becomes significant only with very thick spectacle lenses. Wearers of plastic spectacles must still forego the comfort of photochromism. Photochromic plastics remain reversible for only very limited periods.

CR39 monomer is synthesized from allyl alcohol, phosgene, and diethylene glycol and subjected to crosslinking polymerization at the two allyl groups with the aid of a dialkyl peroxydicarbonate, *e.g.* diisopropyl- (IPP) or dicyclohexyl peroxydicarbonate.



C R 39-Monomer

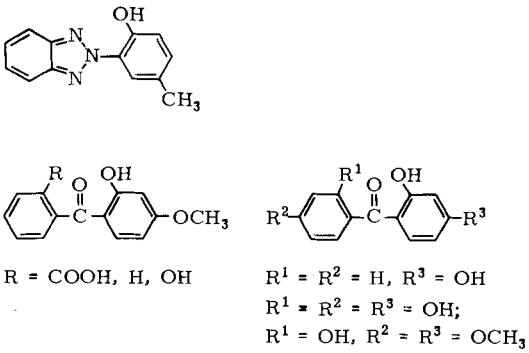


IPP

The monomer is introduced, together with 3—4 % of peroxide into a mold consisting of two glass half-molds with an optically perfect internal surface separated by an elastic spacer ring. On polymerization, induced by heating, the volume contracts by 14 %; the two half-molds to which the polymer tends to adhere—a problem in its own right—follow the contracting mass. There results a lens which requires no aftertreatment provided that it is of low focal power. In the range of medium focal power, it proves possible to impart the final curvature to only one side. The other receives its ultimate shape by grinding and polishing. At high focal powers, deviations from the shape of the mold are so large that only a rough casting can be produced by polymerization. Polyfocal lenses can also be produced by polymerization[32].

High-quality sunglass lenses are produced analogously from CR39. Polymerization may take hours. Since the mold is tied during this time, considerable costs result. For this reason, non-correcting lenses are preferably produced from large flat sheets of CR39 about 2 mm thick which are then sawn and worked similarly to glass. The disks are softened by heating and pressed or sucked into a curved mold; they retain this shape on cooling. When in use, their temperature should not be allowed to attain values leading to restoration of the original flat shape.

The UV stability of CR39 and the UV opacity of a spectacle lens can be adjusted in the finished product by several minutes' immersion in a boiling aqueous suspension of UV absorber (Fig. 5).



R = COOH, H, OH

$R^1 = R^2 = H$, $R^3 = OH$
$R^1 = R^2 = R^3 = OH$;
$R^1 = OH$, $R^2 = R^3 = OCH_3$

Fig. 5. Examples of UV absorbers based on hydroxyphenylbenzotriazole and hydroxybenzophenone.

The absorber diffuses a few μm into the surface where it is retained so strongly that it cannot be removed by water[33]. The depth of penetration is controlled by the nature of the substituent(s) at C-4 (and C-4'), and the position of the UV absorption edge by the number and position of the OH groups. This is a very apt example of "doubly tailored molecules".

The advantage of this method lies in its versatility, speed, and effective protective action (UV barrier), and also in the saving in expensive UV absorber and avoidance of a certain yellow tinge observed on bulk UV stabilization of optical material. The process can also be applied to other plastics. Choice of an inert solvent, which may not lead to swelling of the plastic, is of critical importance; water is often ideal for this purpose[34].

CR39 will probably retain its distinctive role mainly in the case of correcting glasses, variations being possible by copolymerization. Preliminary studies on epoxy resins have revealed various advantages with regard to rates of curing and coloring; a serious disadvantage is the sensitivity of the surface to wiping which is greater than that of CR39 and this has to be overcome by coating[35]. Epoxy resin lenses can be cast in plastic molds to which they do not adhere[36].

3.2. Other Products[22, 24, 37, 38]

3.2.1. Photographic Optics

The use of plastics [poly(methyl methacrylate), polycarbonate (which is increasingly replacing polystyrene), and polystyrene-acrylonitrile copolymers] in the image-forming optical system of a camera is limited to simpler cameras. The image-producing units in high-quality cameras remain a domain of glass owing to the temperature dependence of optical properties. The viewfinder optics of even expensive equipment is nowadays made almost entirely of plastic (lenses, Fresnel lenses, *etc.*). Practically the only exception is the bulky pentaprism of single lens reflex cameras. The narrow tolerances of the angles and the planarity of the surfaces are unattainable with plastics. A possible solution could lie in the use of a hollow prism.

A balanced mixture of plastic and glass is used in camera production. However, a trend toward the use of plastics cannot be denied, especially in "integral plastic optics" in which the optical components as well as mounting and centering components are produced in one piece. A classical example is the "Polaroid Land Super Swinger Camera", in which the transition to plastics is reported to have incurred cost saving of up to 95% for the optical system[16]. Viewed realistically savings of 30% can be expected. It is of considerable significance that aspherical plastic lenses are very easy to produce; just one such lens is said to replace several spherical glass lenses in many applications. (Pro's and con's are compiled in[23].)

3.2.2. Lighting Optics

Lighting optics is a field of application for plastics provided that high temperatures are not involved, such as occur in studio lighting[4].

3.2.3. Strain Optics

Transparent plastics having various strain-optical constants have proved of value[1].

3.2.4. Signal Optics

Plastics (frequently PMMA owing to the resistance to weathering often required) have cornered a considerable market and have replaced glass (*e.g.* automobile reflectors, warning signs, traffic signs). The colored disks of traffic lights can also be produced from polycarbonate by injection molding. Good flow properties of plastics permit highly rational production methods.

3.2.5. Polarization Optics

Poly(vinyl alcohol) and poly(vinyl acetate) films colored with iodine and stretched have long been in use[1]. Plane polarizers made of plastic have also been described for the infrared and ultraviolet spectral regions[39].

3.2.6. Filter Optics

Apart from colored transparent plastic disks, photographic filters are also made in sandwich form, consisting of a colored gelatin or cellulose acetate filter between glass layers, *e.g.* Kodak Wratten filters[40]. The variety of spectral transmission and the possibility of precise adjustment are considerable (for recent improvements see Section 4).

Protective welding spectacles having the required high IR absorption also belong in this Section. Again, plastics are seeking to penetrate into a domain of glass. Cast PMMA is used for protective glasses for electric welding, while injection-molded cellulose propionate is employed in those for autogeneous welding. It would appear that only American Cyanamid produces organic IR absorbers that can be used—to a limited extent—in practice. Protective glasses for welding are often coated with a transparent layer of gold to reflect strong IR radiation.

Goggles affording protection against laser light are produced from plastics by Glendale Optical Corp., USA. Dyes having extremely high extinction coefficients are incorporated into the plastics[41].

Narrow bandpass filters have been developed for the region between 2000 and 3000 Å[42]. For this purpose, organic absorbers are dissolved in partly condensed methylpolysiloxane which is then cured. This plastic was selected as "host material" owing to its high UV transmission.

3.2.7. Grating Optics

Original diffraction gratings are produced with extreme precision by scratching of glass and metal and may bear up to several thousand lines per millimeter. Plastic replicas of the valuable originals are made, *e.g.* gelatine replicas, which in turn serve as masters for the production of polyester replicas. Styrene or methyl methacrylate may also be polymerized in contact with the original gratings. The fidelity of reproduction is excellent (see also Section 4).

3.2.8. Fresnel Optics

Fresnel lenses, prisms, and mirrors are produced both by injection and by machining; these techniques are suitable for plastics. The principal material used is poly(methyl methacrylate).

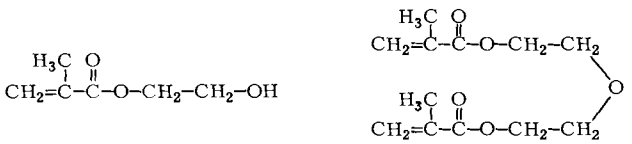
3.2.9. Optical Cements

The classical optical cement, Canada balsam, can be replaced by plastics. Presumably the epoxy resins already used for this purpose will find wider use. Examples are cemented glass filter packs. Such cements can be formulated as desired in considerable variety from numerous combinations of resin and curing agent. Their good adhesion to glass, attributable to chemical reaction of the Si—OH groups of the glass surface with the epoxy or OH groups of the resin, can be further

enhanced by admixture of specific adhesion promoters (silicon compounds having "glass-functional" and "resin-functional" groups). On cementing lenses with non-thermoplastic cements, the elegant possibility of "fine adjustment" in the warm state is renounced.

3.2.10. Contact Lenses

Apart from hard plastics used as contact lenses, particular interest attaches to the hydrogels developed by *Wichterle*[43] which permit the production of soft lenses[44]. Crosslinking copolymerization of hydroxymethyl methacrylate with, *e.g.*, diethylene glycol dimethacrylate, reduces the water solubility of the former to water swellability.



Silicone rubber with a hydrophilized surface has also recently been used as a contact lens material[45]. Its high permeability to oxygen represents a considerable advantage.

3.2.11. Laser Optics

Even though numerous laser effects of rare earth chelates in solid solution are known, *e.g.* in PMMA, as are other laser-active organic compounds (metal phthalocyanines and dyes), we have to assume that the significance of "plastic lasers" made in this way will remain limited to special scientific problems. Some 50 organic dyes provide overlapping coverage of the range between 3900 and 10000 Å, and this range of variation is where their strength lies. Plastics have proved of value as "host material" for laser dyes, *e.g.* rhodamine G in polyurethane films[46,47].

3.2.12. Aspherical Optics

While the production of aspherical glass lenses requires time-consuming working of individual components, an aspherical steel mold will provide large numbers of aspherical plastic lenses. The economic advantages of plastic lenses become particularly significant with very large lenses (680 mm diameter)[16,28].

3.3. Light Guide Optics

In light guides, a rod or fiber of transparent material with a high refractive index (n_1) is surrounded with a transparent cladding of lower refractive index (n_2). Light falling on the end surface is conducted through the guide as a result of total reflection (Fig. 6).

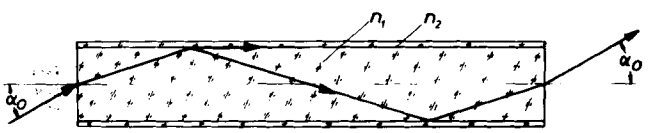


Fig. 6. Principle of light guide optics.

In order to ensure high light transmission and large aperture angle, the core material should have excellent transmittance, the likewise transparent coating should be in excellent contact with the core, and the difference between the refractive indices $n_1 - n_2$ should be as large as possible for it determines the aperture angle $2\alpha_0$, according to

$$n_0 \cdot \sin\alpha_0 = \sqrt{n_1^2 - n_2^2}$$

where n_0 is the refractive index of the surrounding medium.

Although light guide optics, and especially fiber optics, is a domain of glass, the contribution of plastics can no longer be overlooked.

The $n_d - \nu_d$ diagram (Fig. 3) shows the availability of several suitable and industrially accessible "pairs of plastics". Thus polystyrene core fibers ($n_d = 1.59$) have been cladded with poly(methyl methacrylate) ($n_d = 1.49$).

Better known are the Crofon® light guide fibers manufactured by Du Pont[48], which are produced from poly(methyl methacrylate) core fibers by extrusion and stretching. The cladding is applied continuously in a coating bath. Since the PMMA preferentially used as core material for optical reasons already has a relatively low refractive index, none of the mass-produced plastics can serve as cladding (with a necessarily lower refractive index). Use is therefore made of fluorinated esters of acrylic and methacrylic acid[49] (see Section 4.1).

Sheath and core should not absorb nor scatter light, *i.e.* should be noncrystalline or only slightly crystalline. According to *Schreyer*[4], scattering losses account for the major part of losses in plastic light guides. Absorption losses are effective mainly in the ultraviolet and the infrared spectral region. Optical contact is said to be good in Crofon®.

The development of fibers for communications has led to further optimization of plastic light guides. Meanwhile, glass-glass communications fiber optics having extremely low losses of only a few dB/km are available[50].

Plastics cannot meet these extreme requirements, at least as core material. Use of plastics as sheath material is considered in Section 4.1. Whereas Crofon® cables exhibit losses of 1100 dB/km, values of 470 dB/km have been reported for the new PFX fiber produced by Du Pont[51].

Plastic light guides are used mainly for control and illumination purposes.

Planar waveguides made of plastics have proved of interest for integral optical systems[46]. To this end, thin films are produced from solution or by plasma polymerization. Although the energies in the plasma are so high that only relatively inert structures have a chance of survival, this underinvestigated field would appear to offer numerous possibilities. Alkylpolysiloxanes and fluorinated polymers have been examined in more detail; they afford glass-clear films of low pore density.

4. Glass-Plastics Combinations for Optical Applications

4.1. Light Guide Optics

4.1.1. UV Fiber Light Guides

The fundamentals are presented in Section 3.3. Fiber optics have long been used for conducting visible light; until recently,

however, conduction of UV light was possible only by classical methods using lenses and prisms made of silica glass. UV fiber optics cannot be made from combinations of glass with glass or plastic with plastic; only glass-plastic combinations offer this possibility.

The only material transparent down to wavelengths of 200 nm that can be drawn out to fibers is silica glass having refractive indices of $n_{546} = 1.460$, $n_{365} = 1.475$, and $n_{255} = 1.506$. A glance at Figure 3 shows that there is no glass with a sufficiently low refractive index to serve as a possible cladding material, while plastics have such refractive indices. Since this cladding material should also be UV transparent and nonscattering, two readily accessible materials appear likely candidates from Figure 1, *viz.* methylpolysiloxane and Teflon FEP: in more general terms, alkylpolysiloxanes and extensively, if possible completely, fluorinated polymers insofar as they are glass-clear. The wavelength dependence of the refractive indices of Teflon FEP is shown in Figure 7[52].

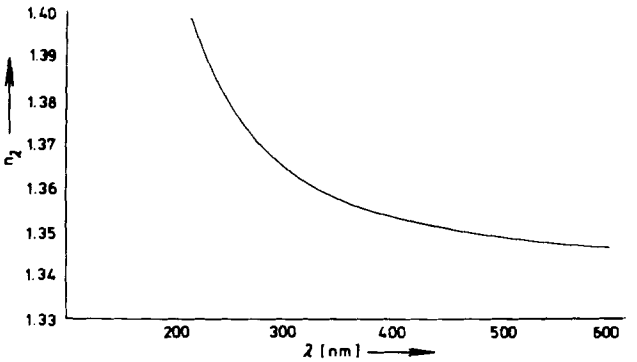


Fig. 7. Refraction by a Teflon film as a function of wavelength.

On this basis, JENAer Glaswerk Schott & Gen., Mainz, produced UV fiber optics[11-13] which provided the first means of conveniently handling UV light, and represent a new tool for use in medical technology, medicine, and numerous technical and scientific applications. The spectral transmittance is shown as an essential property in Figure 8. Further information will be found in company literature[11, 53] which also gives details concerning development.

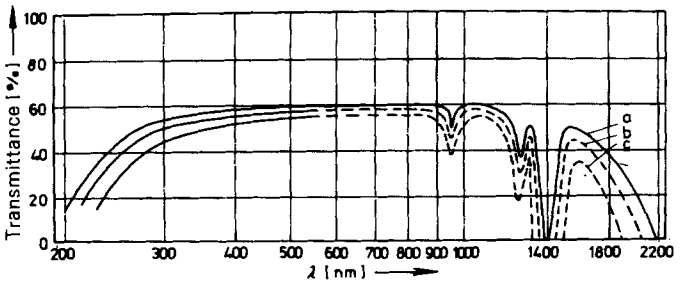


Fig. 8. Spectral transmittance of flexible UV light guides made of silica glass coated with Teflon FEP. Length of light guide: (a) 500 mm, (b) 1000 mm, (c) 1800 mm.

4.1.2. Communications Fibers

After this, to our knowledge the first, application of coatings made of transparent plastic on glass core material[12, 13], developments were reported which were aimed at producing low-loss fibers for transmission of information by the same principle[54-58]. The light to be conducted is usually 800 to 1060-nm radiation from a laser source; the excellent transparency of certain silica glasses is exploited and a low-refractive-index material is therefore required as coating; the same problem has already been solved in the case of UV fiber optics. Accordingly, the same plastics (fluoropolymers and alkylpolysiloxanes) are described as cladding for these (step index) communications fibers. Other plastics are unsuitable. Examples are shown in Figure 9.

$CF_2{=}CF_2$	Tetrafluoroethylene
$CF_2{=}CF{-}CF_3$	Hexafluoropropylene
$CH_2{=}CHF$	Vinyl fluoride
$CH_2{=}CF_2$	Vinylidene fluoride
$CF_3{-}O{-}CF{=}CF_2$	Perfluorovinyl methyl ether
$CF_2{=}CClF$	Monochlorotrifluoroethylene
$CH_2{=}C(CH_3){-}CO{-}O{-}CH(CF_3)_2$	Hexafluoroisopropyl methacrylate
$CH_2{=}C(CH_3){-}CO{-}O{-}CH(CF_3)CH_3$	Trifluoroisopropyl methacrylate

Fig. 9. Fluorinated monomers for optical cladding.

To our knowledge the resulting fibers having exceptionally low losses of a few dB/km are not in technical use. We can expect considerable investment in scientific and technical development in this "hotly contested" field in the near future. The two classes of compounds are fixed; however, variations are possible within these classes.

In conclusion, it should be mentioned that glass-plastic combinations are not essential in this field. The best prospects exist for glass-glass systems, in the form of gradient fibers. It is interesting to note that after achieving 470 dB/km with their PFX fiber[51], Du Pont has switched to the glass-plastic area and so far achieved 80 dB/km[59]. The core of these fibers consists of undoped silica glass and the cladding of an unnamed polymer. The price of this PFX-S-108-RO2 cable is presently 5 dollars per meter.

4.2. Grating Optics

The reader is referred to Section 3.2.7 for a description of the production of plastic gratings. Owing to the high thermal expansion of plastics, the line separations are dependent upon temperature. Some glass ceramics show practically no thermal expansion over a wide range of temperatures. If a drop of monomeric diethylene glycol diallyl biscarbonate is polymerized between a block of a glass ceramic and an original glass grating (Fig. 10) one obtains a plastic grating which is likewise not subject to expansion. In order to separate the original grating from the replica, the former is "siliconized", *i. e.* treated with methylchlorosilanes, prior to copying (Fig. 11). This procedure is rendered possible by the Si—OH groups of the glass. These groups are also responsible for the very firm adhesion between the plastic and the glass ceramic by copolymerization of "grafted" vinyl groups (Fig. 11)[60]. There results a plastic lattice some μm thick which is chemically bonded to the substrate.

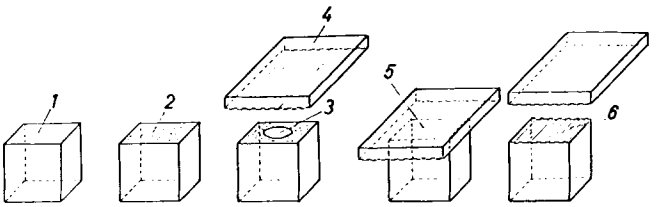


Fig. 10. Bonding of a grating of polymeric diethylene glycol diallyl biscarbonate to a glass support. 1 = glass block, 2 = vinylation of the surfaces, 3 = drop of diethylene glycol diallyl biscarbonate, 4 = original glass grating with a methylated surface, 5 = polymerization of the drop after spreading, 6 = plastic grating bonded to the glass block.

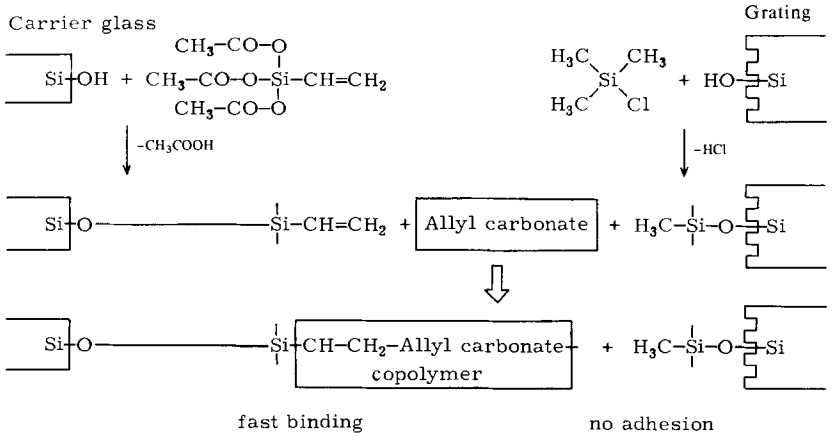


Fig. 11. Polymerization of diethylene glycol diallyl biscarbonate ("allyl carbonate") between the vinylated surface of a glass support and the methylated surface of a glass grating (schematic).

This example[61], which is not employed in practice, illustrates the chemistry of a glass-plastic composite and its potential.

4.3. Filter Optics

Optical filters for photographic or scientific purposes can be made from glass or plastic. Glass filters generally meet all the optical requirements made of them and stability requirements. Certain limitations do apply to their spectral scope, particularly if other properties are desired simultaneously, *e.g.* lack of fluorescence.

Plastics have almost unlimited spectral possibilities, but are less robust in use and prone to scratch. Moreover, plastic filters cannot be produced with the same high degree of planarity as ground and polished glass filters.

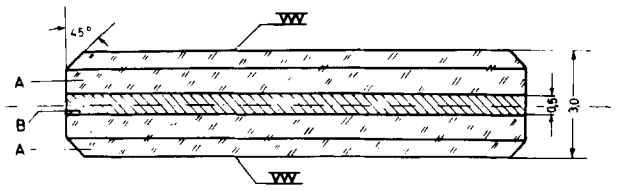


Fig. 12. Glass-plastic composite filter. A = cover glass, B = plastic composite layer, VVV high polish.

A glass-plastic composite filter as shown in Figure 12 combines the advantages of both materials. In their production, methyl methacrylate is treated with soluble dyes, silane adhesion promoters of the kind described in Section 4.2, and catalysts, and polymerized between two glass sheets separated by spacer strips. Owing to the ready oxidation of many dyes, azodiisobutyronitrile is used as initiator in place of the usual peroxides. These composites produced as large sheets are so firm, that filters can be produced with conventional glass-working machines[62]. Thus maximum planarity and scratch-resistance are ensured, as is resistance to climatic, and even tropical, conditions[63]—properties not found with plastic filters.

On the other hand, plastics offer ideal means of introducing absorbing materials which are impossible with glass. For example, a series of extremely sharp-edged UV suppression filters can be produced with extremely narrow tolerance with regard to the wavelength of the absorption edges, and having very low intrinsic fluorescence (Fig. 13)[64].

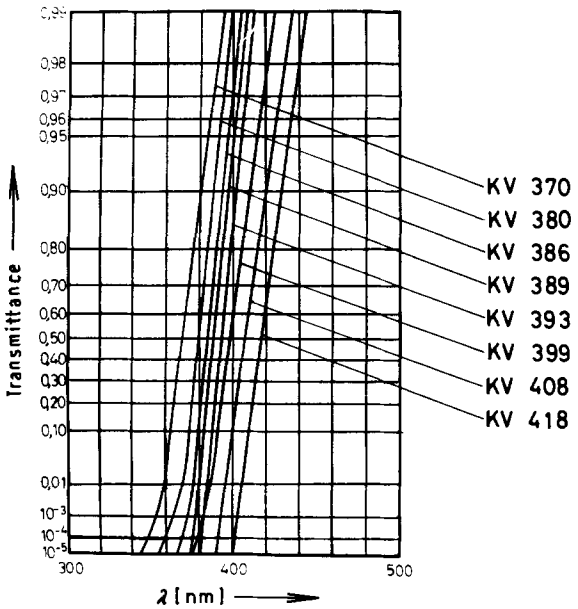


Fig. 13. UV suppression filter. KV 370 to KV 418 signify the values of internal transmission = 0.50.

Such combinations are accordingly suitable as UV suppression filters, as fluorescence suppression filters, as filters for the study of excitation conditions, and as conversion filters[65].

While plastic is protected by glass in these filters, we shall now consider cases in which inorganic material requires protection by plastic. This is the case with IR-transparent materials such as single crystals or polycrystals of alkali or alkaline earth halides. These products, which are often very expensive, are sensitive to moisture. They can be protected by coatings which, however, must also be IR-transparent.

For example, a polycrystalline lithium fluoride disk, which is transparent down to about 5—6 μm acquires excellent protection against water from a film of Teflon FEP just a few μm thick, which is applied as a dispersion, without losing its IR transparency[66]. Films applied in this way enclose LiF disks so well that they can be kept for years under water. The protective layer of Teflon FEP can be also applied by sputtering (see, *e.g.* [67]). As a rule, however, this leads to far-reaching structural changes.

4.4. Insulating Windows

It may appear surprising to find mention of windows in an article about optical materials. And yet, in these days of rising energy prices, a window no longer merely fulfills the function of mechanical protection against the whims of nature through which light falls and people can look out. Its protective function has meanwhile also become optical in nature, *e.g.* sunshielding glasses in high-rise buildings which reduce the load on air conditioning plant on sunny days or conversely prevent the escape of longwave IR radiation in winter. Reflecting coatings best serve both purposes, *e.g.* layers of TiO_2 at interference layer thicknesses or of metals such as Au, Ag, Cu[68]. Of course, this is a domain of glass. Triply-glazed windows, of which one pane may also bear a reflecting coating, have very low heat transfer coefficients (k values). The third pane, which leads to considerably greater weight and greater thickness of the overall system, can be replaced by a coated plastic film. Thus a doubly-glazed window is transformed into a triply-glazed window without any significant increase in weight; coating of the film and carefully chosen gas filling of the intermediate spaces leads to very low heat transfer and—where desired—affords protection against sunlight[69]. Table 1 shows the astonishing extent to which the k value of such a "film window" can be reduced. The k value of 0.65 kcal m^{-2} h^{-1} K^{-1} corresponds to a 0.5-m solid brick wall.

Table 1. k values of window glazing.

Kind of glazing	k [kcal m^{-2} h^{-1} K^{-1}]
Single glazing	5.0
Double glazing (12 mm air)	2.6
Triple glazing (2 × 12 mm air)	1.8
Double glazing (12 mm air) (gold)	1.55
Double glazing (12 mm krypton) (gold)	1.06
Film window (metal) (2 × 6 mm air)	1.46
Film window (metal) (2 × 12 mm air)	0.95
Film window (metal) (2 × 6 mm krypton)	0.79
Film window (metal) (2 × 8 mm krypton)	0.65

Such windows have been made on an experimental basis; however, many questions still surround their use in practice.

It was the author's intention to close a rather sober account of plastics in optics with a somewhat futuristic section, in order to show that plastics can often provide solutions for freshly occurring problems in spite of all their limitations. It is not the material itself which should be placed in the foreground, but the solution of problems. The question of the material—plastic or glass—is admittedly important, but nevertheless secondary.

While thanking many colleagues for their kind support, I would like to mention two co-workers specifically. Karl-Heinz Wiesner has promoted the entire development of plastics thanks to his dedicated engagement and understanding, and Paul Hinz has done the same for the unorthodox glass synthesis and the coating processes. The author wishes to express his particular thanks to them and their co-workers for more than ten years of cooperation.

Received: January 23, 1978 [A 254 IE]
German version: Angew. Chem. *91*, 52 (1979)

[1] Polaroid Corporation, OSRD-Report No. 4417, PB 28553 (1945).
[2] *G. Schreyer*, Kunststoffe *51*, 569 (1961).
[3] *G. Schreyer*, Umschau Wiss. Tech. *9*, 269 (1962).
[4] *G. Schreyer* in: Konstruieren mit Kunststoffen. Hanser, München 1972.
[5] *W. Geffcken* in Landolt-Börnstein: Zahlenwerte und Funktionen aus Physik, Chemie, Astronomie, Geophysik und Technik. 6th Edit. Springer, Berlin 1957, Vol. 4, Part 3, pp. 925ff.
[6] *O. Lindig* in Landolt-Börnstein: Zahlenwerte und Funktionen aus Physik, Chemie, Astronomie, Geophysik und Technik. 6th Edit. Springer, Berlin 1962, Vol. 2, Part 8, pp. 465ff.
[7] *J. D. Torbin, Yu. F. Daminov*, Sov. J. Opt. Technol. *41*, 492 (1974).
[8] *H. Schröder, N. Neuroth*, Optik *26*, 381 (1967).
[9] *A. J. Burzinski, M. R. Eliot*, DOS 1595062 (1965), Owens-Illinois.
[10] *H. Dislich*, Lecture at Macromolecular Symposium, Budapest 1969, Preprints Vol. 1.
[11] *H. Dislich, A. Jacobsen*, Angew. Chem. *85*, 468 (1973); Angew. Chem. Int. Ed. Engl. *12*, 439 (1973).
[12] *H. Dislich, A. Jacobsen*, DBP 1494872 (1965), JENAer Glaswerk Schott & Gen.
[13] *H. Dislich, A. Jacobsen*, DBP 1494874 (1966), JENAer Glaswerk Schott & Gen.
[14] *R. H. Wiley, G. M. Brauer*, J. Polym. Sci. *3*, 455 (1948).
[15] *R. F. Weeks*, Optics News *5*, (Sept. 1975).
[16] VDI-Nachr. *44*, 24 (Oct. 75).
[17] *H. Fricke*, DBP 2501991 (1975), DBP 2204830 (1972), Deutsche Spiegelglas AG.
[18] *H. Schröder*, Opt. Acta *9*, 249 (1962).
[19] *H. Dislich*, Angew. Chem. *83*, 428 (1971); Angew. Chem. Int. Ed. Engl. *10*, 363 (1971).
[20] *H. Dislich*, Glastech. Ber. *44*, 1 (1971).
[21] *H. Dislich, P. Hinz, R. Kaufmann*, DBP 1941191 (1969), JENAer Glaswerk Schott & Gen.; *H. Schroeder*, Phys. Thin Films *5*, 87 (1969).
[22] *L. D. Bronson*, Mod. Plast. *35*, 118 (1957).
[23] Pop. Photogr. *1972*, 52.
[24] *P. J. Wernicke*, Feinwerktech., Messtech. *84*, 74 (1976).
[25] *H. Lucke*, Kunstst.-Rundsch. *9*, 273 (1962); Company Literature of Combined Optical Industries Ltd., Slough, England.
[26] *H. O. Mulfinger, H. Dutz, H. G. Krolla*, DBP 1696110 (1968), JENAer Glaswerk Schott & Gen.
[27] *I. Kaetsu, A. Ito, Y. Maeda*, Plast. Ind. News Jpn. *20*, 81 (1974).
[28] *L. Wray*, Manuf. Opt. Int. *1976*, 331.
[29] *I. E. Muskat, F. Strain*, US-Pat. 2370565 (1945), Pittsburgh Plate Glass.
[30] *M. Faulstich, V. Geiler, G. Gliemeroth, L. Meckel*, US-Pat. 3898093 (1975), JENAer Glaswerk Schott & Gen.
[31] *B. Kratzer, H. Gottlob*: Schwerflint 64, ein neues Brillenrohglas. Firmenschrift Carl Zeiss, Oberkochen.
[32] *E. Crundall*, Manuf. Opt. Int. *1976*, 629.
[33] *H. Dislich*, Lecture at Internat. Symp. on Degradation and Stabilization of Polymers, Brüssel 1974.
[34] *H. Dislich*, DBP 1569046 (1964), JENAer Glaswerk Schott & Gen.
[35] *J. Reiner, O. Hinterhofer*, SOZ *11*, 778 (1974).
[36] *H. Fricke, H. Dislich*, DBP 2416830 (1974), Deutsche Spiegelglas AG.
[37] *H. J. Lorkowski*, Plaste Kautsch. *23*, 318 (1976).
[38] *H. Zscheek*, Plaste Kautsch. *23*, 321 (1976).

[39] *L. Drechsel*, Lecture at Macromolecular Symposium Prag 1965, Preprint 342.
[40] Kodak Wratten Filter, Company Literature of Kodak AG, Stuttgart-Wangen.
[41] *A. E. Sherr et al.*, AD-A009511, National Technical Information Service, U. S. Department of Commerce.
[42] *S. F. Pellicori, C. A. Johnson, F. T. King*, Appl. Opt. *5*, No. 12, p. 1916 (1966).
[43] *O. Wichterle*, DBP 1084920 (1956).
[44] *M. Smetana*, Aussenhandel der Tschechoslowakei *2*, No. 8, p. 28 (1962).
[45] *P. Feneberg*, Süddtsch. Optiker-Ztg. *2*, 1 (1976).
[46] *H. P. Weber, W. J. Tomlinson, E. A. Chandross*, Opt. Quant. Electronics *7*, 465 (1975).
[47] *J. Schubert*, Bull. Schweiz. Elektrotech. *61*, 657 (1970).
[48] Du Pont de Nemours International AS, Genf, Company Publication on Crofon®.
[49] *A. L. Breen, J. R. Green*, DBP 1494721 (1965), Du Pont.
[50] *W. G. French, J. B. MacChesnay, A. D. Pearson*, Annu. Rev. Mater. Sci. *5*, 373 (1975).
[51] Du Pont de Nemours & Co., Wilmington, Data sheet PFX Fiberoptic.
[52] *W. Geffcken*, personal communication.
[53] JENAer Glaswerk Schott & Gen., Mainz, Company publication on UV Light Guides.
[54] *D. A. Pinnow, L. G. van Uitert*, Br. Pat. 1389263 (1972), Western Electric.
[55] *S. Shiraishi, Y. Kumagai, S. Kurosaki*, DOS 2333873 (1973), Sumitomo Electric Industries.
[56] *L. L. Blyler, A. C. Hart, R. F. Jaeger, P. Kaiser, T. J. Miller*, Lecture at Topical Meeting on Optical Fiber Transmission, Williamsburg 1975, Preprint.
[57] *Y. Suzuki, H. Kashiwagi*, Appl. Opt. *13*, 1 (1974).
[58] *H. Kashiwagi*, Lecture at Topical Meeting on Optical Fiber Transmission, Williamsburg 1975, Preprint.
[59] Genschow Technischer Informationsdienst, Auslandsschnellbericht 31 – 1976.
[60] *H. Dislich, E. Hildebrandt*, Optik *28*, 126 (1968/69).
[61] *H. Dislich, E. W. Deeg*, DBP 1214864 (1962), JENAer Glaswerk Schott & Gen.
[62] *H. Dislich, K. H. Wiesner*, DBP 1704743 (1967), JENAer Glaswerk Schott & Gen.
[63] *H. Dislich, K. H. Wiesner*, Optik *30*, No. 4, p. 1 (1970).
[64] JENAer Glaswerk Schott & Gen., Mainz, Company Publication on Glass-Plastic Composite Filters.
[65] Deutsche Spiegelglas AG, Grünenplan, Company Publication on Conversions Filters, Daylight Composite Filters, and Skylight Filters.
[66] *H. Dislich, K. Warnach*, DBP 1604572 (1966), JENAer Glaswerk Schott & Gen.
[67] *R. H. Hopkins, R. A. Hoffmann, W. E. Kramer*, Appl. Opt. *14*, 2631 (1975).
[68] *W. Klein*, Glaswelt *25*, 217 (1972).
[69] *H. Dislich, H. Hussmann, P. Hinz*, DAS 2263353 (1972), JENAer Glaswerk Schott & Gen.

COMMUNICATIONS

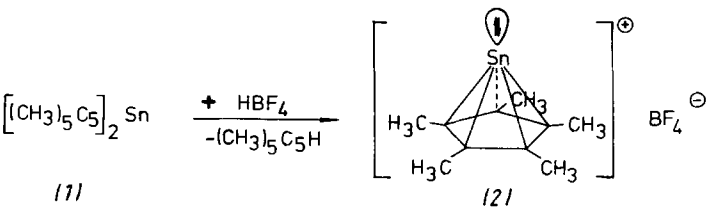
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying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

Synthesis and Structure of the *nido*-Cluster $(CH_3)_5C_5Sn^+$ [**]

By *Peter Jutzi, Franz Kohl*, and *Carl Krüger*[*]

Species of the type $R_5C_5Sn^+$ have previously only been observed in the mass spectra of dicarbonyl(η^5-cyclopentadienyl)ferriostannanes[1] and some cyclopentadienyl compounds of divalent and tetravalent tin[2]. We have now been able to isolate for the first time such an ion as the tetrafluoroborate and to elucidate its structure by X-ray crystallography.

Treatment of bis(pentamethylcyclopentadienyl)tin *(1)*[2d] with tetrafluoroboric acid leads to formation of pentamethylcyclopentadiene and the salt $(CH_3)_5C_5Sn^+BF_4^-$ *(2)*, whose cation exists in the form of an axially symmetric pentagonal bipyramidal *nido*-cluster:



(1) *(2)*

Compound *(2)*, which is isolable as colorless crystalline needles, is air- and moisture-sensitive and rapidly turns violet on exposure to daylight. On the other hand, no decomposition is observed over several weeks when it is stored at −20°C and in the dark. *(2)* is readily soluble in strongly aprotic solvents (acetonitrile, nitromethane, dichloromethane). ^{1}H-NMR (in CH_2Cl_2): $\delta CH_3 = 2.15$ (s); ^{11}B-NMR (in CD_3CN, ext. $BF_3 \cdot OEt_2$): $\delta BF_4^- = -0.53$ (s); ^{19}F-NMR (in CD_3CN, ext. $CFCl_3$): $\delta BF_4^- = 146.8$ (s). Conductivity (in CH_3NO_2, 20°C): $\Lambda = 127.4\ \Omega^{-1}\ cm^2\ mol^{-1}$ (1.035×10^{-3} M) [comparative measurement on $C_6H_5CH_2N(C_2H_5)_3^+Cl^-$: $\Lambda = 130.5\ \Omega^{-1}\ cm^2\ mol^{-1}$ (1.010×10^{-3} M)]. Molecular weight determination (cryoscopic in HMPT): 175 [M_r for *(2)* = 340.7].

The orbital and electron requirements for clusters are predicted from MO considerations and established rules[3]. The new cation in *(2)* can be placed quite neatly in the series

[*] Prof. Dr. P. Jutzi, Dipl.-Chem. F. Kohl
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg
Dr. C. Krüger
Max-Planck-Institut für Kohlenforschung
Lembkestrasse 5, D-4330 Mülheim-Ruhr 1 (Germany)

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

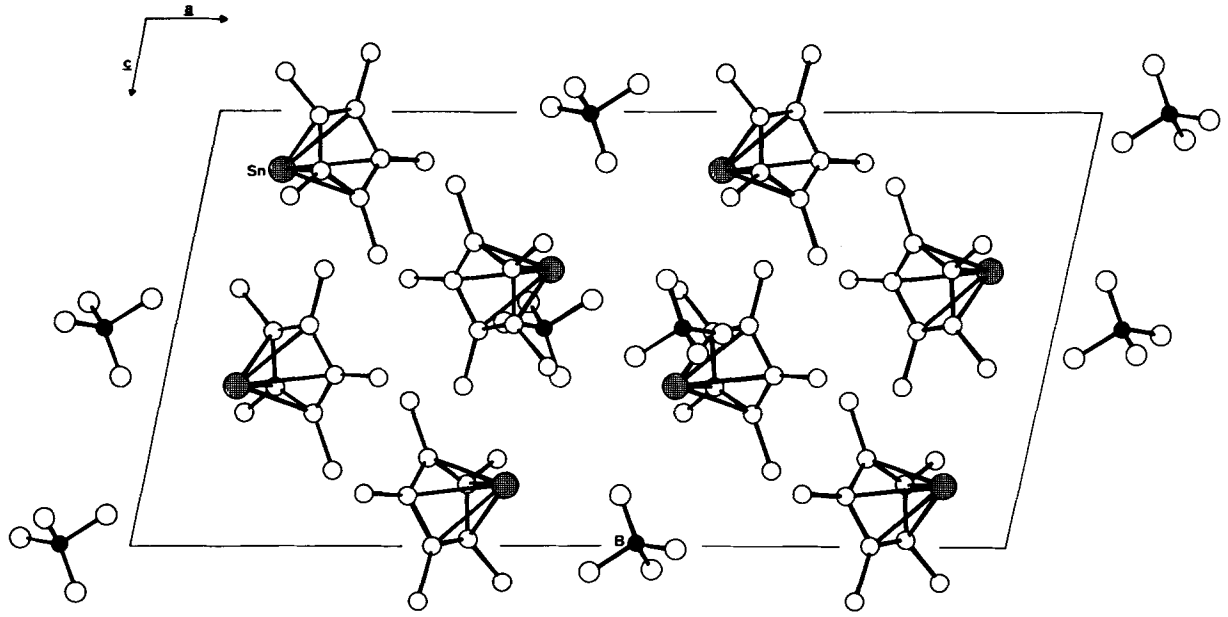


Fig. 1. Crystal structure of η^5-pentamethylcyclopentadienyltin(II) tetrafluoroborate *(2)*.

of well-known pentagonal-pyramidal *nido*-clusters[4]. As in the case of comparable cyclopentadienyl systems the accuracy of the X-ray structure analysis[5] of *(2)* is reduced because of rotational disorders which manifest themselves in high thermal vibration parameters of the lighter atoms.

The Sn—C bond length in *(2)* ($2.462 \pm 0.016 \times 10^{-10}$ m) is considerably shorter than in Cp_2Sn[6] (2.71) or CpSnCl[2b] (2.61 mean value); in the ring the average bond length is 1.39 ± 0.03, the C-methyl bond length 1.51 ± 0.03. Surprisingly[7], the methyl groups are oriented away from the central atom in the same fashion, and are bent at an average angle of $\theta = -4°$ (corresponding to 0.11) to the plane through the Cp ring (planar ± 0.01). The shortest SnB distance in the lattice is 3.590 (Sn—F 2.97—2.99).

Experimental

A 54 % ether solution of HBF_4 (14.3 mmol) is added dropwise with stirring to a solution of *(1)* (5.59 g, 14.4 mmol) in 300 ml diethyl ether cooled to −78 °C. After concentration of the mixture to *ca.* 50 ml the resulting pale yellow precipitate is filtered off, recrystallized from toluene and dried in a high vacuum. Yield: 1.50 g (31 %) of *(2)*, m.p. 210—218 °C (decomp).

Received: October 6, 1978 [Z 117 IE]
German version: Angew. Chem. *91*, 81 (1979)

[1] *J. Lewis, A. R. Manning, J. R. Miller, J. M. Wilson*, J. Chem. Soc. *A 1966*, 1663.
[2] a) *P. G. Harrison, J. J. Zuckerman*, J. Am. Chem. Soc. *92*, 2577 (1970); b) *K. D. Bos, E. J. Bulten, J. G. Noltes*, J. Organomet. Chem. *39*, C52 (1972); c) *H. J. Albert, U. Schröer, ibid. 60*, C6 (1973); d) *P. Jutzi, F. Kohl, ibid.*, in press.
[3] *K. Wade*, Chem. Br. *11*, 177 (1975); *R. W. Rudolph*, Acc. Chem. Res. *9*, 446 (1976).
[4] *P. Jutzi*, Nachr. Chem. Tech. Lab. *26*, 422 (1978).
[5] Crystallographic data: $a = 21.555(2)$, $b = 11.6905(8)$, $c = 10.7813(7)$ (all data in 10^{-10} m), $\beta = 101.925(6)°$, space group C2/c, $Z = 8$, $d_{calc} = 1.703$ g cm^3; $\mu = 19.46$ cm^{-1} ($Mo_{K\alpha}$), 3832 corrected reflections, 1139 unobserved (2σ), $R = 0.057$ ($R_w = 0.075$).
[6] *A. Almenningen, A. Haaland, T. Motzfeldt*, J. Organomet. Chem. *7*, 97 (1967).
[7] Cf. *D. M. P. Mingos*, Adv. Organomet. Chem. *15*, 33 (1977), and references cited therein.

Bis(trimethylsilyl)zinc and -cadmium[**]

By *Lutz Rösch* and *Gerald Altnau*[*]

Organozinc derivatives number among the first organometallic compounds to be synthesized and are well established reagents in preparative chemistry. In contrast, the homologous silylzinc derivatives were hitherto virtually unknown; the first representative of this series of compounds, bis(triphenylsilyl)-zinc was only briefly described in 1963[1].

We have now been able to synthesize the first alkylsilylzinc compound bis(trimethylsilyl)zinc *(1)* by reaction of zinc chloride or zinc acetate with lithium tetrakis(trimethylsilyl)aluminate[2] in diethyl ether.

$$2\,MX_2 + LiAl(SiMe_3)_4 \cdot 2DME \xrightarrow{Et_2O} 2\,M(SiMe_3)_2 + \cdots$$

X = Cl, CH_3COO — *(1)*, M = Zn
DME = 1,2-Dimethoxyethane — *(2)*, M = Cd

The pale yellow crystalline product *(1)*, which is isolable by vacuum sublimation, ignites spontaneously and is readily soluble in ethers, benzene and pentane. On treatment with dilute hydrochloric acid, a strongly exothermic reaction ensues with formation of trimethylsilane. The composition of *(1)* was confirmed by elemental analysis and by the mass spectrum (molecular peak with calculated isotope distribution). The ^{1}H-NMR spectrum (benzene) shows a sharp signal at $\delta = 0.20$. Only one absorption band is observed in the expected range for the ZnSi stretching vibration, both in the IR spectrum (305 cm^{-1}) and in the Raman spectrum (330 cm^{-1}). These findings indicate that the molecule is linear, *i. e.* the structure corresponds to that of the homologous bis(trimethylsilyl)mercury[3]. Compound *(1)* is not very stable thermally; slow decomposition with separation of metal takes place even at room temperature. However, it can be stored for *ca.* three weeks at −20 °C.

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

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

Bis(trimethylsilyl)cadmium *(2)*, which was likewise previously unknown, can be synthesized in the same way. Its properties are similar to those of the zinc compound. However, it is even less stable thermally; at $-20°C$, *(2)* decomposes within *ca.* 2 days with precipitation of the metal. The ^{1}H-NMR spectrum contains only one signal near that of the TMS standard, which still shows no splitting at $-10°C$. This signal would be expected to be flanked by two satellite bands [coupling with ^{111}Cd (13 %, $I=1/2$) and ^{113}Cd (12 %, $I=1/2$)]. The absence of satellites points to rapid exchange of the trimethylsilyl groups, as observed in the case of dimethylcadmium[4] and divinylcadmium[5]. According to the IR spectrum (CdSi stretching vibration at 320 cm^{-1}), *(2)* should also be a linear molecule; a Raman spectrum could not be recorded because the compound is very sensitive to light.

The preparatively important bis(trimethylsilyl)mercury can also be conveniently synthesized by reaction of lithium tetrakis(trimethylsilyl)aluminate with mercury acetate. We are presently investigating the general utility of this synthetic route as a method for the preparation of trimethylsilylmetal compounds.

Experimental

All operations must be carried out in the absence of air and moisture (argon as inert atmosphere).

(1): $Zn(OOCCH_3)_2$ (0.9 g) is added portionwise at room temperature to a vigorously stirred solution of $LiAl(SiMe_3)_4 \cdot 2DME$ in Et_2O (50 ml) with continuous passage of argon. After one hours' stirring, the solvent is removed at 0 °C in an oil-pump vacuum. Sublimation of the residue (room temperature/$-20°C$) from the reaction flask affords pale yellow star-shaped crystals, which immediately ignite and decompose on exposure to air. Yield 0.23 g (25 %).

(2): $CdCl_2$ (1.8 g) is allowed to react in the same way as above. $Cd(SiMe_3)_2$ is obtained in the form of yellow crystals, yield 0.35 g (27 %). This compound is also light-sensitive, and can be stored for only short periods in an ice-box.

Received: October 10, 1978 [Z 120 IE]
German version: Angew. Chem. *91*, 62 (1979)

[1] *E. Wiberg, O. Stecher, H.-J. Andrascheck, L. Kreuzbichler, E. Staude*, Angew. Chem. *75*, 516 (1963); Angew. Chem. Int. Ed. Engl. *2*, 507 (1963).
[2] *L. Rösch*, J. Organomet. Chem. *121*, C 15 (1976); *L. Rösch, G. Altnau*, unpublished.
[3] *H. Bärger*, Organomet. Chem. Rev. *A 3*, 425 (1968); *P. Bleckmann, M. Soliman, K. Reuter, W. P. Neumann*, J. Organomet. Chem. *108*, C 18 (1976).
[4] *W. Bremser, M. Winokur, J. D. Roberts*, J. Am. Chem. Soc. *92*, 1080 (1970).
[5] *H. D. Visser, L. P. Stodulski, J. P. Oliver*, J. Organomet. Chem. *24*, 563 (1969).

Coordination Number 3 in Co^{II}: $Na_{10}[Co_4O_9]$, an Oligooxocobaltate(II)[1]

By *Wilfried Burow* and *Rudolf Hoppe*[*]

In the newly prepared oxide $Na_{10}[Co_4O_9]$ we find the first example of cobalt coordinated in an almost trigonal planar environment. Lustrous red, robust single crystals of $Na_{10}[Co_4O_9]$ are obtained on heating an intimate mixture of Na_2O and "active" CoO in a cobalt tube[2] [Na:Co = 2.2:1, 500 °C, 30 d]. The crystals are extremely sensitive towards moisture (hydrolysis) and immediately deliquesce on exposure to air. The reaction product was therefore handled under absolutely dry argon, and single crystals were selected and picked out under the microscope.

According to Weissenberg photographs $Na_{10}[Co_4O_9]$ crystallizes triclinically with $a=12.18_1$, $b=8.52_7$, $c=8.32_2$ Å; $\alpha=119.96_7$, $\beta=87.89_1$, $\gamma=116.75_7°$; $Z=2$ (four circle diffractometer data). The structure was determined with 4928 symmetry independent reflections (Mo-Kα, graphite monochromator, $3° \leq \theta \leq 34°$)[3] by direct methods[4] and interpretation of the three-dimensional Patterson synthesis. Refinement with anisotropic temperature parameters for all particles gave for 3364 reflections the R value 6.10 % (space group $P\bar{1}$).

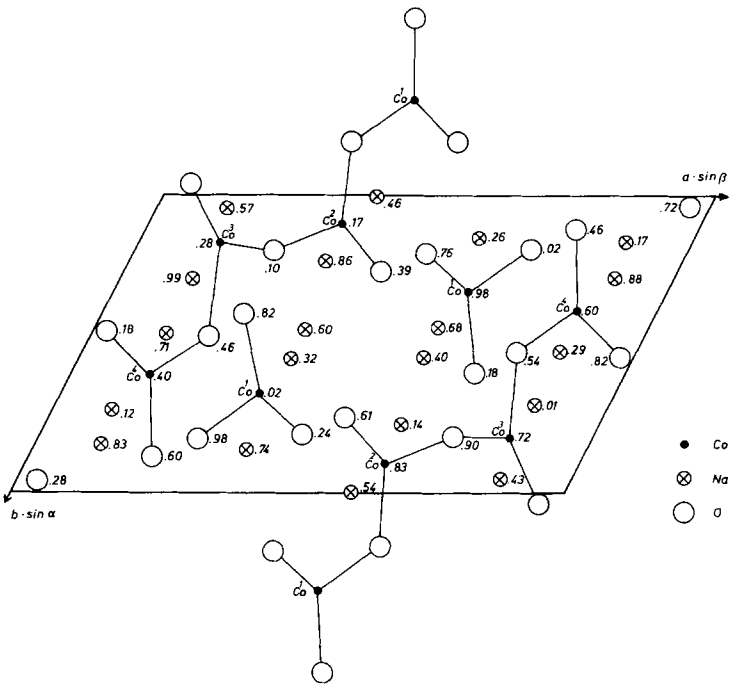


Fig. 1. Crystal structure of $Na_{10}[Co_4O_9]$; projection along [001]. Heights z in fractions of c.

Primary structure: Each Co atom is surrounded trigonal planar by three O atoms [bridging O atoms (Co—O bond

Table 1. Assignment of atoms in $Na_{10}[Co_4O_9]$.

Na^1	$\{O^1\ Ø^7\}\ \{O^6\}\ \{O^4\}$	C.N. 4
Na^2	$\{O^3\}\ \{O^2\}\ \{Ø^7\ Ø^9\}$	4
Na^3	$\{O^2\}\ \{O^5\}\ \{O^5\}\ \{O^8\}$	4
Na^4	$\{O^2\ O^6\}\ \{O^4\}\ \{O^4\}$	4
Na^5	$\{O^2\ Ø^3\}\ \{O^5\}\ \{O^8\}\ \{Ø^9\}$	4+1
Na^6	$\{Ø^3\ Ø^7\}\ \{O^5\}\ \{O^8\}$	4
Na^7	$\{O^1\}\ \{Ø^3\}\ \{O^6\ Ø^9\}$	4
Na^8	$\{O^2\ O^6\}\ \{O^5\}\ \{Ø^7\}$	4
Na^9	$\{O^1\}\ \{O^1\}\ \{O^4\}\ \{Ø^9\}$	4
Na^{10}	$\{Ø^3\ O^8\}\ \{O^8\}\ \{O^6\}$	4
O^1	$Na_1^1Na_1^2Na_1^7Na_2^9Co_1^4$	C.N. 6
O^2	$Na_1^2Na_1^3Na_1^4Na_1^5Na_1^8Co_1^4$	6
$Ø^3$	$Na_1^2Na_1^6Na_1^7Na_1^{10}Co_1^3Co_1^4$	6
O^4	$Na_1^1Na_2^4Na_1^9Co_1^3$	5
O^5	$Na_1^3Na_1^5Na_1^6Na_1^8Co_1^1$	6
O^6	$Na_1^1Na_1^4Na_1^7Na_1^8Na_1^{10}Co_1^1$	6
$Ø^7$	$Na_1^1Na_1^2Na_1^6Na_1^8Co_1^2Co_1^3$	6
O^8	$Na_1^3Na_1^5Na_1^6Na_2^{10}Co_1^2$	6
$Ø^9$	$Na_1^2Na_1^5Na_1^7Na_1^9Co_1^1Co_1^2$	6
Co^1	$O_1^5O_1^6O_{1\ 2}^9$	3
Co^2	$O_{1\ 2}^7O_1^8O_{1\ 2}^9$	3
Co^3	$O_1^3{}_2O_1^4{}_2O_{1\ 2}^7$	3
Co^4	$O_1^1O_2^3{}_2$	3

Ø: Symbol for bridging oxygen atoms of the $[Co_4O_9]$ group; particles in { } belong to a $[Co_4O_9]$ group.

[*] Prof. Dr. R. Hoppe, Dipl.-Chem. W. Burow
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

lengths 1.86—1.96 °A) and terminal O atoms (Co—O bond lengths 1.76—1.82 Å)]. In contrast, not all Na particles are coordinatively equivalent. This follows obligatorily from the composition if it is presupposed that all Co atoms have the coordination number (C.N.) 3 and all Na atoms and O atoms must as far as possible be coordinatively equivalent (cf. Table 1). One Na particle and one O particle (Na^5 and O^4) each differ coordinatively from the others. The equivalence of all the remaining Na towards O, as given in Table 1, refers only to the coordination number, not to the function of Na as bridge between various $[Co_4O_9]$ groups. Seven Na particles each link three asymmetric $[Co_4O_9]$ groups; Na^3, Na^5 and Na^9 each link four such groups, while Na^3 and Na^4 are unique insofar as they do not belong to any bridging oxygen.

Secondary structure: In a $[Co_4O_9]$ group the bridging O atoms form O—Co—O angles of 116.47, 96.32 and 115.99° with the Co atoms. The conformation of the group is difficult to explain: one half of the group (with Co^1 and Co^2) is almost planar, the other half (with Co^3 and Co^4) is both twisted with respect to the first as well as being twisted itself.

Tertiary structure: In the projection along [001] the assumed valency bonds between each two Co atoms of a $[Co_4O_9]$ group are almost parallel to [010]. It thus follows that the $[Co_4O_9]$ groups are also parallel [010] but out of phase with each other. This results in the formation of channels along [001] in which Na particles reside. The Madelung Part of the Lattice Energy (MAPLE[5] = 15843.3 kcal/mol) agrees with the sum of the MAPLE values of the binary oxides (15654.6 kcal/mol, Δ MAPLE = 1.1 %).

Received: October 18, 1978 [Z 118 IE]
German version: Angew. Chem. 91, 71 (1979)

[1] Part of a dissertation by *W. Burow*, Universität Giessen.

[2] We thank Bayer AG, Leverkusen, for supplying the electrolytic cobalt, and Prof. *Predl* and his co-workers of the Max-Plauck-Institut für Metallforschung, Stuttgart, for casting the cobalt rods (length 10 cm, diameter 7 mm).

[3] The measurements were carried out by Dr. *M. Jansen* in our laboratories with a Philips PW 1100 automated four-circle diffractometer.

[4] SHEL-X-Programmsystem; *G. Sheldrick*, unpublished.

[5] *R. Hoppe*, Angew. Chem. *78*, 52 (1966); *82*, 7 (1970); Angew. Chem. Int. Ed. Engl. *5*, 95 (1966); *9*, 25 (1970); Adv. Fluorine Chem. *6*, 387 (1970).

Extreme Liquid Chromatographic Separation Effects in the Case of Diastereomeric Amides Containing Polar Substituents[**]

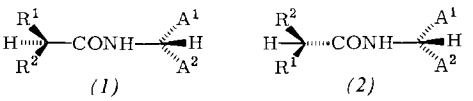
By *Günter Helmchen, Günter Nill, Dieter Flockerzi, Willi Schühle*, and *Mohamed S. K. Youssef*[*]

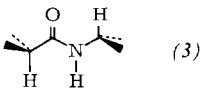
In contrast to the classical method *via* fractional crystallization of diastereomeric salts the separation of the enantiomers of chiral carboxylic acids and amines can be carried out by liquid adsorption chromatography of diastereomeric amides in a directed way, *i. e.* with pre-estimation of separation effects[1a] and with simultaneous determination of the enantiomeric purity[1b] and absolute configuration[1c]. Besides the low efficiency of the—now superseded—conventional column chromatography[2], non-optimal separation factors and especially the extreme difficulty of amide hydrolysis[3] were obstacles to wider preparative application of the method.

We have now developed reagents which not only ensure very high separation factors but also ready hydrolysis (cf. [4]).

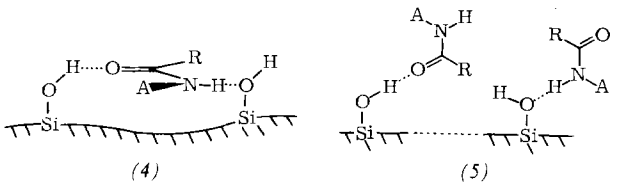
Particularly well suited for demonstrating the effects are the diastereomeric amides *(1)/(2)*, since their conformation in solution, the starting point of our model considerations, is well defined[1a] and the substituents R and A can be easily varied. From chromatographic data (adsorbent: silica gel[5]) four simple postulates were derived which serve as guidelines in the search for structural features necessary for high separation effects.

1. The conformation of the amides is the same in the dissolved state and in the adsorbed state[6]. In cases *(1)/(2)*, for both diastereomers it is determined by the planar structural element *(3)* (common plane) provided neither R^1 nor R^2 form a hydrogen bond to the amide group[7].





2. Binding to silica gel preferentially takes place *via* hydrogen bonding[9]. Hence the contribution of the amide group, which can be bound as described by *(4)* and *(5)*, is particularly high.



3. Significant diastereoselectivity is to be expected only for the state *(4)*. This arrangement is perturbed in favor of unbound or states *(5)* by substituents R and A with weak affinity to the silica gel. The perturbing effect of a substituent must be determined empirically. We assess it formally by the designations chromatographically large (cL) and small (cS), since for alkyl and aryl groups it approximately parallels the steric bulk in the direction perpendicular to the amide plane[9].

4. (Configuration rule) The groups R^1 and R^2 as well as A^1 and A^2 are classified according to their perturbing effect as R^{cL} and R^{cS} and A^{cL} and A^{cS}. Due to the better shielding of the amide group, the diastereomer whose R^{cL}/A^{cL} groups are situated on opposite faces of the common plane is eluted first.

Which structural features, according to these postulates, ought to lead to particularly good separating effects, as assessed by the separation factor α? Postulate 3 implies that α increases with the difference in steric bulk between A^1 and A^2 or R^1 and R^2. This is so for the amides *(a)* and *(b)* (cf. Table 1) but not in the series *(c)—(e)*, even though postulate 4 remains correct. Apparently the proportion of diastereoselectively acting states *(4)* decreases for *both* diastereomers with increasing size—especially broadening—of the apolar substituents. An extreme case is *(f)*.

[*] Dr. G. Helmchen, Dipl.-Chem. G. Nill, Dipl.-Chem. D. Flockerzi, W. Schühle, Dr. M. S. K. Youssef
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] Directed Resolution of Enantiomers *via* Liquid Chromatography of Diastereomeric Derivatives, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft (Projekt He 880/6).—Part 3: [1a].

Table 1. High-pressure liquid chromatographic separation [a] of diastereomeric amides *(1)*/*(2)* [b] on silica gel (23 °C; hexane/ethyl acetate (x:y) [c]).

	R^1 (cS)	R^2 (cL)	A^1 (cS)	A^2 (cL)	α[d]	$-\Delta(\Delta G)$ [cal] [e]	(x:y)
(a)	Et	Ph	Me	Ph	1.51	242	4:1
(b)	Et	Ph	Me	*p*-C_6H_4Ph	1.70	313	4:1
(c)	Me	Ph	Me	Ph	1.81	348	4:1
(d)	Me	CH_2Ph	Me	Ph	1.68	306	4:1
(e)	Me	$CHPh_2$	Me	Ph	1.45	220	4:1
(f)	Me	$CHPh_2$	Me	$CHPh_2$	1.15	82	4:1
(g)	Me	Ph	CH_2OH	Ph	2.56	553	1:1
(h)	Me	CH_2Ph	CH_2OH	Ph	2.56	553	1:1
(i)	Me	$CHPh_2$	CH_2OH	Ph	2.73	591	1:1
(i)					3.06	658	4:1
(j)	CH_2OH	Ph	Me	Ph	2.81	608	1:1
(k)	$(CH_2)_2OH$	Ph	Me	Ph	2.83	613	1:1
(l)	$(CH_2)_3OH$	Ph	Me	Ph	2.13	445	1:1
(m)	CH_2OAc	Ph	Me	Ph	2.06	424	4:1
(n)	CH_2CO_2Me	Ph	Me	Ph	1.91	380	1:1
(o)	$(CH_2)_2CO_2Me$	Ph	Me	Ph	1.71	314	1:1
(p)	$(CH_2)_2OH$	Ph	CH_2OH	Ph	5.77	1031	0:1
(q)	CH_2CO_2Me	Ph	CH_2OH	Ph	3.36	713	1:1

[a] Apparatus: see [1b]; pressure: 150 bar; inert substance: pentane; column: 30 × 0.3 cm for *(a)*–*(f)*, 20 × 0.3 cm for *(g)*–*(q)*, packed with Merckosorb SI 60, 5 µm. [b] All the new compounds were prepared diastereomerically pure and gave correct analyses and spectra; the configuration of *(l)* and *(o)* was confirmed by ^{1}H-NMR (method: *G. Helmchen*, Tetrahedron Lett. *1974*, 1527), otherwise by synthesis. [c] The composition of the eluent could not be held constant because of the difference in polarity of the compounds. As shown by case *(i)*, α decreases with increasing content of ethyl acetate. [d] $\alpha = (t_2 - t_0)/(t_1 - t_0)$; t_1, t_2: retention time of the first and second eluted amide, respectively; t_0: retention time of pentane. [e] $\Delta(\Delta G) = -RT\ln\alpha$.

In order to counteract this undesirable effect polar groups were introduced for the stabilization of *(4)*. The OH group proved particularly effective for this purpose. Thus, the series *(g)*–*(i)* corresponding to *(c)*–*(e)* shows (comparison of $A^1 = CH_3$ with $A^1 = CH_2OH$) not only a considerably higher α-level but also the expected increase with increasing difference in bulkiness of the apolar substituents. Equally favorable as that of the amine moiety is a polar group of the acyl moiety; compare *(a)* with *(j)* or *(k)*.

As to be expected on the basis of the proposed structure *(4)* the influence of the polar group is dependent upon its position. This manifests itself for the OH group in the series *(j)*–*(l)* and for the ester group, whose overall effect is weaker, in the series *(m)*–*(o)*. That the effect is particularly large in the case of a hydroxyl group in the γ position relative to the carbonyl C makes it "chemically" useful.

A further increase is observed with compounds containing polar groups in both moieties; see *(p)* and *(q)*. The postulates 1–4 are valid also for these extreme cases regarding separation if the polar groups are formally assigned to the cS class.

Separation factors $\alpha > 2$ are rarely found, even for cyclic diastereomers. The significance of such values in practice must be judged in relation to the number of theoretical plates of the chromatographic system[2]. Assuming typical conditions ($k'_2 = 5$), with $\alpha = 1.05$, 1.2, 1.5, 2.0, and 5, *ca.* 15000, 1200, 300, 130, and 50 theoretical plates, respectively, are necessary[8] for a baseline separation ($R_s = 1.2$). Accordingly, separations with α above ≈ 2 can be readily carried out even on primitive columns.

Received: October 25, 1978 [Z 122a IE]
German version: Angew. Chem. *91*, 64 (1979)

CAS Registry numbers:
(1a), 64314-07-4; *(1b)*, 68854-56-8; *(1c)*, 64314-03-0; *(1d)*, 68854-13-7; *(1e)*, 68843-75-4; *(1f)*, 68843-76-5; *(1g)*, 68843-77-6; *(1h)*, 68843-85-6; *(1i)*, 68843-78-7; *(1j)*, 68844-06-4; *(1k)*, 64284-07-7; *(1l)*, 68854-55-7; *(1m)*, 64284-05-5; *(1n)*, 68843-79-8; *(1o)*, 68843-80-1; *(1p)*, 68843-81-2; *(1q)*, 68854-54-6; *(2a)*, 64314-06-3; *(2b)*, 68854-53-5; *(2c)*, 64314-02-9; *(2d)*, 68854-52-4; *(2e)*, 68843-82-3; *(2f)*, 68843-83-4; *(2g)*, 68843-84-5; *(2h)*, 68843-85-6; *(2i)*, 68843-86-7; *(2j)*, 68843-87-8; *(2k)*, 64284-06-6; *(2l)*, 68843-88-9; *(2m)*, 64284-04-4; *(2n)*, 68843-89-0; *(2o)*, 68843-90-3; *(2p)*, 68843-91-4; *(2q)*, 68854-51-3

[1] a) *G. Helmchen, H. Völter, W. Schühle*, Tetrahedron Lett. *1977*, 1417; b) *G. Helmchen, W. Strubert*, Chromatographia *7*, 713 (1974), see also footnote 13 in [1c]; c) *G. Helmchen, R. Ott, K. Sauber*, Tetrahedron Lett. *1972*, 3873.

[2] Reproducible long-lived (> 1 year) preparative glass columns (45 × 4 cm; 300 g silica gel Merck LiChroprep 15–25 µm) with 10000 ± 1000 theoretical plates (naphthalene, hexane/ethyl acetate (95:5), 50 ml/min) can even be prepared by beginners: *B. Glatz, G. Helmchen*, unpublished. Under the same test conditions conventional open columns have 50–300 theoretical plates, TLC plates or Merck-Lobar columns 600–1200.

[3] Previously, the only alternative to the hydrolysis was the rearrangement of the corresponding nitrosamides, in which the amine is destroyed: *G. Helmchen, V. Prelog*, Helv. Chim. Acta 55, 2599 (1972); see in particular p. 2601, paragraph 1.

[4] a) *G. Helmchen, G. Nill, D. Flockerzi, M. S. K. Youssef*, Angew. Chem. *91*, 65 (1979); Angew. Chem. Int. Ed. Engl. *18*, 63 (1979); *G. Helmchen, G. Nill, ibid. 91*, 66 (1979) and *18*, 65 (1979).

[5] For other adsorbents, especially reversed phases, the postulates must possibly be modified.

[6] We are well aware that this postulate might excite contradiction; but in many more than 100 cases so far investigated it has been found to be valid without exception. The Ugi-Ruch method which does not contain the concept of conformation was shown to be inapplicable here: *H. Völter*, Dissertation, Universität Stuttgart 1978.

[7] According to IR and NMR spectra none of the compounds listed in Table 1 shows hydrogen bonding of this kind.

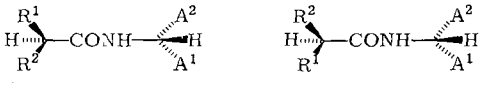
[8] *L. R. Snyder*: Principles of Adsorption Chromatography. Marcel Dekker, New York 1968.

[9] The repulsive perturbation effect of aryl groups towards alumina is smaller; it is known that arenes are also adsorbed on alumina much more strongly than on silica gel [8].

Preparative Scale Directed Resolution of Enantiomeric Carboxylic Acids and Lactones *via* Liquid Chromatography and Neighboring-Group Assisted Hydrolysis of Diastereomeric Amides[**]

By *Günter Helmchen, Günter Nill, Dieter Flockerzi*, and *Mohamed S. K. Youssef*[*]

The diastereomeric amides *(1)*/*(2)* with OH groups located in the γ or δ position to the carbonyl group [R^1 or $R^2 = (CH_2)_nOH$ and/or A^1 or $A^2 = (CH_2)_{n-1}OH$, $n = 2, 3$] show high, in certain cases extreme separation factors in liquid absorption chromatography[1]. We now report that these amides also have favorable chemical properties. Their cleavage takes place under acidic conditions mild enough, so that relati-



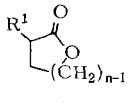
(1) *(2)*

vely sensitive compounds can be worked with, but not under such mild conditions that reaction occurs on the weakly acidic adsorbent silica gel. In cases where R^1 or $R^2 = (CH_2)_nOH$, $n = 2$, 3, reaction with 0.5–1 N mineral acid at 50–90 °C leads to formation of lactones *(3)*, $n = 2$, 3[2] and amines

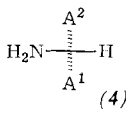
[*] Dr. G. Helmchen, Dipl.-Chem. G. Nill, Dipl.-Chem. D. Flockerzi, Dr. M. S. K. Youssef
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] Directed Resolution of Enantiomers *via* Liquid Chromatography of Diastereomeric Derivatives, Part 5.– This work was supported by the Deutsche Forschungsgemeinschaft (Projekt He 880/6).–Part 4: [1].

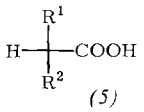
(4). In cases where A^1 or $A^2 = (CH_2)_{n-1}OH$, $n = 2, 3$, *N,O*-acyl transfer[3] occurs, followed by ester hydrolysis to give the carboxylic acids *(5)* and amines *(4)*. Depending upon the properties of R^1 and R^2, 0.5–3 N mineral acid is necessary at *ca.* 50–100 °C. As a rule the yields are almost quantitative.



(3)



(4)



(5)

(4a) $A^1 = CH_2OH$, $A^2 = Ph$
(4b) $A^1 = CH_3$, $A^2 = Ph$

These results thus demonstrate that the sought-after method (see [1]) for directed resolution of enantiomeric carboxylic acids or amines has in principle been realized, as has also a method for the separation of enantiomeric lactones:

1. Racemic carboxylic acids *(5)* *via* the usual activated derivatives (acyl chlorides, imidazolides *etc.*) can be reacted with amino alcohols *(4)*, A^1 or $A^2 = (CH_2)_nOH$, $n = 1, 2$, to give the diastereomeric amides *(1)/(2)*, which can be separated chromatographically and subsequently hydrolyzed. (−)-(*R*)-phenylglycinol *(4a)* is a suitable reagent here, since it is UV-active (chromatographic detection), is commercially available[4], and is easily recoverable almost quantitatively (cf. Table 1 and Experimental). Other compounds that can be prepared from amino acids, *e.g.* phenyl alaninol, alaninol, valinol, leucinol, and amides or esters of serine also give good results[5]. The nitrosamide rearrangement, an alternative for the hydrolysis in the case of extremely sensitive carboxylic acids, can also be employed in the case of *N*-acyl derivatives of amino alcohols, cf. *(5d)* in Table 1.

2. Racemic lactones *(3)* can by direct reaction with amines *(4)* be converted into amides *(1)/(2)*, R^1 or $R^2 = (CH_2)_nOH$, $n = 2, 3$ (catalyst: 2-hydroxypyridine[6]). Since these amides show high separation factors even in the case of apolar substituents A^1, A^2[1], amines such as (−)-(*S*)-1-phenylethylamine *(4b)*[7] are sufficiently good separating reagents. Cleavage of the chromatographically separated amides affords (apart from in the case where $R^1 = Ph$) enantiomerically pure lactones *(3)* (cf. Experimental and Table 1).

Such lactones have a strong tendency to racemization. We have therefore determined the enantiomeric purity of the particularly sensitive lactone *(3c)* in the following way: (+)-*(3c)* (for data see Table 1) was treated with hydrogen bromide/glacial acetic acid and then with zinc/glacial acetic acid; the 2-benzylbutyric acid formed was > 99.9 % enantiomerically pure [HPLC of the diastereomeric amides with *(4b)*][8].

3. Enantiomerically pure lactones *(3)* are now readily available for the first time. However, they are not suitable as separating reagents for amines since they partially racemize upon direct conversion to amides (for a solution to this problem see [9]).

Experimental

(1)/(2) from *(5)*: 1 mol *(5)* is converted with oxalyl chloride into the crude acyl chloride, whose solution in anhydrous dioxane is added dropwise to a solution of 1.0 mol *(4a)* and 1.2 mol triethylamine in dioxane at 5–10 °C. After removal of the solvent 1 N hydrochloric acid is added and the amides *(1)/(2)* are extracted with methylene chloride.

(1)/(2) from *(3)*: A solution of 1 mol *(3)*, 2 mol *(4a)* or *(4b)* and 1 mol 2-hydroxypyridine in 0.5 l anhydrous toluene is heated to boiling for 25 h under an inert gas, then partially evaporated down and the residue partitioned between CH_2Cl_2 and 0.5 N hydrochloric acid.

Separation of *(1)* and *(2)*: The crude mixture of *(1)/(2)* is chromatographed, either on a column as mentioned in Ref.[1] or on a Merck-Lobar column (UV detection, eluent: petroleum ether (low-boiling)/ethyl acetate in a ratio shown to be optimal by TLC). Alternatively, the mixture can be fractionally crystallized with TLC monitoring of the separation progress (in all cases widely separated spots).

Amide cleavage: For recovery of *(3)* the vigorously stirred mixture of 1 mol of the diastereomerically pure *(1)* or *(2)* and 2 l 1 N H_2SO_4 in dioxane/water (1:1) is heated at 80–90 °C for 16 h then diluted with water and extracted with methylene chloride to afford *(3)* in the neutral part. The recovery of *(5)* is carried out analogously, but as a rule up to 3 N H_2SO_4 is used and the mixture is heated to boiling. Since the rate of reaction varies greatly with the nature of the acyl group (reaction time a few minutes to several hours) the conversion

Table 1. Separation of enantiomeric lactones *(3)* and carboxylic acids *(5)* by chromatography of diastereomeric amides *(1)/(2)* ($A^2 = Ph$, $A^1 = CH_2OH$ or CH_3) and their cleavage under acid conditions (cf. Experimental).

	n	R^1	R^2	Separating reagent	*(1)/(2)* [a]	Yield [%] (+)- *(3)* or *(5)* [b]	Yield [%] (−)- *(3)* or *(5)* [b]	$[\alpha]_D$ [°] of *(3)* or *(5)* from first eluted amide [c]	second eluted amide [c]	Configuration according to Lit.	Configuration according to Rule in [1]
(3a)	2	CH_3		*(4b)*	67	76	67	− 23.1	+ 23.1 (*c* = 9.7, EtOH, 23 °C) [d]	(+)-(*R*) [d]	(+)-(*R*)
(3b)	2	n-C_4H_9		*(4b)*	76	99	99	+ 12.5	− 12.5 (*c* = 5.0, MeOH, 20 °C) [e]	(−)-(*R*) [e]	(−)-(*R*)
(3c)	2	CH_2Ph		*(4b)*	77	98	99	+ 67.7	− 67.9 (*c* = 5.0, CCl_4, 20 °C)		(−)-(*R*)
(3d)	2	$(CH_2)_3Ph$		*(4b)*	68	95	95	+ 7.4	− 7.3 (*c* = 10.0, CCl_4, 20 °C)		(−)-(*R*)
(3e)	2	$CHPh_2$		*(4b)*	69	100	100	+206	−210 (*c* = 3.0, CCl_4, 20 °C)		(+)-(*R*)
(3f)	3	CH_2Ph		*(4b)*	93	84	82	+ 63.4	− 63.1 (*c* = 3.0, MeOH, 20 °C)		(+)-(*R*)
(5a)		n-C_3H_7	CH_3	*(4a)*	97	85	91	− 18.8 (25 °C) [f]	+ 18.4 (neat, 16 °C) [g]	(+)-(*S*) [g]	(+)-(*S*)
(5b)		CH_2Ph	CH_3	*(4a)*	93	92	98	− 25.2	+ 25.4 (neat, 22 °C) [h]	(−)-(*R*) [h]	(−)-(*R*)
(5c)		$CHPh_2$	CH_3	*(4a)*	97	95	94	+ 54.3	− 54.6 (*c* = 1.6, $CHCl_3$, 26.5 °C) [i]	(−)-(*S*) [i]	(−)-(*S*)
(5d)		Ph	CH_3	*(4a)*	92	96			+ 86.2 (*c* = 1.2, C_6H_6, 20 °C) [j]	(+)-(*S*) [j]	(+)-(*S*)
(5d)						75 [k]			+ 94.3 (*c* = 2.5, C_6H_6, 20 °C)		

[a] Chromatographically pure compounds; max. difference between *(1)* and *(2)*: 2 %. [b] Analytically pure products; yield w.r.t. the amide. [c] Highest rotation found in the literature. [d] *T. Kaneko, K. Wakabayashi, H. Katsura*, Bull. Chem. Soc. Jpn. *35*, 1149 (1962): $[\alpha]_D^{15} = -21.5°$ (*c* = 5.5, EtOH). [e] $[\alpha]_D^{23} = -12.8°$ (*c* = 9.9, EtOH); *A. I. Meyers, E. D. Mihelich*, J. Org. Chem. *40*, 1186 (1975): $[\alpha]_D^{23} = -7.3°$ (*c* = 9.7, EtOH). [f] *P. A. Levene, R. E. Marker*, J. Biol. Chem. *98*, 5 (1932): $[\alpha]_D^{25} = -18.4°$ (neat). [g] *S. Ställberg-Stenhagen, E. Stenhagen*, Ark. Kemi *23 A*, 7 (1947): $[\alpha]_D^{16} = +18.5°$ (neat). [h] *A. W. Schrecker*, J. Org. Chem. *22*, 33 (1957): $[\alpha]_D^{22} = -24.56°$ (neat). [i] *H. M. Walborsky, C. G. Pitt*, J. Am. Chem. Soc. *84*, 4832 (1962): $[\alpha]_D^{26.5} = -52.6°$ (*c* = 1.6, $CHCl_3$). [j] *K. Petersen*, Ark. Kemi *10*, 283 (1956) (repeated by us): $[\alpha]_D^{20} = +94.2°$ (*c* = 3.1, C_6H_6). [k] Nitrosamine rearrangement; see [1], footnote 3.

is monitored by TLC. For recovery (*ca.* 90%) of *(4a)* the acidic aqueous phases from the extraction step are brought to pH 9–10 and extracted six times with *n*-butanol/ethyl acetate/heptane (2:1:0.02); the organic phase is washed with a little water and evaporated down without previous drying.

Received: October 25, 1978 [Z 122b IE]
German version: Angew. Chem. *91*, 65 (1979)

[1] *G. Helmchen, G. Nill, D. Flockerzi, W. Schühle, M. S. K. Youssef*, Angew. Chem. *91*, 64 (1979); Angew. Chem. Int. Ed. Engl. *18*, 62 (1979), references cited therein.
[2] *L. Zürn*, Justus Liebigs Ann. Chem. *631*, 56 (1960).
[3] *A. P. Phillips, R. Baltzly*, J. Am. Chem. Soc. *69*, 200 (1947).
[4] Of the commercially available products tested by us those obtainable from Sigma showed the highest chemical and enantiomeric purity; E.P. = 99.2%, determined by HPLC according to the method of *G. Helmchen, W. Strubert*, Chromatographia *7*, 713 (1974).
[5] Refractometric detection is necessary for compounds without aryl groups.
[6] *H. C. Openshaw, N. Whittaker*, J. Chem. Soc. *C 1969*, 89.
[7] Enantiomerically pure (>99.9%) (−)-*(4b)* can be obtained from commercially available products (96–99%) by single precipitation of the salt with D-tartaric acid.
[8] This procedure constitutes a new method for the determination of the enantiomeric purity of 2- and 3-substituted butyrolactones (and presumably also valerolactones); for other methods see *G. Saucy, R. Borer, D. P. Trullinger, J. B. Jones, K. P. Lok*, J. Org. Chem. *42*, 3206 (1977), and references cited therein.
[9] *G. Helmchen, G. Nill*, Angew. Chem. *91*, 66 (1979); Angew. Chem. Int. Ed. Engl. *18*, 65 (1979).

Preparative Scale Directed Resolution of Enantiomeric Amines *via* Liquid Chromatography of Diastereomeric 4-Hydroxybutyramides[**]

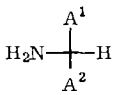
By *Günter Helmchen* and *Günter Nill*[*]

We reported that racemic 2-substituted butyrolactones *(1)*, R ≠ aryl, can be readily resolved into enantiomers by converting them with an enantiomerically pure amine *(2)* into diastereomeric 4-hydroxybutyramides, separating these by liquid chromatography and cleaving the separated products under mild acidic conditions back into lactone and amine[1]. In view of the practical importance of optically active amines *(2)* the converse of this method, the separation of enantiomeric amines by reaction with an enantiomerically pure lactone is of great interest. However, the realization of this concept was at first thwarted by the fact that enantiomerically pure 2-alkylbutyrolactones [investigated for the cases: *(1)*, $R = CH_2C_6H_5$ and *n*-butyl] partially racemize under the influence of catalysts (*e.g.* 2-hydroxypyridine) required for the direct reaction with amines.

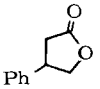
The most advantageous of several solutions[2] to this problem achieved so far was gained from investigations of diastereomeric amides in which the distances between the chirality centers were varied. As can be seen from Table 1, shifting the chirality center of the acyl group from the α- to the β-position with respect to the carbonyl group leads to only a slight decrease in the separation factor α, while displacement to the γ-position leads to a very large decrease in the separation factor. Consequently, not only α- but also β-substituted carboxylic acids and lactones can be separated quite easily *via* diastereomeric amides. Conversely, β-substituted lactones must be suitable reagents for the resolution of amines *(2)*, since they are stable towards racemization.



(1)



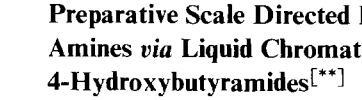
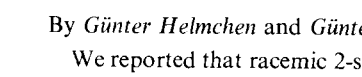
(2)



(3)

We have investigated 3-phenylbutyrolactone *(3)*, the first example of this new class of separating reagents. The preparation of *(3)* and the separation into two pure enantiomers [*via* the diastereomeric amides *(6a, b)*, cf. Table 1] are described in the Experimental section[3].

Table 1. Liquid chromatographic separation factors [a] of diastereomeric amides having differently spaced chirality centers (23 °C; silica gel; hexane/ethyl acetate (1:1); 150 bar).

	R = OH, R′ = H	α	R = H, R′ = OH	α
	(4a, b)	2.81	*(8a, b)*	2.56
	*(5a, b)*	2.83	*(9a, b)*	2.20
	*(6a, b)*	2.07	*(10a, b)*	1.93
	*(7a, b)*	1.10		

[a] For definition of the separation factor α and description of the measuring apparatus see [1a] Table 1.

Directed resolutions of the enantiomers of amines *(2)* are carried out with (−)-*(R)*-*(3)* [or with (+)-*(S)*-*(3)* in the "mirror image" way] according to the method summarized in Scheme 1 (for examples see Table 2). The configurational relationships were determined as follows: 1. The chromatographic model presented in [1] can be applied to the case of the diastereomeric amides with a chirality center in the β-position to the carbonyl group, since the conformation of compounds $R^1R^2CH(CH_2)_nCONHA^1A^2$ (R^1, R^2 = alkyl, aryl, $n \neq 0$) can generally be given[4]. 2. A^{cL} and A^{cS} represent the "chromatographically larger and smaller", respectively, of the groups A^1, A^2 of *(2)* (for the definition of these terms see [1]). 3. The separation of the enantiomers of *(3)* *via* the diastereomeric amides *(6a, b)* already constitutes a directed resolution according to Scheme 1 and establishes the configuration of *(3)*. For unequivocal confirmation (−)-*(R)*-*(3)*, $[\alpha]_D^{20} = -50°$ ($c = 4.7$, MeOH) was converted with hydrogen bromide in glacial acetic acid into 4-bromo-3-phenylbutyric acid, and this in turn with zinc in glacial acetic acid into (−)-*(R)*-3-phenylbutyric acid[5], $[\alpha]_D^{25} = -55°$ ($c = 2$, benzene).

Experimental

Separation of the enantiomers of *(3)*: A mixture of 28.9 g *(3)*[6], 17 g 2-hydroxypyridine, 43.2 g (−)-*(S)*-1-phenylethylamine, $[\alpha]_D^{22} = -40.36°$ (neat), enantiomerically pure, and 50 ml anhydrous toluene is heated under an inert gas at 120 °C

[*] Dr. G. Helmchen, Dipl.-Chem. G. Nill
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] Directed Resolution of Enantiomers *via* Liquid Chromatography of Diastereomeric Derivatives, Part 6. This work was supported by the Deutsche Forschungsgemeinschaft (Projekt He 880/6).—Part 5: [1b].

Table 2. Preparative resolution of chiral amines *(2)* (A^1, $A^2 = A^{cL}$ or A^{cS}) *via* diastereomeric amides *(11a, b)* according to Scheme 1 (cf. Experimental).

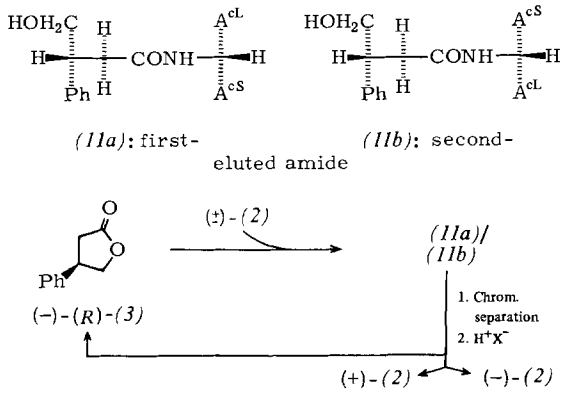
Amine	A^{cL}	A^{cS}	Resolution agent	Yield [%] *(11a, b)*	[a](+)- *(2)*·HCl	(−)- *(2)*·HCl	$[\alpha]_D^{20}$ [°] (MeOH) of *(2)*·HCl from first eluted *(11)*	second eluted *(11)*	Configuration according to Lit.	Scheme 1
(2a)	C_6H_5	C_2H_5	(−)-*(R)*-*(3)*	77	95	92	+17.8	−17.6 (*c* = 5) [b]	(+)-*(S)* [b]	(+)-*(S)*
(2b)	C_6H_5	$CH(CH_3)_2$	(+)-*(S)*-*(3)*	72	94	93	− 7.7	+ 7.8 (*c* = 3) [c]	(+)-*(S)* [c]	(+)-*(S)*
(2c)	n-C_6H_{13}	CH_3	(−)-*(R)*-*(3)*	84	95	96	− 5.1	+ 5.1 (*c* = 5) [d]	(−)-*(S)* [d]	(−)-*(S)*
(2d)	n-$C_{14}H_{29}$	CH_3	(+)-*(S)*-*(3)*	88	89	92	+ 2.7	− 2.4 (*c* = 2)		(−)-*(S)*
(2e)	n-C_3H_7	CH_2CH_2OH	(+)-*(S)*-*(3)*	92	[e]		[f]		(+)-*(S)* [f]	(+)-*(S)*

[a] Chromatographically pure compounds; maximum difference between *(11a)* and *(11b)*: 2%. [b] Neutral sulfate: $[\alpha]_D^{20} = -13.1°$ (*c* = 2, water); cf. *F. M. Jaeger, W. Froentjes*, Proc. Nederl. Acad. Wetenschap. *44*, 140 (1941): $[\alpha]_{589} = -13.5°$ (*c* = 2, water). [c] *N*-acetyl derivative: $[\alpha]_D^{20} = +136.6°$ (*c* = 3.7, MeOH); cf. *O. Cervinka, V. Dudek, L. Hub*, Collect. Czech. Chem. Commun. *35*, 724 (1970): $[\alpha]_D = +72.3°$ (*c* = 3.8, MeOH). [d] According to *F. G. Mann, J. W. G. Porter*, J. Chem. Soc. *1944*, 456: $[\alpha]_D^{17} = +4.67°$ (*c* = 6.23, MeOH). [e] Yield of distilled amino alcohols: (+)-*(2e)* 92%, (−)-*(2e)* 95%. [f] From first eluted *(11)*: $[\alpha]_D^{22} = +1.30°$ (neat), from second eluted *(11)*: $[\alpha]_D^{22} = -1.31°$ (neat); HPLC determination of the enantiomeric purity with *O*-methylmandelic acid according to *G. Helmchen, W. Strubert*, Chromatographia *7*, 713 (1974) gave > 99.5% for (+)-*(2e)*. These facts contrast with the literature data; cf. *G. Habermehl, H. Andres*, Justus Liebigs Ann. Chem. *1977*, 800: $[\alpha]_D^{22} = +3.4°$ (neat) for (*S*)-*(2e)*.

for 26 h. Dichloromethane (1 l) is then added and the solution extracted several times with 1 N hydrochloric acid and water. The crude product after evaporation of the organic phase is chromatographed in 4 g portions (column: see [1a]; eluent: ethyl acetate, flow-rate: 40 ml/min; UV detection at 254 nm): baseline separation, $t_R(6a) = 22$ min, $t_R(6b) = 35$ min. 25.2 g (100%) of *(6a)* and 23.3 g (92%) of *(6b)* are obtained.

A vigorously stirred mixture of 22.7 g *(6b)* and 160 ml 2 N sulfuric acid/dioxane (1:1) is heated under an inert gas at 90°C for 14 hours. The mixture is then worked up in the same manner as described above. 12.95 g (100%) of (−)-(*S*)-*(3)* is obtained. For the elemental analysis a sample is distilled bulb-to-bulb (70—80°C/0.001 torr): m.p. 61—61.5°C, $[\alpha]_D^{20} = +50.4°$C (*c* = 5, methanol). (−)-(*R*)-*(3)* is obtained in an analogous way from *(6a)*.

Separation of enantiomeric amines *(2)*: The same procedure as above (or as is described in [1b]) is employed, but with lactone/hydroxypyridine/amine in the molar ratio (2:2:1). The excess lactone is recovered quantitatively from the front fraction on chromatographic separation of the amides. The amines are isolated in the usual way from the acidic aqueous phases after hydrolysis.



Scheme 1. Directed resolution of the enantiomeric amines (±)-*(2)* *via* diastereomeric amides *(11a)* and *(11b)*. The oxygen of the Z amide group (with its plane perpendicular to the plane of the paper) is pointing upwards.

Received: October 25, 1978 [Z 122c IE]
German version: Angew. Chem. *91*, 66 (1979)

[1] a) *G. Helmchen, G. Nill, D. Flockerzi, W. Schühle, M. S. K. Youssef*, Angew. Chem. *91*, 64 (1979); Angew. Chem. Int. Ed. Engl. *18*, 62 (1979); b) *G. Helmchen, G. Nill, D. Flockerzi, M. S. K. Youssef, ibid. 91*, 65 (1979) and *18*, 63 (1979).

[2] *G. Nill*, Planned Dissertation, Universität Stuttgart.

[3] All the new compounds gave correct elemental analyses and spectra.

[4] *H. Völter*, Dissertation, Universität Stuttgart 1978.

[5] *V. Prelog, H. Scherrer*, Helv. Chim. Acta *42*, 2227 (1959).

[6] Freshly distilled 2-oxo-2-phenylethyl acetate is allowed to react with diethyl(methoxycarbonyl) phosphonate according to the standard method, the crude reaction product subjected to catalytic hydrogenation (5% Pd/C/glacial acetic acid), and (once again the crude product) lactonized with 4 N sulfuric acid/dioxane (1:1). The total yield of *(3)* after purification by distillation is 80—90%.

$Xe(OTeF_5)_6$, A Deep-Colored Noble Gas Compound, and $O{=}Xe(OTeF_5)_4$—The Existence of $Kr(OTeF_5)_2$[**]

By *Dieter Lentz* and *Konrad Seppelt*[*]

Since the —OTe_5 group has been shown to have fluorine-like ligand properties[1a] we have tried using it for the synthesis of nobel-gas compounds having the highest possible oxidation states. Recently, the stable $Xe(OTeF_5)_4$ was reported[1b].

We have now succeeded in synthesing $Xe(OTeF_5)_6$ *(1)*: XeF_6 reacts very slowly with $B(OTeF_5)_3$[2] (molar ratio 1:2) in perfluoro-*n*-pentane at −40°C with liberation of BF_3 and precipitation of *(1)* as a reddish violet finely crystalline solid. The xenon hexakis(pentafluorotellurate(VI)) was characterized by its defined decomposition to $Xe(OTeF_5)_4$ and F_5TeOO-TeF_5. This decomposition can be induced either thermally at −10°C or by exposure to daylight at temperatures as low as −230°C. The photolysis is analogous to the decomposition of XeF_6 into XeF_4 and F_2 by UV light[3]. Yet $Xe(OTeF_5)_6$ decomposes in UV light to one part Xe and 3 parts $F_5TeOOTeF_5$.

$$XeF_6 + 2\,B(OTeF_5)_3 \xrightarrow[n\text{-}C_5F_{12}]{-40°C} 2\,BF_3 + \underset{(1)}{Xe(OTeF_5)_6}$$

$$(1) \xrightarrow{-10°C;\ h\nu(VIS)} Xe(OTeF_5)_4 + F_5TeOOTeF_5$$

$$(1) \xrightarrow{h\nu(UV)} Xe + 3\,F_5TeOOTeF_5$$

The sensitivity of *(1)* makes spectroscopic investigations difficult. Apart from the recently described species Xe_2^+ (green)[4],

[*] Priv.-Doz. Dr. K. Seppelt, Dipl.-Chem. D. Lentz
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

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

no other deeply colored noble-gas compounds have previously been reported, where the color is due to the noble gas. The color of *(1)* must be a consequence of the bonding of the hexavalent xenon, which has a lone pair of electrons; the tellurium compound $Te(OTeF_5)_6$[5] has no lone pair and is colorless. From the color we conclude that *(1)* exists as a monomeric molecule with covalent bonds and does not form intermolecular bridges, as have been observed in the case of XeF_6, both in the liquid and the solid state[6]; so, even monomeric XeF_6 is pale yellow in color. An accurate X-ray structure analysis of *(1)* would thus also allow conclusions to be drawn about the structure of monomeric XeF_6.

In contrast to XeF_6 the new compound $Xe(OTeF_5)_6$ is moderately stable towards hydrolysis, presumably because of the shielding effect of the large $OTeF_5$ groups. The first isolable product of hydrolysis, $O{=}Xe(OTeF_5)_4$ *(2)*, is a colorless, remarkably stable compound (m. p. 56 °C, subl. 35 °C/10^{-2} mbar) which can be obtained better directly from $XeOF_4$.

$$3\,XeOF_4 + 4\,B(OTeF_5)_3 \xrightarrow[n\text{-}C_5F_{12}]{-30\,^\circ C} 4\,BF_3 + 3\,O{=}Xe(OTeF_5)_4 \quad (2)$$

$$XeOF_4 + (2) \rightleftharpoons O{=}XeF_3(OTeF_5) + \textit{cis}\text{-}O{=}XeF_2(OTeF_5)_2 + \textit{trans}\text{-}O{=}XeF_2(OTeF_5)_2 + O{=}XeF(OTeF_5)_3$$

The identity of *(2)* was easily established by spectral data [MS (75 eV): $m/e = 871$ $OXe(OTeF_5)_3^+$, 646 $O_2Xe(OTeF_5)_2^+$ *etc.*; Raman (cm^{-1}): *inter alia* 886 $\nu_{Xe=O}$, 667 ν_{TeF_4}, 477 $\nu_{Xe=O}$; ^{19}F-NMR: AB_4 spectrum with $\delta_A = 47.8$, $\delta_B = 35.3$, $J_{AB} = 183$ Hz] and elemental analysis. Of particular importance is the ^{129}Xe-NMR spectrum (Fig. 1)[7].

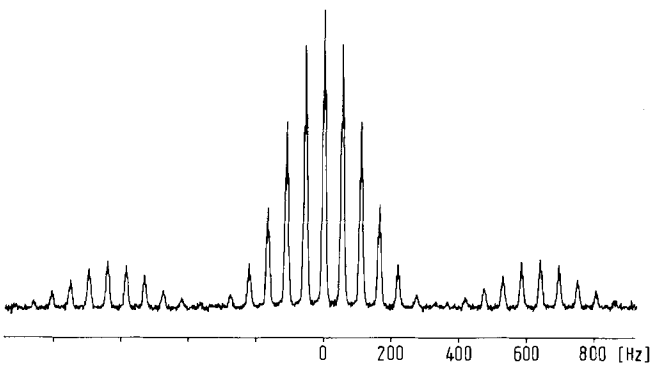


Fig. 1. ^{129}Xe-NMR spectrum (55.33 MHz) of $O{=}Xe(OTeF_5)_4$, dissolved in $C_2F_4Cl_2$: $\delta = -5121$ rel. Xe; $^3J_{Xe-F_{ax}} = 4$ Hz, $^3J_{Xe-F_{eq}} = 55$ Hz, $^2J_{Xe-^{125}Te} = 1281$ Hz.

Coupling is observed with the 16 equatorial fluorine atoms and with the four axial fluorine atoms, and also with the tellurium isotope ^{125}Te (7 % natural abundance, nuclear spin 1/2). Since the pentafluorotellurates are the most stable xenon derivatives after the fluorides [decomp.: $Xe(OTeF_5)_2$ 130 °C[8] > $O{=}Xe(OTeF_5)_4$ 90 °C > $Xe(OTeF_5)_4$ 72 °C[1b] > $Xe(OTeF_5)_6$ −10 °C] we tried to synthesize an analogous krypton compound.

$$3\,KrF_2 + 2\,B(OTeF_5)_3 \xrightarrow[FClO_3]{-100\,^\circ C} 2\,BF_3 + 3\,[Kr(OTeF_5)_2] \quad (3)$$

$$(3) \xrightarrow{-100\,^\circ C} Kr + F_5TeOOTeF_5$$

Even under the most carefully controlled reaction conditions only $F_5TeOOTeF_5$ could be detected besides krypton. Since, however, the peroxide is the typical decomposition product of all xenon derivatives, we assume intermediary formation of $Kr(OTeF_5)_2$ (or $FKr{-}OTeF_5$). Indeed, the reaction proceeds in a very clear fashion and, despite the extremely powerful fluorinating property of KrF_2, no TeF_6 can be detected. Reactions with the $OSeF_5$ ligands proceed analogously. It would appear, therefore, that the synthesis of a compound containing a krypton-oxygen bond is impossible with todays state of synthetic chemistry—apart perhaps by means of the matrix technique. KrF_2 so far remains the only compound of krypton, and it can be converted into the ions KrF^+ and $Kr_2F_3^+$[9].

Received: October 10, 1978 [Z 119 IE]
German version: Angew. Chem. *91*, 68 (1979)

[1] a) *D. Lentz, K. Seppelt*, Angew. Chem. *90*, 390 (1978); Angew. Chem. Int. Ed. Engl. *17*, 355 (1978); b) *ibid. 90*, 391 (1978) and *17*, 356 (1978).
[2] *F. Sladky, H. Kropshofer, O. Leitzke*, J. Chem. Soc. Chem. Commun. *1973*, 134.
[3] UV photolysis of XeF_6 is the best method for preparing pure XeF_4: *K. Seppelt*, Inorg. Synth., in press.
[4] *L. Stein, J. R. Norris, A. J. Downs, A. R. Minihan*, J. Chem. Soc. Chem. Commun. *1978*, 502.
[5] *D. Lentz, H. Pritzkow, K. Seppelt*, Angew. Chem. *89*, 741 (1977); Angew. Chem. Int. Ed. Engl. *16*, 729 (1977); Inorg. Chem. *17*, 1926 (1978).
[6] *H. H. Rupp, K. Seppelt*, Angew. Chem. *86*, 669 (1974); Angew. Chem. Int. Ed. Engl. *13*, 613 (1974); Z. Anorg. Allg. Chem. *409*, 331 (1974); *R. D. Burbank, G. R. Jones*, J. Am. Chem. Soc. *96*, 43 (1974).
[7] We are grateful to Dr. *Hull* of the Bruker Company, Karlsruhe, for recording the ^{129}Xe-NMR spectra
[8] *K. Seppelt, D. Nöthe*, Inorg. Chem. *12*, 2727 (1973).
[9] *H. Selig, R. D. Peacock*, J. Am. Chem. Soc. *86*, 3895 (1964); *D. E. McKee, C. J. Adams, A. Zalkin, N. Bartlett*, J. Chem. Soc. Chem. Commun. *1973*, 26; *R. J. Gillespie, G. J. Schrobilgen, ibid. 1974*, 90; *B. Frlec, J. Holloway*, Inorg. Chem. *15*, 1263 (1976).

Vinyl Ketenimines by Nucleophilic Ring Cleavage of Cyclopropenes with *tert*-Butyl Isocyanide[**]

By *Günter Ege* and *Karlheinz Gilbert*[*]

Dedicated to Professor Hans Plieninger on the occasion of his 65th birthday

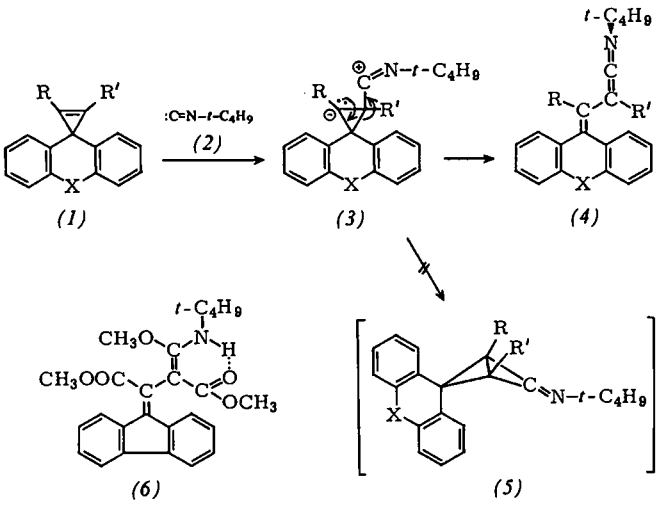
Isocyanides react with activated double[2] and triple bonds[3] to give primary products, which nearly always add to further isocyanide or also to the multiple bond, with formation of cyclic compounds.

On reaction of the cyclopropenes *(1)*[4], activated by electron-acceptor groups, with *tert*-butyl isocyanide *(2)* in benzene solution at room temperature and allowing the reaction mixture to stand for several days in the dark we obtained the vinyl ketenimines (1-aza-1,2,4-pentatrienes) *(4)* which showed characteristic ketenimine bands in the IR spectrum at 2025 to 2060 cm^{-1}. Boiling under reflux shortened the reaction time, but reduced the yields.

The vinylketenimines *(4a)*—*(4d)* (Table 1) could be purified by chromatographic methods. On attempted crystallization, *(4b)* added one equivalent of methanol on standing to give the vinylketene *O,N*-acetal *(6)*[5]. Though *(4e)* could be separated by column chromatography it has so far not been obtained in the pure state.

[*] Prof. Dr. G. Ege, Dipl.-Chem. K. Gilbert
Organisch-Chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

[**] Reactions with Cyclopropenes, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft, BASF AG, Bayer AG, and Haarmann-Reimer GmbH.—Part 1: Ref. [1].



R = $COOCH_3$

in the dark. After removal of all volatile components in a rotary evaporator at 30°C the crude oil is separated on a silica gel medium-pressure column with anhydrous petroleum ether (60—70°C)/ether (2:1). The main fraction (IR band at 2060 cm^{-1}) is evaporated in a rotary evaporator; the resulting colorless oil crystallizes. *(4a)*, yield after recrystallization from anhydrous petroleum ether (60—70°C)/ether (1:1) 1.6 g (82%), melts at 146—148°C.

Received: September 4, 1978 [Z 116 IE]
German version: Angew. Chem. *91*, 62 (1979)

[1] *G. Ege, B. Hahn*, Justus Liebigs Ann. Chem. *763*, 39 (1972); cf. also *B. Schrader*, Tetrahedron Lett. *1971*, 2993.
[2] *W. J. Middleton*, J. Org. Chem. *30*, 1402 (1965); *N. Obata, T. Takizawa*, Tetrahedron Lett. *1969*, 3403.
[3] *H. J. Dillinger, G. Fengler, D. Schumann, E. Winterfeldt*, Tetrahedron *30*, 2553 (1974); *T. Takizawa, N. Obata, Y. Suzuki, T. Yanagida*, Tetrahedron Lett. *1969*, 3407; *A. Krebs, H. Kimling*, Angew. Chem. *83*, 401, 540 (1971); Angew. Chem. Int. Ed. Engl. *10*, 409, 509 (1971).

Table 1. Data for the vinyl ketenimines *(4a)*—*(4e)*.

	X	R′	M.p. [°C]	Yield [%]	UV (CH_2Cl_2) λ_{max} [nm] (ε)	IR [cm^{-1}]	^{1}H-NMR (60 MHz, δ-values; in $CDCl_3$/TMS	HMS(*m/e*) calc. obs.
a	H, H	$COOCH_3$	146—148	82	326 (8000), 251 (21200)	2060	1.16 (s, 9H, *t*-C_4H_9), 3.50 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 6.4—8.1 (m, 10H, aromat. H)	391.1783 391.1767
b	Direct linkage	$COOCH_3$	30—35 [a]	62	372 (8100), 319 (6500), 303 (7600), 264 (37300), 255 sh (30900), 244 (28400)	2060	1.32 (s, 9H, *t*-C_4H_9), 3.77 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 7.1—7.9 (m, 8H, aromat. H)	389.1627 389.1642
c	$C(CH_3)_2$	$COOCH_3$	130—131	63	321 (8600), 266 (8600)	2050	1.33 (s, 9H, *t*-C_4H_9), 1.67 (s, 6H, $C(CH_3)_2$), 3.47 (s, 3H, OCH_3), 3.58 (s, 3H, OCH_3), 7.0—7.8 (m, 8H, aromat. H)	431.2096 431.2099
d	CH_2—CH_2	$COOCH_3$	92—94	53	312 (5600), 260 (19100)	2060	1.27 (s, 9H, *t*-C_4H_9), 2.4—3.8 (m, 4H, CH_2CH_2), 3.46 (s, 3H, OCH_3), 3.56 (s, 3H, OCH_3), 6.9—7.5 (m, 8H, aromat. H)	417.1940 417.1929
e	Direct linkage	H	oil [b]	43	—	2025	1.34 (s, 9H, *t*-C_4H_9), 3.90 (s, 3H, OCH_3), 6.9—7.9 (m, 8H, aromat. H), 8.0 (s, 1H, olefin. H)	—

[a] Yellow glassy mass. [b] Not pure.

The reaction is initiated by nucleophilic attack of the *tert*-butyl isocyanide *(2)* at the reactive double bond of the cyclopropene *(1)*. The dipolar compound *(3)* is formed, in which the negative charge on the cyclopropane ring is stabilized by the electron acceptor R. Subsequent opening of the cyclopropane ring in *(3)* leads to the conjugated ketenimine *(4)*. This ring cleavage opens up a new entry to vinylketenimines *(4)*, only one example of which has hitherto been described in the literature[6].

The constitutionally specific ring-opening of the adduct *(3)* rules out intermediary formation of a bicyclobutanone imine *(5)*: the unsymmetrically substituted *(3e)* affords exclusively *(4e)*. The structure of *(4e)* follows from the long-wave position of the ketenimine band at 2025 cm^{-1} [*(4a)*—*(4d)*: 2050 to 2060 cm^{-1}] and the downfield position of the ^{1}H-NMR signal of the $COOCH_3$ group at δ = 3.90 [*(4b)*: δ = 3.95 and 3.77].

Experimental

Synthesis of *(4a)*: *(1a)*[1] (1.54 g, 5 mmol) is dissolved in anhydrous benzene (30 ml), treated with 0.42 g (5 mmol) *(2)* and allowed to stand for three days at room temperature

[4] *(1a)* see [1]; *(1b)*: *G. Ege*, Tetrahedron Lett. *1963*, 1667; *(1c)*, *(1d)*: *K. Gilbert*, projected Dissertation, Universität Heidelberg 1979; *(1e)*: *H. Reimlinger*, Chem. Ber. *100*, 3097 (1967).
[5] *(6)*: yellow crystals, m.p. 187—189°C (CH_3OH); UV (CH_2Cl_2): 412 (12800), 287 (22600), 272 sh (34400), 264 (35600), 250 (41000) nm; IR (KBr): 3240 (NH), 1715, 1645, 1600 cm^{-1} (enamino ester); ^{1}H-NMR (90 MHz, $CDCl_3$): δ = 1.37 (s, 9H, *t*-C_4H_9), 3.64 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 7.0—7.7 (m, 8H, aromat. H), 9.64 (s, 1H, NH, exchangeable).
[6] *E. Sonveaux, L. Ghosez*, J. Am. Chem. Soc. *95*, 5417 (1973); regarding a dienylketenimine cf. *H. H. Eckhardt, H. Perst*, Angew. Chem. *90*, 497 (1978); Angew. Chem. Int. Ed. Engl. *17*, 465 (1978).

Oxidation of Hydrocarbons with Benzyl(triethyl)ammonium Permanganate

By *H.-Jürgen Schmidt* and *Hans J. Schäfer*[*]

CH bonds can be oxidized with permanganate ions; however, the use of this method is greatly restricted by the insolubility of the alkanes in aqueous solution[1]. A further disad-

[*] Prof. Dr. H. J. Schäfer, Dipl.-Chem. H.-J. Schmidt
Organisch-chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

vantage is that alkylarenes are degraded to arenecarboxylic acids[2]. The advantages of oxidation in organic solvents have hitherto been exploited only in isolated cases. Olefins can be cleaved to carboxylic acids with potassium permanganate in benzene, if the potassium ion is complexed with a crown ether[3]. In pyridine, alcohols and aldehydes can be oxidized to carboxylic acids with tetrabutylammonium permanganate[4].

We report here on the oxidation of alkanes with benzyl(triethyl)ammonium permanganate *(1)* in dichloromethane or glacial acetic acid (Table 1). *(1)* precipitates as a violet salt on treatment of an aqueous solution of the corresponding chloride with potassium permanganate[5]. It is thermally stable at 100°C, resistant to shock, and readily soluble in dichloromethane and glacial acetic acid (0.3—0.5 mol/l), in which it is relatively stable.

Table 1. Products of the oxidation of alkanes with benzyl(triethyl)ammonium permanganate *(1)*.

Alkane	Oxidation products, Yields [a]
Cumene *(2)* [b]	2-Phenyl-2-propanol, 28 % (98 %); acetophenone, 1 %
sec-Butylbenzene *(3)* [c]	2-Phenyl-2-butanol, 12 % (61 %); acetophenone, 1 %; propiophenone, 1 %; (1-methyl-1-phenylpropyl)acetate, 2 % (12 %)
Isobutylbenzene *(4)* [d]	Isobutyrophenone, 26 % (51 %); 2-methyl-1-phenyl-2-propanol, 3 %; (α,α-dimethylphenethyl)acetate, 20 % (38 %)
n-Butylbenzene *(5)* [e]	*n*-Butyrophenone, 44 % (61 %); (1-phenylbutyl)acetate, 26 % (37 %)
3-Ethylpentane *(6)* [f]	3-Pentanone, 12 % (25 %); 3-ethyl-2-pentanone, 13 % (25 %); 3-ethyl-3-pentanol, 12 % (24 %); (1,1-diethylpropyl)acetate, 5 % (10 %)
Methylcyclohexane *(7)* [g]	1-Methylcyclohexanol, 23 % (72 %); 2-methylcyclohexanone, 3 %
trans-Decalin *(8)* [h]	*trans*-9-Decalol, 11 % (37 %); *trans*-1-decalone, 13 % (43 %); *trans*-2-decalone, 3 %
cis-Decalin *(9)* [h]	*cis*-9-Decalol, 33 % (67 %)

[a] Chromatographically determined yields, based on original amount of alkane and (in brackets) on consumed alkane. [b] 50 mmol *(2)*, 52 mmol *(1)*, 6 mmol pyridine, 3 d at 40°C in CH_2Cl_2. [c] 50 mmol *(3)*, 50 mmol *(1)*, 2 d at 40°C in glacial acetic acid. [d] 50 mmol *(4)*, 10 mmol *(1)*, 100 mmol $KMnO_4$, 4 d at 30°C in glacial acetic acid. [e] As in [d] but only 2 d. [f] As in [d] but at 50°C. [g] As in [d] but 2 d at 60°C. [h] as in [d] but only 3 d.

Benzylic methylene groups [*(4)*, *(5)*] are oxidized to the ketone; cleavage to benzoic acid is suppressed. Tertiary benzylic CH-groups [*(2)*, *(3)*] are smoothly transformed into tertiary alcohols. Some aliphatic methine groups [*(4)*, *(6)*—*(9)*] require higher reaction temperatures and activation of the permanganate by glacial acetic acid as solvent, whereupon the alcohol formed is partially dehydrated and/or secondary methylene groups are also oxidized. Hydroxylation of the decalins [*(8)*, *(9)*] proceeds stereospecifically with retention of configuration.

In the oxidation of alkanes with *(1)* the yields obtained are not as high as those achieved by dry ozonolysis[6]; however, the former method appears to be advantageous for the oxygenation of alkylarenes, which are degraded to alkylcarboxylic acids by ozone[7].

Experimental

Preparation of benzyl(triethyl)ammonium permanganate *(1)*[5]: A solution of benzyl(triethyl)ammonium chloride (227.8 g, 1.00 mol) in 200 ml water is added dropwise and slowly to a solution of potassium permanganate (158.0 g, 1.00 mol) in 4.7 l water. The violet crystals are recovered by filtration and dried at 40°C/0.2 torr. Yield of *(1)* 294.8 g (0.947 mol, 95 %; over 99 % pure (iodometrically)); m.p. (decomp.) 127—129°C.

Received: November 6, 1978 [Z 123a IE]
German version: Angew. Chem. *91*, 77 (1979)

[1] *D. G. Lee* in *R. L. Augustine*: Oxidation. Marcel Dekker, New York 1969, Vol. 1, p. 3.
[2] *R. Stewart* in *K. B. Wiberg*: Oxidation in Organic Chemistry. Academic Press, New York 1965, Part A, p. 39; *C. F. Cullis, J. W. Ladbury*, J. Chem. Soc. *1955*, 2850.
[3] *D. J. Sam, H. E. Simmons*, J. Am. Chem. Soc. *94*, 4024 (1972); *G. W. Gokel, H. D. Durst*, Synthesis *1976*, 168.
[4] *T. Sala, M. V. Sargent*, J. Chem. Soc. Chem. Commun. *1978*, 253.
[5] *T. Claussen*, Diplomarbeit, Universität Münster 1977.
[6] *Z. Cohen, E. Keinan, Y. Mazur, T. H. Varkony*, J. Org. Chem. *40*, 2141 (1975).
[7] *H. Klein, A. Steinmetz*, Tetrahedron Lett. *1975*, 4249.

Oxidation of Ethers with Benzyl(triethyl)ammonium Permanganate

By *H.-Jürgen Schmidt* and *Hans J. Schäfer*[*]

Ruthenium tetraoxide has long been known to be a particularly suitable reagent for the oxidation of alkyl ethers[1]. Other oxidizing agents have also been used. For example, chromium trioxide[2] and trichloroisocyanuric acid[3] oxidize ethers to esters and lactones, respectively. Reaction with bromine[4], uranium hexafluoride[5], lead tetraacetate[6] or ozone[7], as well as anodic oxidation[8], leads *via* oxidative cleavage of the ethers to carboxylic acids, ketones and alcohols. Ruthenium tetroxide is, of course, only suitable for the oxidation of dialkyl ethers, since aryl groups are oxidatively degraded. This disadvantage is overcome on oxidation with benzyl(triethyl)ammonium permanganate *(1)*, which oxidizes ethers cleanly and chemoselectively to esters (Table 1).

Table 1. Products of the oxidation of ethers with benzyl(triethyl)ammonium permanganate *(1)*.

Ether	Oxidation products, Yields [a]
Dibutyl ether *(2)* [b]	Butyl butyrate, 58 % (80 %)
Dibenzyl ether *(3)* [c]	Benzyl benzoate, 80 % (84 %); methylene dibenzoate, 8 %
Benzyl butyl ether *(4)* [d]	Butyl benzoate, 90 % (99 %)
Butyl methyl ether *(5)* [e]	Methyl butyrate, 23 % (40 %)
Methyl octyl ether *(6)* [f]	Methyl octanoate, 41 % (79 %)
Benzyl (1-ethylpropyl) ether *(7)* [g]	(1-Ethylpropyl) benzoate, 84 % (85 %)
Benzyl methyl ether *(8)* [g]	Methyl benzoate, 83 % (84 %)
Butyl (1-ethylpropyl) ether *(9)* [h]	(1-Ethylpropyl) butyrate, 45 % (73 %); 3-pentanone, 3 %
Benzyl (1-phenylethyl) ether *(10)* [i]	(1-Phenylethyl) benzoate, 71 % (83 %); acetophenone, 6 %
Benzyl phenyl ether *(11)* [j]	Phenyl benzoate, 42 % (94 %)
Butyl (1-phenylethyl) ether *(12)* [k]	Acetophenone, 38 % (67 %); (1-phenylethyl) butyrate, 3 %; butyl benzoate, 2 %
Butyl phenyl ether *(13)* [f]	Phenyl butyrate, 11 % (92 %)

[a] Yields based on initial amount of ether and (in brackets) amounts of ether consumed; determined by gas-chromatography. [b] 30 mmol *(2)*, 10 mmol *(1)*, 50 mmol $KMnO_4$ in 100 ml H_2O, 100 ml CH_2Cl_2, 14 d at 30°C. [c] 30 mmol *(3)*, 60 mmol *(1)* in CH_2Cl_2, 6 d at −5 to 20°C. [d] As in [c], but 8 d at 0°C. [e] As in [b], but 10 d at 42°C. [f] As in [b], but at 42°C. [g] As in [c], but 7 d at −5°C. [h] As in [b], but 30 to 42°C. [i] As in [c], but 9 d at 5°C. [j] As in [c], but 9 d at 0°C. [k] As in [b], but 8 d at 25°C.

[*] Prof. Dr. H. J. Schäfer, Dipl.-Chem. H.-J. Schmidt
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

The esters formed from the unsymmetrical ethers and the reaction times and temperatures indicate the following reactivity sequence for the individual CH-bonds: benzyl > phenylalkyl > *primary*-alkyl > *secondary*-alkyl, methyl > phenyl. In phenyl ethers the phenyl group deactivates the CH-group of the alkyl residue.

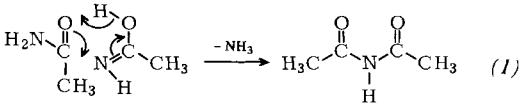
Received: November 6, 1978 [Z 123b IE]
German version: Angew. Chem. 91, 78 (1979)

[1] *L. M. Berkowitz, P. N. Rylander*, J. Am. Chem. Soc. *80*, 6682 (1958); *M. E. Wolff, J. K. Kerwien, F. F. Owings, B. B. Lewis, B. Blank*, J. Org. Chem. 28, 2729 (1963); *D. G. Lee, M. van den Engh* in *W. S. Trahanovsky*: Oxidation in Organic Chemistry. Academic Press, New York 1973, Part B, p. 222.
[2] *I. T. Harrison, S. Harrison*, J. Chem. Soc. Chem. Commun. *1966*, 752; *W. Hückel, H. Bretschneider*, J. Prakt. Chem. *11*, 61 (1938); *H. B. Henbest, B. Nicholls*, J. Chem. Soc. *1959*, 227.
[3] *E. C. Juenge, M. D. Corey, D. A. Beal*, Tetrahedron *27*, 2671 (1971); *E. C. Juenge, D. A. Beal*, Tetrahedron Lett. *1968*, 5819.
[4] *N. C. Deno, N. H. Potter*, J. Am. Chem. Soc. *89*, 3550 (1967).
[5] *G. A. Olah, J. Welch, T. L. Ho*, J. Am. Chem. Soc. *98*, 6717 (1976).
[6] *V. Franzen, R. Edens*, Justus Liebigs Ann. Chem. *735*, 47 (1970).
[7] *K. A. Pollart, R. E. Miller*, J. Org. Chem. *27*, 2392 (1962).
[8] *T. Shono, Y. Matsumura*, J. Am. Chem. Soc. *91*, 2803 (1969).

Intermolecular Ene Reactions in a High-Pressure/High-Temperature Flow Apparatus[**]

By *Jürgen Metzger* and *Peter Köll*[*]

In the thermal degradation of chitin in supercritical acetone[1] we were able to demonstrate the presence of large amounts of diacetamide *(1)*, which can be formed by dimerization of the acetamide molecules in the sense of an ene reaction.

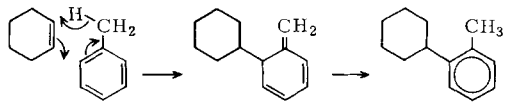


(1)

This finding encouraged us to investigate some ene reactions[2], as example of the numerous types of thermal pericyclic reactions[3], in the same high-pressure/high-temperature apparatus ("HP-HT" apparatus)[1], which enables relatively unproblematical operation at pressures of up to *ca.* 500 bar and temperatures of up to *ca.* 700 K, and is readily built from commercially available HPLC and GC equipment. The apparatus offers all the advantages of a flow reactor, such as exceptionally rapid withdrawal of sensitive products from the reaction zone and the possibility of quickly changing the reaction parameters with slightest consumption of substances.

Whereas numerous *intra*molecular ene reactions, even with *nonactivated* enophiles, have already been reported[4], *inter*molecular ene reactions generally require *active* enophiles[2]. It was predicted, however, that if the latter reactions were to be carried out at high pressures, besides the usual conditions employed for ene reactions, namely high temperatures and long reaction times, then *inter*molecular ene reactions with *nonactivated* enophiles should also be possible. Thus, the reactions carried out at high temperatures under pressure by *Nemtsov et al.*[5] in 1938 with the aim of polymerizing olefins may be regarded as ene reactions. The reaction of acetylene as moderately active enophile with olefins at 623 K and 170 bar to give 1,4-dienes—likewise in a flow reactor—also demonstrates the influence of pressure in such reactions[6].

In all the examples so far investigated by us (cf. Table 1) the expected products were seen to be formed in the overall main reaction. Even toluene was found to react as "deactivated" ene component with non-activated enophiles; reaction with cyclohexene afforded *o*-cyclohexyltoluene *(2)*.



(2)

The yields quoted in Table 1 are not optimized and might easily be increased to preparatively satisfactory values by increasing the residence time of the reactants (incorporation of a longer reaction capillary or reduction in the rate of flow of reactants). A typical example here is the synthesis of 3-cyclohexylcyclohexene from cyclohexene (see Experimental). Such a dimerization apparently proceeds regiospecifically, corresponding to the expected pericyclic mechanism. (With longer residence times, however, about 5 % of the primary product isomerizes to 1-cyclohexylcyclohexene.) Thus, the thermal olefin-dimerization and the alkylation of toluene described here are superior to the catalytic methods, at least as far as regioselectivity is concerned.

Table 1. Some intermolecular ene reactions with non-activated enophiles. Reaction conditions: 673 K, 450 bar, 10 min residence time, ene:enophile = 10:1, conversion based on enophile. Characterization of the products by GC-MS.

Ene	Enophile	Reaction product(s)	Conversion [%]
1-Hexene	1-Hexene	Mixture of isomeric dodecenes	5
Cyclohexene	Cyclohexene	3-Cyclohexylcyclohexene	4.5
Acetone	Cyclohexene	Cyclohexylacetone	0.5
Toluene	Cyclohexene	*o*-Cyclohexyltoluene	1.2
Toluene	Tolan	1,2-Diphenyl-1-tolylethylene	15

Experimental

Synthesis of 3-cyclohexylcyclohexene: Cyclohexene (20 g) is pumped through the "HP-PT" apparatus[1] at 673 K and 460 bar at a flow-rate of 0.12 ml/min and with a residence time of *ca.* 50 min. A 15-m long stainless steel capillary (O.D. 1.6 mm, I.D. 0.7 mm) can be used as reactor. Unreacted cyclohexene (16 g) is removed by distillation. The residue (3.4 g, 17 %) mainly consists of pure 3-cyclohexylcyclohexene, which is further purified by distillation: b.p. 98 °C/10 torr, $n_D^{20} = 1.4912$ (b.p. 224 °C/760 torr, $n_D^{20} = 1.4941$[7]). The IR, NMR, and mass spectra are consistent with the given structure.

Received: September 29, 1978 [Z 130a IE]
German version: Angew. Chem. 91, 74 (1979)

[*] Prof. Dr. P. Köll, Dr. J. Metzger
Fachbereich 4 (Naturwissenschaften) der Universität
Ammerländer Heerstr. 67—99, D-2900 Oldenburg (Germany)

[**] Part 2 of High-Pressure/High-Temperature Reactions in a Flow Reactor.—Part 1: [1].

[1] *P. Köll, J. Metzger*, Angew. Chem. *90*, 802 (1978); Angew. Chem. Int. Ed. Engl. *17*, 754 (1978).
[2] *H. M. R. Hoffmann*, Angew. Chem. *81*, 597 (1969); Angew. Chem. Int. Ed. Engl. *8*, 566 (1969).
[3] *J. B. Hendrickson*, Angew. Chem. *86*, 71 (1974); Angew. Chem. Int. Ed. Engl. *13*, 47 (1974).

[4] W. Oppolzer, V. Snieckus, Angew. Chem. 90, 506 (1978); Angew. Chem. Int. Ed. Engl. 17, 476 (1978).
[5] M. S. Nemtsov, T. V. Nizovkina, E. A. Soskina, J. Gen. Chem. (USSR) 8, 1303, 1324 (1938); Chem. Abstr. 33, 4206 (1939).
[6] N. F. Cywinski, J. Org. Chem. 30, 361 (1965).
[7] W. Hückel, R. Bross, O. Fechtig et al., Justus Liebigs Ann. Chem. 624, 142 (1959).

Thermal Pericyclic Reaction between Alkynes and Alkanes[1]

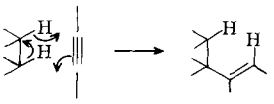
By *Jürgen Metzger* and *Peter Köll*[*]

From results of intermolecular ene reactions[2] in a high-pressure/high-temperature flow reactor ("HP-HT" apparatus) it was predicted that hitherto presupposed but unobserved thermal pericyclic reactions ought to be realizable at high pressures and temperatures with rapid removal of reaction products. We first examined the reaction of 1-hexyne in *n*-hexane (1 : 10) under such conditions, expecting to observe not only the trimerization of the alkyne to benzene derivatives but also a dimerization in the sense of an ene reaction, which should lead to allene derivatives. A hexyne dimer was indeed detectable in small amounts by combined GC-MS. Surprisingly, however, we obtained alkenes as major products (0.9 % octene, 0.9 % nonene, 1 % decene, 6 % dodecene, 2.6 % tributylbenzene; in each case isomeric mixtures; yields based on starting 1-hexyne). These alkenes could only have been formed by reaction of 1-hexyne with *n*-hexane.

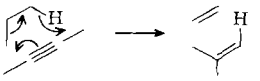
To check the possible generalization of this surprising observation we examined the reaction of cycloalkanes with alkynes in the same HP-HT reactor[3]. As shown in Table 1, in each of the cases investigated the alkenylcycloalkanes are formed as major products in a remarkably uniform reaction.

Owing to the extremely drastic reaction conditions free radicals were assumed to be involved in the reaction, particularly since the formation of vinylcyclohexane is known to take place in the presence of radical-forming species[4, 5]. Addition of radical scavengers, however, did not influence the yield of main product. In our opinion, this finding rules out a radical chain reaction.

The reaction is apparently another novel type of thermal pericyclic reaction, which also ought to be possible on theoretical grounds[6]. The formation of the major products can best be described by the general scheme:



As side reaction an alkyl group obviously can migrate (with cleavage and reformation of a CC σ-bond) instead of a hydrogen atom. This would explain the formation of octene, nonene, and decene in the reaction of *n*-hexane with 1-hexyne, as well as the fact that undecene is not observed:



The new pericyclic reaction might be of interest both for the functionalization (vinylation) and for the fragmentation (thermal non-radical cracking) of alkanes to alkenes.

General Procedure

The alkynes are dissolved in an excess of alkane; in the case of gaseous alkynes, the alkane is saturated in an autoclave with the alkyne. The solution is pumped through the HP-PT apparatus[3]. As reactor for the present series of experiments we used a stainless steel capillary (length 12 m, O.D. 1.6 mm, I.D. 0.7 mm). The following reaction conditions proved to be suitable: $T = 623$—673 K, $p = 350$—500 bar, flow rate 1—3 ml/min.

Table 1. Reactions of alkanes and alkynes (reaction conditions: $T = 673$ K, in the case of Nos. 1 and 2, 633 K; $p = 400$ bar). The products were identified by GC-MS and determined gas chromatographically using an internal standard. The major products were isolated by distillation (Nos. 2, 4, 5) or by preparative thin-layer chromatography (No. 3) and investigated by NMR and IR-spectroscopy.

No.	Alkane	Alkyne	Alkane : Alkyne	Residence time [min]	Main product(s)	Yield [%] [a]
1	*n*-Hexane	1-Hexyne	10 : 1	4	Dodecene isomers	6
2	Cyclohexane	1-Hexyne	20 : 1	2	*trans*-1-Cyclohexyl-1-hexene	7.5
					cis-1-Cyclohexyl-1-hexene	2.6
					2-Cyclohexyl-1-hexene	0.8
3	Cyclohexane [b]	Tolan	100 : 1	4.5	*E*- and *Z*-1-Cyclohexyl-1,2-diphenylethylene	20.0
4	Cyclohexane	Acetylene	0.5 bar [c]	2	Vinylcyclohexane	0.2
5	Methylcyclopentane [d]	Acetylene	1.0 bar [c]	4	Methyl(vinyl)cyclopentane (isomeric mixture)	1.5

[a] Yields based on alkyne; in the case of Nos. 4 and 5 on alkane. [b] Same result on addition of 1 % 2,6-di-*tert*-butyl-4-methylphenol (based on cyclohexane). [c] Saturated with acetylene at the given excess pressure. [d] Same result on addition of 1 % hydroquinone (based on methylcyclopentane).

Received: November 16, 1978 [Z 130b IE]
German version: Angew. Chem. 91, 75 (1979)

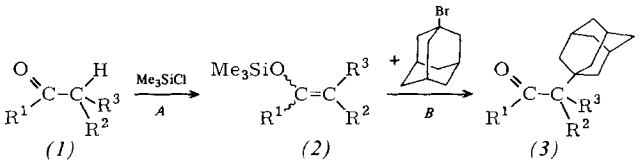
[*] Prof. Dr. P. Köll, Dr. J. Metzger
Fachbereich 4 (Naturwissenschaften) der Universität
Ammerländer Heerstr. 67—99, D-2900 Oldenburg (Germany)

[1] Part 4 of High-Pressure/High-Temperature Reactions in a Flow Apparatus.—Part 3: *P. Köll, E. Steinweg, U. Lackmann, J. Metzger*, Tetrahedron Lett., in press.
[2] *J. Metzger, P. Köll*, Angew. Chem. 91, 74 (1979); Angew. Chem. Int. Ed. Engl. 18, 70 (1979).
[3] *P. Köll, J. Metzger*, Angew. Chem. 90, 802 (1978); Angew. Chem. Int. Ed. Engl. 17, 754 (1978).
[4] *N. I. Shuikin, B. L. Lebedev, V. G. Nikol'ski*, Neftekhimiya 6, 544 (1966).
[5] *R. Srinivasan, K. H. Carlough*, Can. J. Chem. 45, 3209 (1967).
[6] *J. B. Hendrickson*, Angew. Chem. 86, 71 (1974); Angew. Chem. Int. Ed. Engl. 13, 47 (1974).

General Synthesis of Potentially Antiviral α-Adamantyl Carbonyl Compounds[**]

By *Manfred T. Reetz, Wilhelm F. Maier, Konrad Schwellnus,* and *Ioannis Chatziiosifidis*[*]

Recently, it was discovered[1] that certain α-adamantyl carbonyl compounds are considerably more active as antiviral agents and a great deal less toxic than 1-aminoadamantane[2]. The multistep syntheses which were described in [1] are based on phenols as starting materials, and are therefore restricted to the cyclohexanone framework. We wish to report that our method of α-*tert*-alkylation of carbonyl compounds can be applied generally to the introduction of 1-adamantyl groups[3]. Silylenol ethers *(2a)—(2h)*, which are easily obtained from ketones *(1a)—(1h)*[4], react smoothly with 1-bromoadamantane in the presence of titanium tetrachloride at −40 °C to −50 °C to afford the desired α-adamantyl ketones *(3)* in good yields (Table 1). Table 1 shows that structurally



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

Table 1. α-Adamantylation of ketones *(1a)—(1h)* (A: triethylamine; B: $TiCl_4$; −40 to −50 °C) and carboxylic esters *(1i)—(1l)* (A: lithium diisopropylamide; B: catalytic amounts of $ZnCl_2$; room temperature).

	R^1	R^2	R^3	Yield [%] [a]
a		$-(CH_2)_3-$	H	66 (78)
b		$-(CH_2)_4-$	H	89 (95)
c		$-(CH_2)_6-$	H	73 (90)
d	$(CH_3)_2CH$	CH_3	CH_3	62 (75)
e	$-(CH_2)_2-$	$-CHCH_3-CH_2-$	H	72 (80)
f	C_2H_5	CH_3	H	75 (80)
g	$(CH_3)_3C$	H	H	82 (89)
h		[b]		70 (80)
i	OCH_3	$-(CH_2)_5-$		80
j	OCH_3	CH_3	H	47
k	OCH_3	C_2H_5	H	77
l	OC_2H_5	$(CH_3)_3C$	H	70 [c]

[a] The yields are based on isolated products in the reaction *(2)* → *(3)*; the values in brackets were determined by ^{1}H-NMR spectroscopy. [b] 1-Trimethylsiloxy-4-methyl-3,4-dihydronaphthalene *(2h)* → 2-(1-adamantyl)-4-methyl-1-tetralone *(3h)*. [c] Yield *(1l)* → *(2l)*: 84%.

quite different ketones can be alkylated. Also noteworthy is the smooth adamantylation of diisopropyl ketone *(1d)*, which affords the derivative *(3d)* having two neighboring *quaternary* carbon atoms.

In a similar manner carboxylic acid alkyl esters *(1i)—(1h)* can be adamantylated *via* the corresponding ketene ketals *(2i)—(2l)*[5], using catalytic amounts of zinc chloride as Lewis acid at room temperature. Compounds containing *two* tertiary groups on *one* carbon atom can also be prepared, *e.g. (3l)*.

[*] Doz. Dr. M. T. Reetz, Dipl.-Chem. W. F. Maier, K. Schwellnus, I. Chatziiosifidis
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg (Germany)

Present address:
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Straße 1, D-5300 Bonn (Germany)

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

According to *Dubois et al.*[6] it is possible to convert bulky carboxylic acid esters into ketones *via* the corresponding acid chlorides on using Grignard reagents in the presence of copper salts. Combination of the methods allows the synthesis of ketones having adamantyl groups in specific positions.

Concerning the antiviral activity of the compounds *(3)*, *in vitro* tests with viruses of the Newcastle disease show that for example 2-(1-adamantyl)-4-methylcyclohexanone *(3e)* is about three times more active and half as toxic as 1-aminoadamantane[1].

Experimental:

Synthesis of 2-(1-adamantyl)cyclohexanone *(3b)*: A cooled solution (−50 °C) of 3.8 g (20 mmol) titanium tetrachloride in 10 ml dry methylene chloride is added within two minutes to a cooled mixture (−50 °C) of 3.5 g (20 mmol) 1-trimethylsiloxycyclohexene and 4.5 g (20.9 mmol) 1-bromoadamantane in 60 ml of dry methylene chloride. The reaction mixture is stirred for 30 minutes, hydrolyzed, and the solvent of the organic phase evaporated off. Recrystallization of the residue from methanol affords 3.5 g of pure 2-(1-adamantyl)cyclohexanone as well as 1.0 g from the mother liquor: yield 89%; m.p. 86 °C; ^{1}H-NMR (CCl_4): $\delta = 1.72$ (s, 15H), 1.42—2.4 (m, 9H); IR (KBr): 2960, 2930, 2895, 2840, 1695, 1445, 1345, 1310, 1205, 1130, 1120, 1110, 1065 cm^{-1}.

Received: June 19, 1978 [Z 114 IE]
Publication delayed at authors' request
German version: Angew. Chem. *91*, 78 (1979)

[1] *K. Aigami, Y. Inamoto, N. Takaishi, K. Hattori*, J. Med. Chem. *18*, 713 (1975).
[2] Reviews: *R. C. Bingham, P. v. R. Schleyer*, Fortschr. Chem. Forsch. *18*, 83 (1971); *J. S. Wishnok*, J. Chem. Educ. *50*, 780 (1973).
[3] *M. T. Reetz, W. F. Maier*, Angew. Chem. *90*, 50 (1978); Angew. Chem. Int. Ed. Engl. *17*, 48 (1978); see also *T. H. Chan, I. Paterson, J. Pinsonnault*, Tetrahedron Lett. *1977*, 4183.
[4] *H. O. House, L. J. Czuba, M. Gall, H. D. Olmstead*, J. Org. Chem. *34*, 2324 (1969).
[5] *M. T. Reetz, K. Schwellnus*, Tetrahedron Lett. *1978*, 1455.
[6] *C. Lion, J. E. Dubois, Y. Bonzougou*, J. Chem. Research (S) *1978*, 46.

C-Acylation under Virtually Neutral Conditions[**]

By *Dee W. Brooks, Linda D.-L. Lu,* and *Satoru Masamune*[*]

During the course of studies directed toward the total synthesis of macrolide antibiotics, the pressing need for an efficient method of *C*-acylation on acid- and base-sensitive synthetic intermediates became evident[1]. We wish to describe here a practical solution of this fundamental problem.

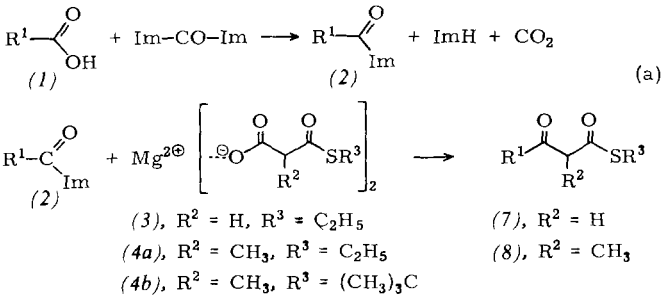
The method is operationally very simple; it involves successive addition of two reagents to a carboxylic acid *(1)* in tetrahydrofuran (THF) [reaction (a)]. Carbonyldiimidazole converts the acid *(1)* into the corresponding imidazolide *(2)*[2], which, without isolation, is treated with the *neutral* magnesium salt of a malonic or methylmalonic acid half thiol ester of type *(3)* or *(4)*. The condensation proceeds in excellent yields and under mild conditions (see Table 1). The β-ketothiol esters of type *(7)* and *(8)* which are obtained are apparently

[*] Dr. D. W. Brooks [+], Ms. L. D.-L. Lu [+], and Professor Dr. S. Masamune [+]
Department of Chemistry, University of Alberta, Edmonton, Alberta T6G 2G2 (Canada)

[+] Present address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139 (USA)

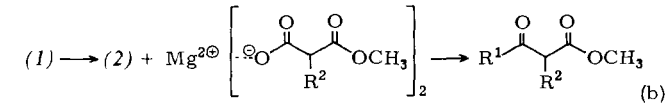
[**] This work was supported by the National Research Council of Canada.

not complexed with magnesium and are readily isolated, either directly by thin layer chromatography or by aqueous work-up.—The reaction can also be carried out with the neutral magnesium salts of the esters *(5)* and *(6)* [Reaction (b); Table 1].



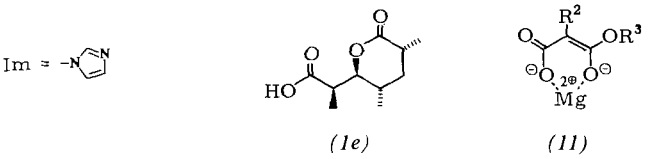
(a)

(3), $R^2 = H$, $R^3 = C_2H_5$ — *(7)*, $R^2 = H$
(4a), $R^2 = CH_3$, $R^3 = C_2H_5$ — *(8)*, $R^2 = CH_3$
(4b), $R^2 = CH_3$, $R^3 = (CH_3)_3C$



(b)

(5), $R^2 = H$; *(6)*, $R^2 = CH_3$ — *(9)*, $R^2 = H$; *(10)*, $R^2 = CH_3$



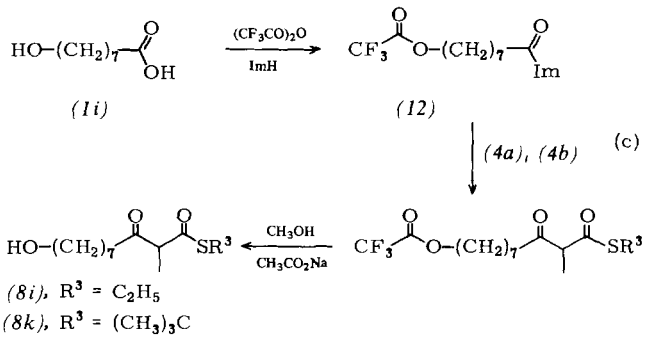
(1e) *(11)*

Table 1. Conversion of carboxylic acids *(1)* into β-ketoesters *(7)*–*(10)* *via* reactions (a) and (b).

No.	Carboxylic acid	R^1	Reagent, conditions [a]		Product	Yield [%] [b]
1	*(1a)*	$C_6H_5(CH_2)_2$	*(3)*	A	*(7a)*	100
2	*(1b)*	*c*-C_6H_{11}	*(3)*	B	*(7b)*	100
3	*(1c)*	$(CH_3)_3C$	*(3)*	B	*(7c)*	100
4	*(1a)*	$C_6H_5(CH_2)_2$	*(4a)*	B	*(8a)*	100
5	*(1a)*	$C_6H_5(CH_2)_2$	*(4b)*	B	*(8b)*	100
6	*(1b)*	*c*-C_6H_{11}	*(4a)*	C	*(8c)*	90
7	*(1d)*	$CH_3CO(CH_2)_2$	*(4a)*	B	*(8d)*	85
8	*(1e)*	[c]	*(3)*	B	*(7d)*	88
9	*(1e)*	[c]	*(4b)*	D	*(8e)*	75
10	*(1f)*	C_6H_5	*(4b)*	D	*(8f)*	85
11	*(1g)*	*t,t*-$CH_3(CH{=}CH)_2$	*(4b)*	D	*(8g)*	95
12	*(1h)*	$CH_3(CH_2)_5CHOH(CH_2)_{10}$	*(4b)*	B	*(8h)*	95
13	*(1a)*	$C_6H_5(CH_2)_2$	*(5)*	B	*(9a)*	100
14	*(1h)*	$CH_3(CH_2)_5CHOH(CH_2)_{10}$	*(5)*	B	*(9b)*	95
15	*(1b)*	*c*-C_6H_{11}	*(5)*	B	*(9c)*	85
16	*(1a)*	$C_6H_5(CH_2)_2$	*(6)*	B	*(10)*	95

[a] Conditions A: 4h, 25°C; B: 18h, 25°C; C: 6h, 35°C; D: 24h, 35°C. [b] Yield of isolated, pure product. [c] Formula, see above; cf. *R. Anliker, D. Dvornik, K. Gubler, H. Heusser, V. Prelog*, Helv. Chim. Acta 39, 1785 (1956); *C. Djerassi, J. A. Zderic*, J. Am. Chem. Soc. 78, 9390 (1958); synthesis: *S. Masamune, C. U. Kim, K. E. Wilson, G. O. Spessard, P. E. Georghiou, G. Bates, ibid.* 97, 3512 (1975); new synthesis: *S. Masamune et al.*, unpublished.

Because of the slightly enhanced reactivity of a primary hydroxy group toward carbonyldiimidazole as compared with a secondary hydroxy group, the above method requires modification when applied to ω-hydroxycarboxylic acids. Thus, treatment of 8-hydroxyoctanoic acid *(1i)* (1.0 mmol) in 4 ml THF with excess imidazole (4.4 mmol) and trifluoroacetic acid anhydride (2.1 mmol) gave the imidazolide *(12)*, which in turn was allowed to react with 1.2 mmol *(4a)* or *(4b)*. Methanolysis in the presence of sodium acetate (25°C for 2h) afforded the ω-hydroxy-β-ketothioester in 90% yield [reaction (c)].



(1i) *(12)*

(c)

(8i), $R^3 = C_2H_5$
(8k), $R^3 = (CH_3)_3C$

The efficient *C*-acylation resulting from reaction of the *neutral* magnesium compounds of type *(3)* or *(4)* with an acid imidazolide *(2)* is surprising and offers distinct advantages in many respects over an earlier, superficially similar method which involves reaction of the *basic* magnesium enolate *(11)* with an acid chloride or imidazolide[3]. With this earlier method, *e.g.*, the acid derivatives of *(1d)* and *(1e)* provided, at best, 25—32% yields of the corresponding products listed in Table 1. Protection of the hydroxy group is normally required before the reaction with *(11)* (cf. entries 12 and 14 in Table 1). Furthermore, the present *C*-acylation proceeds unaffected by the presence of 1 equivalent of cyclohexanecarboxaldehyde, which is recovered intact.

The use of malonic acid half thiol esters patterns the scheme proposed for a similar process involved in the biosynthesis of fatty acids[4]. Early and recent model studies for the enzymatic process[5] have aided us in developing the present synthetically useful procedure.

Experimental

Synthesis of *(4a)*: Magnesium ethoxide (0.49 g, 5 mmol) is added to a solution of methyl malonic acid half ethanethiol ester (1.62 g, 10 mmol) in THF (25 ml) and the mixture is stirred for 1 h. The solvent is removed at reduced pressure (25°C/0.1 torr) to give a slightly hygroscopic white salt which is used directly.

Synthesis of *(8a)* (Table 1, entry 7): Carbonyldiimidazole (180 mg, 1.1 mmol) is added to a solution of levulinic acid *(1d)* (116 mg, 1.0 mmol) in THF (5 ml). After stirring at room temperature for 6 h, the magnesium salt *(4a)* prepared above (380 mg, 1.1 mmol) is added. The mixture is stirred for 18 h at 25°C and then the solvent is removed at reduced pressure. The residue is partitioned between ether (20 ml) and aqueous 0.5 N HCl (20 ml) and the layers are separated. The aqueous phase is further extracted with ether (10 ml). The combined ether extracts are washed with aqueous saturated $NaHCO_3$ (20 ml), dried over anhydrous Na_2SO_4, and filtered. The solvent is evaporated at reduced pressure to give 185 mg (85%) of the β-ketoester *(8d)*; ^{1}H-NMR ($CDCl_3$): $\delta = 1.26$ (t, 3H, $J = 7.5$ Hz), 1.38 (d, 3H, $J = 7.0$ Hz), 2.16 (s, 3H), 2.75 (m, 4H), 2.91 (q, 2H, $J = 7.5$ Hz), 3.82 (q, 1H, $J = 7.0$ Hz); MS: $m/e = 216.0819 = C_{10}H_{16}O_3S$ (M^+).

Received: October 19, 1978 [Z 113 IE]
German version: Angew. Chem. 91, 76 (1979)

[1] For a concise review of acylation of active methylene compounds, see *H. O. House*: Modern Synthetic Reactions. Benjamin, Menlo Park 1972, Chap. 11; For the use of Meldrum's acid for acylation, see *Y. Oikawa,*

K. Sugano, O. Yonemitsu, J. Org. Chem. *43*, 2087 (1978), and references cited therein.
[2] *H. A. Staab, M. Lüking, F. H. Dürr*, Chem. Ber. 95, 1275 (1962).
[3] *R. E. Ireland, J. A. Marshall*, J. Am. Chem. Soc. *81*, 2907 (1959); *G. Bram, M. Vilkas*, Bull. Soc. Chim. Fr. *1964*, 945.
[4] *F. Lynen* in *R. M. S. Smellie*: Chemical Reactivity and Biological Role of Functional Groups in Enzymes. Academic Press, New York 1970, p. 1ff.; *K.-I. Arnstadt, G. Schindlbeck, F. Lynen*, Eur. J. Biochem. *55*, 561 (1975), and references cited therein.
[5] a) *G. E. Lienhard, W. P. Jencks*. J. Am. Chem. Soc. *87*, 3863 (1965); b) *H. Wenck, M. Schallies*, Helv. Chim. Acta *56*, 3059 (1973); c) *Y. Kobuke, J. Yoshida*, Tetrahedron Lett. *1978*, 367. Reaction (a) described herein resembles in some respects the enzyme model reaction described by these authors which appeared during the course of our present study. Their reaction, however, proceeds rather inefficiently and is synthetically applicable to only the condensation of *primary* carboxylic acids with malonic thiol half ester [$R^1 = CH_3$, $R^2 = H$, $R^3 = C_4H_7$, in reaction (a), reaction time 87 h, yield 60 %]; d) For an intramolecular acylation reaction, see *A. I. Scott, C. J. Wiesner, S. Yoo, S.-K. Chung*, J. Am. Chem. Soc. 97, 6277 (1975).

Cyclooligocondensation of Amino Acids: Macrocyclic Amides of β-Alanine[**]

By *Manfred Rothe* and *Dietger Mühlhausen*[*]

The formation of large ring molecules—in competition with polymer formation—from monomers in macrocyclization equilibria or from polymers by degradation has recently attracted increasing theoretical interest[1]. We have investigated the system β-alanine/cyclooligo(β-alanyls)/poly-β-alanine, which is of interest with respect to the industrial production of fiber-forming poly-β-amides (nylon 3) from β-lactams[2].

We first synthesized cyclic oligoamides of β-alanine *c*-$(NHCH_2CH_2CO)_n$ *(2)* up to the hexamer ($n=2$—6) in crystalline form by stepwise synthesis of the linear oligoamides $H(NHCH_2CH_2CO)_nOH$ *(1)*, $n=2$—6, according to the methods of peptide chemistry (*via* mixed anhydrides with isobutyl chloroformate, benzyloxycarbonyl protecting group removed with HBr/glacial acetic acid) and ring closure of *(1) via* active esters $H(NHCH_2CH_2CO)_n\ SC_6H_5$ in dimethylformamide or phosphorous anhydrides $H(NHCH_2CH_2CO)_n—O—P(OR)_2$ in diethyl phosphite (DEP) according to the dilution principle. With the exception of cyclo-di-β-alanyl *(2)*, $n=2$[3] (m.p. 298—299 °C), the cyclic amides *(2)* decompose without melting only above 350 °C.

The results of the cyclization of the linear oligoamides *(1)* in the form of their active phosphite derivatives are listed in Table 1. These findings cannot be explained in terms of a specific "doubling" resulting from antiparallel association of two oligoamide chains with formation of hydrogen bonds[4], but by polycondensation with subsequent cyclization, especially as an alternative reaction to formation of strained medium-sized rings. Consequently, higher ring homologues are also formed.

We subsequently condensed the "monomeric" amino acid β-alanine according to the phosphite method[5] in moderately dilute solution in DEP ($c=0.1$ mol/l) with *o*-phenylene chlorophosphite (*o*-phenylene phosphorochloridite) at 140 °C. After removal of the linear oligoamides *(1)* with ion exchangers in aqueous solution a cycloamide mixture was obtained which could be separated by gelchromatography (Merckogel PGM 2000/water) into a homologous series of polymeric rings with up to 44 ring atoms [*(2)*, $n=2$—11]. The assignment of the peaks was accomplished with the aid of the synthesized authentic cycloamides by plotting the elution volumes of the gel chromatograms against the logarithm of the molecular weight (in homologous series of polymers a straight line is obtained within a certain range), and by mass spectrometry of the isolated compounds.

Table 1. Cyclization of phosphite derivatives of the linear oligoamides $H(NHCH_2CH_2CO)_nOH$ *(1)* in 0.01 M solution.

	(1), n =	*c*-$(NHCH_2CH_2CO)_n$ *(2)*, n =					
Products	2	2	4	6	8	10	12
Ring atoms		8	16	24	32	40	48
Yield		23 %	44 %	10 %	3 %	1 %	0.5 %
Products	3	3	6	9			
Ring atoms		12	24	36			
Yield		58 %	11 %	2.5 %			
Products	4	4	8				
Ring atoms		16	32				
Yield		68 %	2.5 %				

Remarkably, the monomeric four-membered ring (β-propiolactam) *(2)*, $n=1$, could not be detected, even at larger dilutions; and also the eight-membered ring *(2)*, $n=2$, containing two *cis*-peptide bonds (detected IR spectroscopically: NH 3195, 3080; amide I 1660; amide II 1440; amide III 1330 cm^{-1}) was formed in only moderate yields. In each case the cyclo-tri- and cyclo-tetraamide (12 and 16 ring atoms, respectively; Table 2) were obtained as the main products.

Table 2. Cyclization of β-alanine according to the phosphite method [a]. The yields of *(2)* are given in %.

c	*c*-$(NHCH_2CH_2CO)_n$ *(2)*, n =								
[mol/l]	2	3+4	5	6	7	8	9	10	11
0.001	21	17	4	2	2				
0.01	19	48	6	3	2				
0.1	3	27	11	7	2	1	0.5	0.2	0.2

[a] Conditions: see Experimental procedure b.

The formation of macrocyclic rings can be compared with that of large rings containing up to 63 ring atoms during the polymerization of caprolactam[6]. According to X-ray structure investigations[7] such very large rings are present—at least in the nylon-6 series—as parallel chains, closed at the ends. They therefore resemble the linear polymers in their physical properties, especially in their spectra and solubility. Hence their separation from the chains, and even their detection is always problematical with increasing ring size. Nevertheless, our previous studies (cf. Ref. [6, 8]) show that very large ring molecules are obviously always formed—besides the simplest small rings—during the formation of polymers. Heteroatoms[9] as well as increasing temperature and concentration favor the formation of large rings.

The chromatographic separation of the rings could be achieved quantitatively (baseline separation) up to the heptamide or octamide (after repeated GPC). Complete separation of the tri- and tetramide can be carried out by GPC on Biogel P2. Thus, cycloamides with up to eight amide groups

[*] Prof. Dr. M. Rothe, Dr. D. Mühlhausen
Lehrstuhl Organische Chemie II der Universität
Oberer Eselsberg, D-7900 Ulm
sowie Organisch-chemisches Institut der Universität Mainz (Germany)

[**] Linear and Cyclic Oligomers, Part 25. This work was supported by the Fonds der Chemischen Industrie.—Part 24: *M. Rothe* in *J. Brandrup, E. J. Immergut*: Polymer Handbook. 2nd Edit. Wiley-Interscience, New York 1975, VI-1.

were readily made available in a one-step reaction. The cycloamides *(2)* can be converted by reduction with $LiAlH_4$ in THF suspension into cycloamines $c\text{-}(NHCH_2CH_2CH_2)_n$ of the same size, which as aza-crown ethers form alkali metal ion complexes. This method of formation—also starting from other ω-amino acids—may constitute the simplest route to such ring compounds.

Experimental

a) Cyclization of tri-β-alanine *(1)*, $n=3$: *(1)*, $n=3$, 695 mg (3.0 mmol) is dissolved with warming and stirring in 500 ml DEP, treated with 7 ml diethylethylene pyrophosphite, and heated for 2 h at 140°C under nitrogen. All but 10 ml of the solvent is removed *in vacuo*, and the crystalline precipitate filtered off and washed with acetone; yield of crude product 579.1 mg (91%). After gel chromatographic purification (Sephadex G 10/H_2O) 156.1 mg (65%) of *(2)*, $n=3$, 30.7 mg (13%) of *(2)*, $n=6$, and 5.9 mg (2.5%) of *(2)*, $n=9$, are obtained. Cyclo-tri-β-alanyl *(2)*, $n=3$, crystallizes from H_2O as long entangled needles which sublime above 280°C and do not melt below 350°C.

b) Cyclooligocondensation of β-alanine: 223 mg (2.5 mmol) of dried and sieved β-alanine is dissolved by heating in 25 ml DEP at 140°C. After addition of a twofold molar excess of *o*-phenylene chlorophosphite (873 mg) and subsequent addition of a threefold molar excess of anhydrous triethylamine (1.05 ml) the solution is allowed to stand under N_2 for 30 min. The DEP is removed in a rotary evaporator (oil pump vacuum), the residue dissolved in 30 ml H_2O and neutralized with strongly basic ion exchanger and then passed through cationic and anionic exchangers (Merck I, Amberlite IRA 410). The colorless eluate is removed in a rotary evaporator *in vacuo* and the crystalline cycloamide mixture (64%) separated by gel chromatography on Merckogel PGM 2000/H_2O, the tri-/tetraamide fraction being subsequently separated on Bio-Gel P2.

Received: October 12, 1978 [Z 115 IE]
German version: Angew. Chem. *91*, 79 (1979)

[1] *P. J. Flory, U. W. Suter, M. Mutter*, J. Am. Chem. Soc. *98*, 5733, 5740, 5745 (1976); *J. A. Semlyn*, Adv. Polym. Sci. *21*, 41 (1976).
[2] *H. Bestian*, Angew. Chem. *80*, 304 (1968); Angew. Chem. Int. Ed. Engl. *7*, 278 (1968).
[3] *M. Rothe, R. Timler*, Chem. Ber. 95, 783 (1962).
[4] *R. Schwyzer, P. Sieber*, Helv. Chim. Acta *41*, 2186 (1958).
[5] *M. Rothe, I. Rothe, H. Brünig, K.-D. Schwenke*, Angew. Chem. *71*, 700 (1959).
[6] *M. Rothe*, J. Polym. Sci. 30, 227 (1958); Makromol. Chem. *35*, 183 (1959).
[7] *H. Zahn, J. Kunde*, Justus Liebigs Ann. Chem. *618*, 158 (1958).
[8] *M. Rothe, D. Mühlhausen*, Angew. Chem. *88*, 338 (1976); Angew. Chem. Int. Ed. Engl. *15*, 307 (1976).
[9] *C. Rentsch, R. C. Schulz*, Makromol. Chem. *178*, 2535 (1977).

Thermolysis of Arenediazonium Pentacarbonylcyano-6A-metalates in Various Media: A Route to Novel α-Functionalized Isocyanides[**]

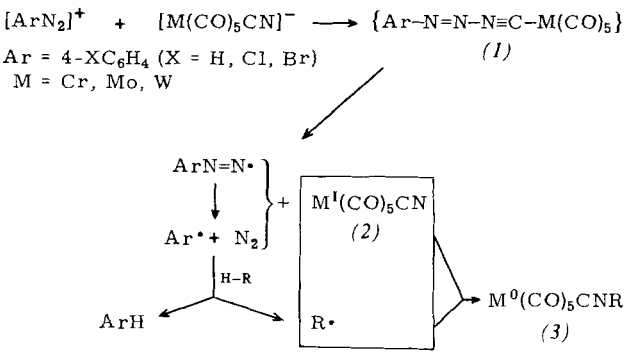
By *Wolf Peter Fehlhammer* and *Fritz Degel*[*]

The stability of diazonium salts is strongly dependent on the nature of the anion. In general, replacement of simple anions (*e.g.* Cl^-) by complex ions such as $SbCl_6^-$, $Fe(CN)_6^{3-}$, $PtCl_6^{2-}$, or $HgCl_3^-$ has a stabilizing effect[1]. Conversely, however, it is also known that even traces of oxidizable anionic metal complexes may catalyze the decomposition of diazonium compounds; this is, in fact, the basic principle of the Sandmeyer reaction[2].

We have now found that pentacarbonylcyano-6A-metalate ions also have a strong labilizing effect on diazonium compounds and have exploited this for the *synthesis of novel isocyanides within metal complexes.*

At temperatures between −50 and −20°C nitrogen is already released from mixtures of $Na[M(CO)_5CN]$ (M = Cr, Mo, W) and arenediazonium chlorides ($[4\text{-}XC_6H_4N_2]Cl$; X = H, Cl, Br) either dissolved or suspended in various media. Reaction in tetrahydrofuran of stoichiometric amounts of these compounds afforded crystalline, sublimable products, which, on the basis of their IR spectra and their fragmentation pattern in the mass spectrometer (−5 CO, $[ML-27(HCN)]^+$, $[MCNH]^+$), were identified as (pentacarbonyl)isocyanide complexes. Surprisingly, these complexes—independent of the arenediazonium components employed—contain the same alkyl isocyanide ligands, the alkyl side chain R of which has been recognized as α-tetrahydrofuranyl by ^{1}H-NMR spectroscopy [*(3)*, M = W: δ (in $CDCl_3$) = 2.28 (m, CH_2, 4H), 4.16 (m, OCH_2, 2H), 5.58 (t, CH, 1H)] and thus originates from the solvent.

For the formation of this novel isocyanide complex we suggest the mechanism outlined in Scheme 1: An electron transfer takes place between diazonium cation and cyanometalate anion, possibly *via* a diazoisocyanide intermediate *(1)* whose existence has, as yet, not been demonstrated[3]. By its stepwise homolytic decomposition (or directly[4]) an energy-rich aryl (or aryldiazenyl) radical is formed, which immediately reacts with the solvent with H abstraction, together with a relatively stable organometallic radical *(2)* which combines with the main radical of the solvent—here an α-tetrahydrofuranyl radical[5].



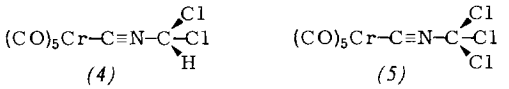
Scheme 1.

Actually, in addition to the isocyanide complexes *(3)* we were also able to detect the reduction product ArH of the diazonium component in each case (Scheme 1). This reaction mechanism is further supported by a) the characterization and controlled thermal decomposition of *p*-dimethylaminobenzenediazonium pentacarbonylcyanochromate[6], b) the earlier isolation of the paramagnetic chromium(I) compound *(2)*[7], and c) the ESR and ^{1}H-NMR spectroscopic detection of paramagnetic species in the reaction solution[6].

If Scheme 1 holds, each change of solvent RH should lead to new isocyanide complexes. This is confirmed by the reactions in di- and trichloromethane, which afford the complexes *(4)* and *(5)* in 25 and 60% yields, respectively.

[*] Dr. W. P. Fehlhammer, Dipl.-Chem. F. Degel
Institut für Anorganische Chemie der Universität Erlangen-Nürnberg
Egerlandstrasse 1, D-8520 Erlangen (Germany)

[**] Isonitrile Syntheses at the Metal, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. -Part 3: *W. P. Fehlhammer, A. Mayr, M. Ritter*, Angew. Chem. *89*, 660 (1977); Angew. Chem. Int. Ed. Engl. *16*, 641 (1977).



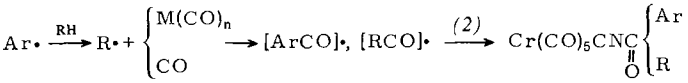
(4) *(5)*

The isocyanides thus formed at the metal are characterized by a high reactivity of the chlorine atoms which can be exploited synthetically. The IR spectra of the two complexes, in particular their low ν(CN)- and high ν(CO) [E]-frequencies, reflect the marked acceptor properties of the dichloro- and trichloromethyl isocyanide ligands.

Characteristic IR data (*n*-pentane; cm^{-1}) of $Cr(CO)_5CNCCl_nH_{3-n}$

		ν(N≡C)	ν(CO) [A_1, E]	
	$n=1$	2135 w	2050 w,	1960 vs
(4)	$n=2$	2122 m	2055 m,	1976 vs
(5)	$n=3$	2120 m	2088 m,	1983 vs

The "radical alkylation of cyano complexes" according to Scheme 1 thus opens up an entry to isocyanides bearing strongly electronegative substituents which are not accessible by the usual methods. The monochloro derivative ($n=1$) still missing from the series $Cr(CO)_5CNCCl_nH_{3-n}$ has so far been detected only in traces by IR and mass spectroscopy. Here, as in other cases where particularly short-lived radicals occur and the volatility of RH necessitates working under pressure, large amounts of *aroyl* and *acyl isocyanide*-metal complexes [*e.g.* $Cr(CO)_5CNCOC_6H_4Cl$, $Cr(CO)_5CNCOCH_2Cl$] are formed instead of the expected products *(3)*. The problem



of whether this variant involves a sequence of free-radical reactions or whether aryl and, correspondingly, aroyl *cations* play a role can only be resolved by further investigations (also under CO pressure).

The reactions in dibromomethane or benzene no longer conform to Scheme 1.

The characterization of all the products clearly shows that, in this instance, bromo- or phenyldediazonization processes occur instead of H abstraction from the solvent.

$CH_2Br_2 + Ar^{\bullet}/Cr^{I}(CO)_5CN \rightarrow ArBr + Cr^{0}(CO)_5CNCH_2Br$
$C_6H_6 + Ar^{\bullet}/Cr^{I}(CO)_5CN \rightarrow ArC_6H_5 + Cr^{0}(CO)_5CNH$

Experimental

Pentacarbonyl(trichloromethyl isocyanide)chromium(0) *(5)*: $Na[Cr(CO_5)CN]$[8] (885 mg, 3.67 mmol) and $[p\text{-}ClC_6H_4N_2]Cl$ (640 mg, 3.67 mmol) are mixed with stirring in 100 ml anhydrous alcohol-free trichloromethane under nitrogen at −78 °C and the mixture allowed to warm to room temperature within 3—4 h. Evolution of gas is observed as soon as the temperature reaches −50 °C. After evolution of gas has subsided the solvent is removed and the solid residue is extracted several times with 20 ml portions of *n*-pentane. Removal of solvent and purification of the crude product by sublimation (30 °C, high vacuum) affords 740 mg of a finely crystalline yellow solid (60 %; decomp. pt 99 °C), which can be stored almost indefinitely at −35 °C.

Received: July 31, 1978 [Z 121 IE]
revised: September 20, 1978
German version: Angew. Chem. *91*, 80 (1979)

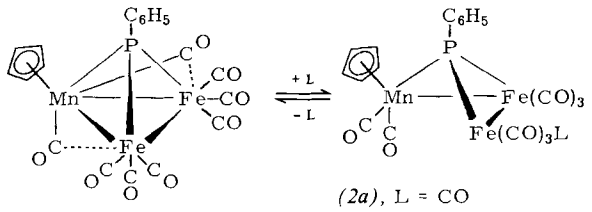
[1] Houben-Weyl: Methoden der organischen Chemie, 4th Edit. Vol. X/3, p. 34ff. Thieme, Stuttgart 1965.
[2] Cf. *H. Zollinger*, Acc. Chem. Res. *6*, 335 (1973).
[3] We could not confirm the existence of the stable arenediazoisocyanides ArN_2NC reported in the literature [*J. Suszko, T. Ignasiak*, Bull. Acad. Pol. Sci., Ser. Sci. Chim. *18*, 669, 673 (1970); *T. Ignasiak, J. Suszko, B. Ignasiak*, J. Chem. Soc. Perkin Trans. 1 *1975*, 2122]. Attempts at their synthesis "at the protecting metal" failed: *W. P. Fehlhammer, F. Degel, P. Buračas*, unpublished.
[4] In the radical dediazonization of diazonium salts, however, "inner-sphere" redox processes are often favored; cf. *e.g. F. Tröndlin, C. Rüchardt*, Chem. Ber. *110*, 2494 (1977).
[5] The last reaction step corresponds to a reversal of the isocyanide reduction by alkali metals $RNC \rightleftarrows RNC^{\bullet-} \rightarrow R^{\bullet} + CN^{-}$; cf. *G. E. Niznik, H. M. Walborsky*, J. Org. Chem. *43*, 2396 (1978).
[6] The compound undergoes decomposition already at room temperature, during the course of which free radicals are formed.—We thank Prof. *W. Jaenicke* and Dipl.-Chem. *G. Grampp* for recording the ESR spectra.
[7] *H. Behrens, D. Herrmann*, Z. Naturforsch. *B 21*, 1236 (1966).
[8] *R. B. King*, Inorg. Chem. *6*, 25 (1967).

Reversible Opening of a Trinuclear Heterometal Cluster[**]

By *Gottfried Huttner, Josef Schneider, Hans-Dieter Müller, Gerhard Mohr, Joachim von Seyerl*, and *Lidwina Wohlfahrt*[*]

Despite numerous investigations on the homogeneous catalytic activity of metal clusters[1], very little is known about their mode of reaction. We have now succeeded in demonstrating for the first time[2] that clusters can add substrates reversibly with opening of metal-metal bonds. Addition of a substrate molecule with rupture of a metal-metal bond, and elimination of the modified substrate with formation of a metal-metal bond, could therefore be the first and last steps, respectively, of a catalytic cycle with cluster participation.

The heterometallic, closed tetrahedral cluster *(1)*[3] can be converted at 20 °C under 2 bar carbon monoxide *via* cleavage of a Mn—Fe bond into the half-closed cluster *(2a)*[4].



(1) *(2a)*, L = CO
(2b), L = $P(C_6H_5)_3$

The yield of *(2a)* is 90 %. At 80 °C under 1-bar N_2, *(1)* is regenerated from *(2a)* quantitatively. At 40 °C and 40 bar CO both Mn—Fe bonds of *(1)* are opened and the metallacyclophosphane complex $C_5H_5(CO)_2MnP(C_6H_5)Fe_2(CO)_8$[5] is formed, which likewise is completely converted into *(1)* under 1 bar N_2 at 80 °C.

(1) reacts analogously with triphenylphosphane: In toluene solutions containing equimolar amounts of *(1)* and PPh_3, the adduct *(2b)* is present to the extent of 73 % at 50 °C, whereas at 80 °C only 31 % of *(2b)* is present in equilibrium with 69 % of *(1)*. The addition of *(1)* to PPh_3 is a second order

[*] Prof. Dr. G. Huttner, J. Schneider, Dr. H.-D. Müller, Dr. G. Mohr, Dipl.-Chem. J. von Seyerl, L. Wohlfahrt
Lehrstuhl für Synthetische Anorganische Chemie, Fachbereich Chemie, der Universität Konstanz
Postfach 7733, D-7750 Konstanz (Germany)

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

reaction, its activation enthalpy is small; the decomposition of *(2b)* to *(1)* and PPh_3 is first order, the activation enthalpy $\Delta H^{\neq} = 115\,kJ\,mol^{-1}$. Overall, the opening of the cluster *(1)* to *(2b)* with $\Delta H = -81\,kJ\,mol^{-1}$ is exothermic. That the structure of the adduct *(2b)* is analogous to that of *(2a)*[4] was confirmed by an X-ray structure analysis[6].

Experimental

All operations must be carried out under an inert atmosphere in anhydrous solvents [mass spectrum: Atlas CH7, direct inlet; structure determination: Syntex P3 diffractometer, λ-Mo = 71.069 pm, graphite monochromator; solution: Syntex-XTL, conventional; kinetic data: Cary 17 UV spectrometer].

Synthesis of (2b): A mixture of *(1)* (300 mg, 0.532 mmol) and PPh_3 (1 g, 3.8 mmol) in 200 ml toluene is stirred for 20 h at 40 °C. The originally red solution gradually takes on the green color of the complex *(2b)*. The crude product is absorbed on 5 g silical gel and gently dried. Chromatography at −10 °C (column 20 × 2.5 cm, silica gel Merck 0.063—0.200 mm, pentane) with *n*-pentane/toluene (1 : 1) affords a small yellow front followed by a broad green zone of *(2b)*; unreacted *(1)* can subsequently be washed from the column with *n*-pentane/toluene (1:2). Recrystallization from 5 ml CH_2Cl_2 and 5 ml *n*-pentane affords 380 mg (86.5 %) of analytically pure *(2b)* as green crystals, m.p. 153 °C (red coloration at 80 °C). The mass spectrum of *(2b)* shows only the molecular ion of *(1)* and its fragments.

Received: October 23, 1978 [Z 124 IE]
German version: Angew. Chem. *91*, 82 (1979)

[1] Review: *E. L. Muetterties*, Angew. Chem. *90*, 577 (1978); Angew. Chem. Int. Ed. Engl. *17*, 545 (1978); Science *196*, 839 (1977); *H. Vahrenkamp*, Struct. Bonding (Berlin) *32*, 1 (1977); *J. R. Shapley*, Strem Chem. *6*, 3 (1978).

[2] A reversible addition of CO has been observed in the case of $Os_3(CO)_{10}H_2$, the addition being to the metal-metal multiple bond: *A. J. Deeming, S. Hasso*, J. Organomet. Chem. *88*, C 21 (1975); *J. R. Shapley, J. B. Keister, M. R. Churchill, B. G. De Boer*, J. Am. Chem. Soc. *97*, 4145 (1975); *J. B. Keister, J. R. Shapley, ibid. 98*, 1056 (1976).—A reversible addition has likewise been observed in the case of $[Rh_{12}(CO)_{30}]^{2-}$; the mechanism of the addition is unknown: *P. Chini, S. Martinengo*, Inorg. Chim. Acta *3*, 299 (1969).

[3] *G. Huttner, A. Frank, G. Mohr*, Z. Naturforsch. B*31*, 1161 (1976).

[4] *G. Huttner, G. Mohr, A. Frank*, Angew. Chem. *88*, 719 (1976); Angew. Chem. Int. Ed. Engl. *15*, 687 (1976).

[5] *G. Huttner, G. Mohr, P. Friedrich, H.-G. Schmid*, J. Organomet. Chem. *160*, 59 (1978).

[6] Space group $P2_1/c$, $Z = 4$; $a = 1262$, $b = 1586$, $c = 1737$ pm, $\beta = 92.99°$; $R_1 = 0.058$; Fe—Mn 291, Fe—Fe 278, Fe—P_{PPh_3} 226, Fe—P_{PPh} 214, 223, Mn—P_{PPh} 223 pm.

Catalytic Alkylation of Benzene with CO and H_2: A Homogeneously Catalyzed Fischer-Tropsch Synthesis

By *G. Henrici-Olivé* and *S. Olivé*[*]

Alkylbenzenes, $C_6H_5(CH_2)_nH$, with $n = 1$—5 (maximum at $n = 2$) are formed in a Fischer-Tropsch type synthesis, if a homogeneous solution of $W(CO)_6$ and $AlCl_3$ in benzene is treated in an autoclave with CO and H_2 under pressure, at 200 °C. No xylenes are detected in the reaction solution, but small amounts of methane, ethane and ethylene are generally present in the gas phase. The yield of alkylbenzenes is increased by the addition of a chelating tertiary phosphane, such as ethylenebis(diphenylphosphane), (diphos), or bis(2-diphenylphosphinoethyl)phenylphosphane, (triphos), in a molar ratio phosphane/tungsten of 1—2. Under otherwise comparable conditions, the catalyst turnover (defined as the number of moles CO converted to side chains, per mole of $W(CO)_6$) increases linearly with the ratio p_{H_2}/p_{CO}, as shown in Table 1. Blank runs under identical conditions except for the omission of either $W(CO)_6$ or $AlCl_3$ result in no detectable production of alkylbenzenes.

Table 1. Catalyst turnover in the $W(CO)_6$ catalyzed formation of alkylbenzenes from C_6H_6, CO and H_2, as a function of the ratio p_{H_2}/p_{CO}. $[W(CO)_6] = [triphos] = 4.7 \times 10^{-3}$ mol/l; $[AlCl_3] = 0.25$ mol/l; $T = 200$ °C; $t = 3$ h.

p_{CO} (atm)	p_{H_2} (atm)	p_{H_2}/p_{CO}	Turnover CO/W
100	20	0.2	7
11	9	0.8	38
60	60	1.0	11 [a]
60	60	1.0	44
60	60	1.0	82 [b]
10	30	3.0	105
20	100	5.0	230

[a] No phosphane added. [b] $t = 14$ h.

Table 1 indicates also that the reaction rate decays with time: after 14 hours, the turnover is only roughly twice that observed after 3 hours. The catalyst, $W(CO)_6$, is retained quantitatively in the reaction solution after the reaction. The decrease in reaction rate is assumed to be due to exhaustion of $AlCl_3$ which is enclosed in Friedel-Crafts type, solid, condensed aromatic byproducts.

The inverse dependence of the turnover on the CO pressure indicates ligand CO dissociation prior to the formation of the catalytically active species—similarly as is known from hydroformylation catalysis[1]. The action of the phosphane appears to be to hold this species in solution. Other metal carbonyls, such as $Rh_6(CO)_{16}$, $Ru_3(CO)_{12}$, $Cr(CO)_6$ and $Co_2(CO)_8$, also catalyze the reaction, but with decreasing turnover in this sequence.

The insertion of CO into an aromatic C—H bond, destabilized by $AlCl_3$, was first reported as early as 1897 by *Gattermann et al.*[2]; *Heck*[3] achieved the insertion of CO into the C—X bond of halogenated arenes with $Ni(CO)_4$; *Casey et al.*[4] were able to carbonylate the phenyl ligand of the complex $[(CO)_5WC_6H_5]^-$. However, in no case was reduction of the inserted $>C{=}O$ to $-CH_2-$ reported, which would be the obvious premise for further chain growth according to a Fischer-Tropsch type reaction.

We suggest that HCl, formed in the reaction

$$AlCl_3 + C_6H_6 \rightleftharpoons HCl + C_6H_5AlCl_2$$

is oxidatively added to the tungsten catalyst; this assumption is based on the observation that the catalytic reaction is inhibited by the presence of a HCl scavenger, such as $CaCO_3$. Ligand exchange between the tungsten center and $C_6H_5AlCl_2$ (Cl versus C_6H_5) may then give an arylated tungsten species, where coordinated CO is inserted into the metal-carbon bond. Further steps in the synthesis of alkylbenzenes are assumed to be analogous to those suggested previously for the heterogeneous Fischer-Tropsch reaction[5].

The Fischer-Tropsch type growth of the alkyl chains is corroborated by their chain length distribution. In the "classical", heterogeneous Fischer-Tropsch catalysis, the primary products have a Schulz-Flory distribution[5a, c]. Table 2 shows the chain length distribution of alkylbenzenes obtained in

[*] G. Henrici-Olivé and S. Olivé
Monsanto Triangle Park Development Center, Inc.
P.O. Box 12274, Research Triangle Park, N.C. 27709 (USA)

two parallel runs with the $W(CO)_6$ system at $p_{CO}=20$ atm, $p_{H_2}=100$ atm (cf. Table 1). This distribution was computed from the gas-chromatographic analysis of the alkylbenzenes. In the Schulz-Flory diagram[6] (Fig. 1) the measurements lie on a reasonably straight line. Interestingly, the points corresponding to ethylbenzene lie considerably above the straight line. Evidently, ethylbenzene is produced by more than one mechanism.

Table 2. Weight distribution of C_nH_{2n+1} chains of alkylbenzenes; conditions as in Table 1, last line.

Length of chain, P	[Alkylbenzene] (10^2 mol/l)	[Alkyl chains] (g/l)	Weight fraction m_P	m_P/P
1	25.3	3.79	0.240	0.240
2	39.0	11.31	0.715	0.357
3	1.3	0.56	0.035	0.012
4	0.11	0.06	0.0038	0.001
5	0.13	0.09	0.0057	0.001
1	23.4	3.51	0.207	0.207
2	42.0	12.18	0.719	0.359
3	2.3	0.99	0.058	0.019
4	0.26	0.15	0.009	0.0022
5	0.17	0.12	0.007	0.0014

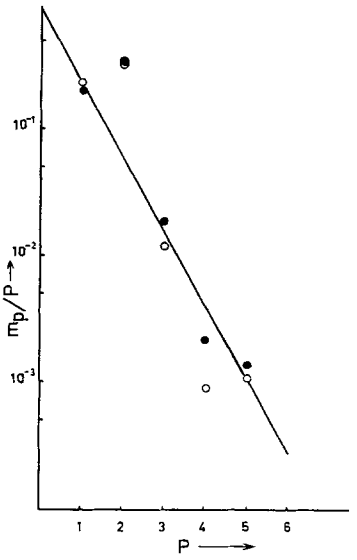


Fig. 1. Chain length distribution of the alkyl chains; graphical representation of data of Table 2 according to $\log(m_P/P)=\log(\ln^2\alpha)+P\log\alpha$ [Schulz-Flory equation, α = probability of chain growth, P = number of carbon atoms in the chain, m_P = weight fraction of chain with length P].

Evidence for homogeneous Fischer-Tropsch catalysis is still scarce. Hydrogenation of CO to hydrocarbons with soluble transition metal-cluster compounds, at low pressure, did not proceed further than to C_2, and with a low turnover[7]; at higher pressures, oxygenated compounds were also produced with soluble clusters[8]. These results led to the assumption[7] that clusters are indispensable for mimicking the solid surface of "classical" Fischer-Tropsch catalysts. However, the recent methanol synthesis by *Rathke* and *Feder*[9], using $HCo(CO)_4$ at 200 °C and 300 atm, is the first example of the catalytic hydrogenation of CO on a soluble, mononuclear species. Some higher alcohols were also found, but were shown to be the products of secondary reactions of methanol, and not of a Fischer-Tropsch type carbon-carbon bond formation.

The synthesis of alkylbenzenes from benzene, CO and H_2 represents the first actual Fischer-Tropsch type chain growth on a soluble, mononuclear catalyst. In contrast to the heterogeneous Fischer-Tropsch catalysts, where chain initiation is assumed to take place at a metal-hydrogen bond[5], the presently described chain growth requires an aryl-metal species to start with. The observed predominance of ethylbenzene, on the other hand, indicates that this particular compound is produced by more than one mechanism. Since small amounts of C_1 and C_2 hydrocarbons are generally found in the reaction gases, it is assumed that ethylene is generated by the "classical" route. (The metal-H bond resulting from the suggested oxidative addition of HCl to the soluble metal complex may be responsible for the initiation of this route.) Ethylene then alkylates the benzene in a Friedel-Crafts reaction.

Received: October 31, 1978 [Z 127 IE]
German version: Angew. Chem. *91*, 83 (1979)

[1] See *e.g. G. Henrici-Olivé, S. Olivé:* Coordination and Catalysis, Chap. 10.2. Verlag Chemie, Weinheim 1977.
[2] *L. Gattermann, J. A. Koch*, Ber. Dtsch. Chem. Ges. *30*, 1622 (1897).
[3] *R. F. Heck*, J. Am. Chem. Soc. *85*, 2013 (1963).
[4] *C. P. Casey, S. W. Polichnowski, R. L. Anderson*, J. Am. Chem. Soc. *97*, 7375 (1975).
[5] a) *G. Henrici-Olivé, S. Olivé*, Angew. Chem. *88*, 144 (1976); Angew. Chem. Int. Ed. Engl. *15*, 136 (1976); b) J. Mol. Catal. *3*, 443 (1978); c) *4*, 379 (1978).
[6] See *e.g. G. Henrici-Olivé, S. Olivé:* Polymerisation – Katalyse, Kinetik, Mechanismen, Chap. 1.6. Verlag Chemie, Weinheim 1969.
[7] *M. G. Thomas, B. F. Beier, E. L. Muetterties*, J. Am. Chem. Soc. *98*, 1296 (1976); *G. C. Demitras, E. L. Muetterties, ibid. 99*, 2796 (1977).
[8] *R. L. Pruett*, Ann. N. Y. Acad. Sci. *295*, 239 (1977).
[9] *J. W. Rathke, H. M. Feder*, J. Am. Chem. Soc. *100*, 3623 (1978).

Ring-Opening of 5-(Bromomethyl)-2-isoxazolines to β,γ-Enoximes—A New Principle for the γ-Substitution of Allyl Bromides by α-Functionalized Alkyl Groups[**]

By *Volker Jäger, Hartmut Grund, and Wilfried Schwab*[*]

2-Isoxazolines represent functionalized carbon skeletons which can be assembled from alkenes and nitrile oxides. This reaction is synthetically useful if suitable methods for the ring cleavage are available[1]. We report here on the ring-opening of 5-(bromomethyl)-[5-(iodomethyl)-]2-isoxazolines *(3)* by reductive elimination: key step of a sequence for the controlled γ-substitution of allyl bromides *(1)*[3] by α-functionalized alkyl groups.

5-(Bromomethyl)-2-isoxazolines *(3)* are accessible in good yield (see Table 1) from *(1)* and chlorooximes as precursors of nitrile oxides *(2)*[4]. On treatment of *(3)* with zinc or zinc/copper [in the case of *(3e)* and *(3f)* after conversion into the iodide], bromine-oxime ether cleavage takes place to furnish β,γ-enoximes *(4)* with the configuration as preconceived in *(3)*. Obvious subsequent reactions are deoximation to *(5)*[5] and oxime reduction to *(6)*, thus completing *acylation* and *α-aminoalkylation* sequences, respectively.

The β,γ-enones *(5a)* and *(5b)* were obtained in $\gtrsim 70\%$ yield *without appreciable isomerization* (see Table 1); the reaction *(4d)*→*(5d)* has so far not been accomplished; likewise the (*E*,*E*)-β-damascone oxime *(7)* (m.p. 123—124 °C), formed

[*] Dr. V. Jäger [+], Dr. H. Grund, Dipl.-Chem. W. Schwab
Institut für Organische Chemie der Universität Giessen
Heinrich-Buff-Ring 58, D-6300 Lahn-Giessen 1 (Germany)
[+] Author to whom correspondence should be addressed.

[**] Syntheses *via* Isoxazolines, Part 7; presented in part in lectures at Brussels (January 21, 1977) and Marburg (July 4, 1977); parts of the dissertation of *H. G.* (1978) and *W. S.* (planned). This work was supported by the Deutsche Forschungsgemeinschaft.—Part 6: [1a].

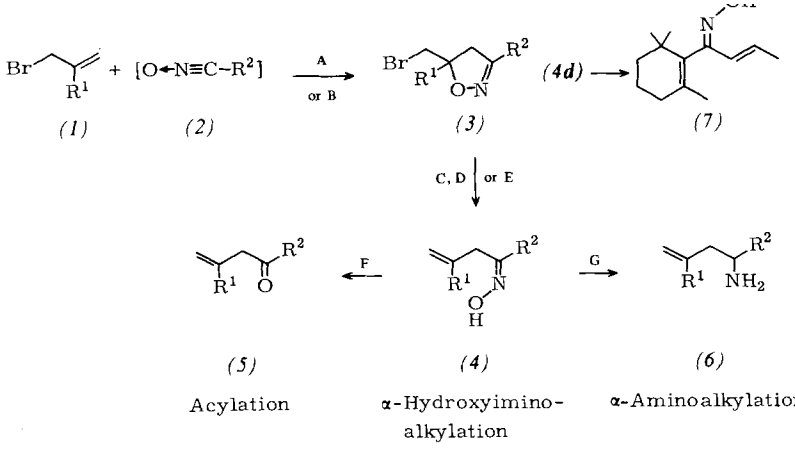


Table 1. 5-(Bromomethyl)isoxazolines *(3)*, β,γ-enoximes *(4)*, β,γ-enones *(5)*, and homoallyl amines *(6)* [a].

	R^1	R^2	*(3)* Yield [%]	*(3)* M.p. [°C] B.p. [°C/torr] [b]	*(4)* Yield [%]	*(4)* M.p. [°C] B.p. [°C/torr] [b]	*(5)* Yield w.r.t. *(3)* [%]	*(5)* B.p. [°C/torr] [b]	*(6)* Yield w.r.t. *(3)* [%]	*(6)* B.p. [°C/torr] [b]
(a)	H	C_6H_5	88 A	60 [c]	80 C	45	71 F [d]	70–75/0.01	59 G	65–70/0.5
(b)	CH_3	C_6H_5	83 A	48–49	65 C	41–43	78 F [d]	80/0.01	64 G	60/0.1–0.2
(c)	H	CH_3	61 A	45–48/0.05	61 D [e]	35/0.25				
(d)	H		65 B	55–56	79 C	47	–			
(e)	H	$COOC_2H_5$	77 A	52	91 E	90/0.2			82 (crude, ^{1}H-NMR) G [f]	
(f)	CH_3	$COOC_2H_5$	59 A [g]	31–36	60 E [g]	37–39			[f]	

[a] Method A: *(2)* from chlorooxime/triethylamine in ether at ≈0°C [4]; B: *(2d)* from β-cyclocitral oxime/*N*-bromosuccinimide/$NaOCH_3$/dimethylformamide (DMF), 0–25°C [9]; C: Zn/80% ethanol, reflux, 1–4.5 h; D: Zn/Cu, DMF/H_2O (3:1), 16 h at ≈25°C; E: NaI, acetone, 6 h reflux [*(3e)*], 110°C [*(3f)*], then Zn/Cu, tetrahydrofuran (THF/H_2O) (4:1), 7h at room temperature; F: $TiCl_3/NH_4OAc$ buffer [5a] H_2O/DMF/pentane (7:1:4), 15h at ≈25°C; G: Al/Hg, THF/H_2O (9:1) [7b], 0–≈25 or 40°C [*(6e)*]. Structures are secured by elemental analyses and spectral data. To our knowledge *(3b)*–*(3f)*, *(4a)*–*(4d)*, *(6b)* and *(7b)* are new compounds. [b] Kugelrohr distillation, bath temperature. [c] Main fraction, m.p. 54–56°C. [d] *(5a)*: α,β-isomer ≲5%; *(5b)*: ≲3% (^{1}H-, ^{13}C-NMR). [e] *(4c)* is configurationally labile: freshly prepared after distillation (*Z*):(*E*)≈7:1 [(*E*)-*(4c)*: δ(CH_2)=3.03; δ(CH_3)=19.5, δ(CH_2)=33.6; (*Z*)-*(4c)*: δ(CH_2)=3.24; δ(CH_3)=13.4, δ(CH_2)=40.3 (in $CDCl_3$)]; after 5 months at 4°C 1:2; using method C a 43:57 (*Z*)/(*E*) mixture was obtained in ≈50% yield. [f] Reduction and conversion into free amino acids, see [7a], yield w.r.t. *(4e)* and *(4f)* 67 and 71%, respectively [7a]. [g] Not optimized.

in 70% yield on isomerization of *(4d)* with hydrochloric acid in 1,4-dioxane, could not be converted into an enone[6].

Enoximes *(4)* activated by phenyl or alkoxycarbonyl[7a] are smoothly converted into the homoallyl amines *(6)* on reduction with aluminum amalgam (see Table 1). This synthesis of the γ,δ-unsaturated α-hydroxyimino esters *(4e)* and *(4f)* (whose reduction has already been described[7a]) constitutes a new entry to γ,δ-unsaturated amino acids; such compounds frequently function as amino acid antagonists inhibiting the growth of microorganisms[8].

Experimental

(5a) from *(3a)*: A mixture of *(3a)* (2.40 g, 10 mmol) and zinc dust (3.27 g, 50 mmol) in 50 ml of 80% ethanol is heated under reflux for 4 h, then evaporated down, treated with water, and twice extracted with ether. The solution is filtered (short column filled with Na_2SO_4) and concentrated in a rotary evaporator. The residue is dissolved in 40 ml of pentane and stirred with a solution of 25 ml $TiCl_3$ (15% in 4% HCl)/12 g NH_4OAc/70 ml water/10 ml DMF for 15 h under argon. For work-up, the mixture is treated with pentane, extracted twice with pentane, washed with H_2O, saturated $NaHCO_3$ solution, again with water, and then dried over Na_2SO_4. Fractionation (rotary evaporator, then Kugelrohr; see Table 1) affords 1.03 g (71%) of *(5a)* as a pale-yellow liquid.

(6b) from *(4b)*: Amalgamated aluminum foil (540 mg, 20 mmol) is added in small pieces (0.5–1 cm^2) to a solution of *(4b)* (360 mg, 2.05 mmol) in 20 ml THF/2 ml H_2O. Vigorous evolution of gas is moderated by ice-cooling; the stirred mixture is then allowed to warm up to 25°C overnight. On completion of reaction (≈27 h, TLC control) the mixture is treated with 20 ml of THF/Na_2SO_4, allowed to stand for 90 min, filtered, and the solids carefully washed with THF/ether and extracted for 24h with refluxing ether. The dried solutes (Na_2SO_4) are evaporated to afford 344 mg of crude product. Distillation of 244 mg thereof yields 231 mg (98%) of pure *(6b)* as a colorless liquid [b.p. ≈60°C (bath temp.)/0.1–0.2 torr; ^{1}H-NMR ($CDCl_3$): δ=1.73 (CH_3), 1.87 (NH_2), 2.3 ("d", J≈7 Hz; CH_2), 4.03 ("t", J≈7 Hz, CHN), 4.8 (=CH_2), 7.3 (C_6H_5).

Received: November 6, 1978 [Z 128 IE]
German version: Angew. Chem. 91, 91 (1978)

[1] a) *V. Jäger, V. Buss, W. Schwab*, Justus Liebigs Ann. Chem., in press. b) Ring cleavage to α,β-enoximes, -enones and γ-amino alcohols (diastereoselective), see previous papers of this series; c) cf. *V. Jäger, H. Grund*, *Angew. Chem. 88*, 27 (1976); Angew. Chem. Int. Ed. Engl. *15*, 50 (1976); *H. Grund, V. Jäger*, Justus Liebigs Ann. Chem., in press; *V. Jäger, W. Schwab*, Tetrahedron Lett. *1978*, 3129.

[2] Cf. olefin synthesis according to *Boord*: review *M. Schlosser* in Houben-Weyl-Müller: Methoden der Organischen Chemie, 4th Edit. Vol. V/1b. Thieme, Stuttgart 1972, p. 213ff.

[3] With organocopper compounds see, *e.g.*, *K. Maruyama, Y. Yamamoto*, J. Am. Chem. Soc. *99*, 8068 (1977); and references cited therein.
[4] *M. Christl, R. Huisgen*, Chem. Ber. *106*, 3345 (1973); *R. Huisgen*, J. Org. Chem. *41*, 403 (1976), and references cited therein.
[5] a) *G. H. Timms, E. Wildsmith*, Tetrahedron Lett. *1971*, 195; b) Surveys: *E. J. Corey, J. E. Richman*, J. Am. Chem. Soc. *92*, 5276 (1970); *B. Unterhalt* in: Methodicum Chimicum. Vol. 6. Thieme, Stuttgart 1974, p. 442f.
[6] In turn, carbonyl derivatives could not be obtained from β-damascone and related compounds; *G. Ohloff, K. H. Schulte-Elte*, private communication; we also are grateful for samples and valuable discussions.
[7] a) *D. J. Drinkwater, P. W. G. Smith*, J. Chem. Soc. *C 1971*, 1305; b) *E. J. Corey, R. J. McCaully, H. S. Sachdev*, J. Am. Chem. Soc. *92*, 2476 (1970); *E. J. Corey, H. S. Sachdev, J. Z. Gougoutas, W. Saenger, ibid. 92*, 2488 (1970).
[8] Survey: *W. Trowitzsch, H. Sahm*, Z. Naturforsch. *C 32*, 78 (1978).
[9] *C. Grundmann, R. Richter*, J. Org. Chem. *33*, 476 (1968); b) *C. Grundmann, K. S. Datta, ibid. 34*, 2016 (1969); *(2d)* is stable at ≈ 25°C, but rearranges to the isocyanate at ≳ 60°C: *C. Grundmann*, private communication (August 20, 1974); see also *H. Grund*, Diplomarbeit, Universität Giessen 1974; we thank Dr. *W. Hoffmann*, BASF AG, Ludwigshafen, for kindly supplying us with β-cyclocitral.

Six-Coordinate Hydrogen: Structure of $[(Ph_3P)_2N]^+[HCo_6(CO)_{15}]^-$ by Single-Crystal Neutron Diffraction Analysis[**]

By *Donald W. Hart, Raymond G. Teller, Chiau-Yu Wei, Robert Bau, Giuliano Longoni, Stefano Campanella, Paolo Chini*, and *Thomas F. Koetzle*[*]

Interstitial H atoms are normally found in the structures of binary metal hydrides. In these materials, it has been shown that H atoms may occupy octahedral and/or tetrahedral sites in the metal lattice[1a], and that intermediate sites of lower symmetry may be occupied as well[1b]. For covalent molecular complexes, however, examples of such "interstitial" hydride ligands are rare[2]. We report here the characterization, *via* single-crystal neutron diffraction measurements, of an interstitial hydride ligand (a six-coordinate H atom) in the metal carbonyl cluster complex $[HCo_6(CO)_{15}]^-$.

The complex anion $[HCo_6(CO)_{15}]^-$ can be prepared by the protonation of $[Co_6(CO)_{15}]^{2-}$, which in turn is formed in the pyrolysis of $Co_2(CO)_8$ in ethanol[3a]. We recently became interested in the structure of $[HCo_6(CO)_{15}]^-$ when it was reported that the ^{1}H-NMR signal of the unique proton in that complex occurred at $\delta = 23.2$[3b], which is unusual for a metal hydride complex. Normally, for hydridometal complexes δ values in the range 0 to -40 are measured[4]. This anomalous downfield shift found here suggested that the H atom in $[HCo_6(CO)_{15}]^-$ might be located in the vicinity of the carbonyl ligands, similarly as in $H_2Fe_3(CO)_{11}$[5].

[*] Prof. Dr. R. Bau, Dr. D. W. Hart, Dr. R. G. Teller, Miss C. Y. Wei
Department of Chemistry
University of Southern California
Los Angeles, Calif. 90007 (USA)
Dr. G. Longoni
Centro del CNR per la Sintesi e la Struttura dei Composti dei Metalli di Transizione nei Bassi Stati di Ossidazione
Via G. Venezian 21, I-20133 Milano (Italy)
Prof. Dr. P. Chini, Dr. S. Campanella
Istituto di Chimica Generale dell'Università
Via G. Venezian 21, I-20133 Milano (Italy)
Dr. T. F. Koetzle
Chemistry Department
Brookhaven National Laboratory
Upton, N. Y. 11973 (USA)

[**] This research was carried out under contract with the U.S. Department of Energy (Division of Basic Energy Sciences), and supported by Grant CHE-77-00360 (to R. B.) from the National Science Foundation. We thank Mr. *J. Henriques* for technical assistance.

$[(Ph_3P)_2N]^+[HCo_6(CO)_{15}]^-$ was prepared by addition of concentrated HCl to an aqueous solution of $K_2[Co_6(CO)_{15}]$, followed by metathesis of the precipitated $K[HCo_6(CO)_{15}]$ with $[(Ph_3P)_2N]Cl$ in acidified isopropyl alcohol. The IR spectrum of this compound (in CH_2Cl_2) consists of the following bands: 2060 (w), 2005 (s), 1975 (ms) and 1830 (ms) cm^{-1}. Salts of $[HCo_6(CO)_{15}]^-$ are unstable in most of the usual solvents where, at room temperature, rapid decomposition to a mixture of $[Co_6(CO)_{15}]^{2-}$, $[Co(CO)_4]^-$ and eventually $Co_4(CO)_{12}$ is observed. The most stable solutions are obtained in diisopropyl ether, and to a somewhat lesser extent in dichloromethane.

The compound $[(Ph_3P)_2N]^+[HCo_6(CO)_{15}]^-$ crystallizes in the monoclinic space group $P2_1/n$, with $a = 17.922(3)$ Å, $b = 17.524(4)$ Å, $c = 16.329(8)$ Å, $\beta = 92.27(2)°$, $Z = 4$ (unit cell parameters measured at -193°C). The neutron diffraction analysis was carried out on a crystal of approximate dimensions $3.0 \times 2.2 \times 0.5$ mm [Brookhaven High Flux Beam Reactor, $\lambda_n = 1.0373(1)$ Å (KBr, $a = 6.6000$ Å, -193°C)]. The positions of the non-hydrogen atoms in the molecule had been determined from an earlier X-ray analysis and this model, together with phenyl H atoms placed in calculated positions, was used to phase the neutron data. A subsequent difference-Fourier synthesis revealed the position of the unique H atom in the anion. Several cycles of least-squares refinement (based on F^2) were then carried out, in which all atoms in the anion were refined anisotropically, and phenyl rings were treated as rigid groups with individual isotropic temperature factors. Final agreement factors are $R(F) = 0.071$, $R(wF) = 0.042$, $R(F^2) = 0.107$ and $R(wF^2) = 0.081$[6] for 3574 unique reflections having $F^2 > 3\sigma(F^2)$.

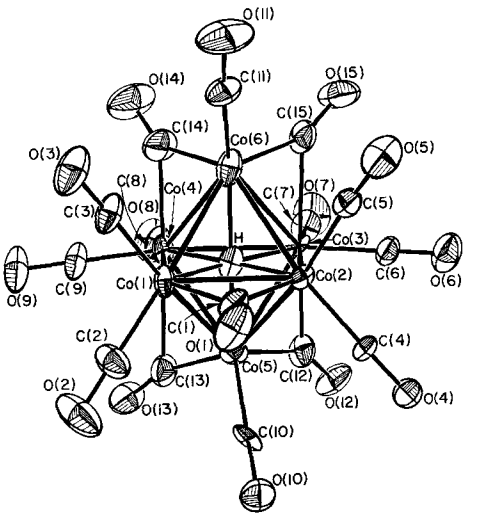


Fig. 1. A molecular plot of the $[HCo_6(CO)_{15}]^-$ anion, showing the six-coordinate H atom at its center. The cluster has approximate C_{2v} symmetry, with ten terminal, one symmetrically bridging and four asymmetrically bridging carbonyl groups. Average H—Co and Co—Co distances are 1.82(1) Å and 2.58(1) Å, respectively.

The structure of the $[HCo_6(CO)_{15}]^-$ anion is shown in Figure 1, which indicates that the lone H atom is located not on the carbonyl ligands but at the center of the Co_6 octahedron. The H—Co distances are nearly equivalent [1.80(2), 1.80(2), 1.81(2), 1.81(2), 1.85(2), 1.87(2) Å; average = 1.82(1) Å], and the H atom is displaced less than one standard deviation from the geometric center of the metal cluster. Co—Co distances range from 2.50(2) to 2.67(2) Å, with an average of 2.579(15) Å, resulting in an apparent radius for the interstitial H atom of $1.82 - (2.58/2) = 0.53$ Å. An interesting observation

is that the insertion of a H atom into the cluster has caused a small but appreciable swelling of the octahedron: the average Co—Co distance increases from 2.509(8) Å in $[Co_6(CO)_{15}]^{2-}$[7] to 2.579(15) Å in $[HCo_6(CO)_{15}]^-$. This was also noticed in the structures of $[HNi_{12}(CO)_{21}]^{3-}$ and $[H_2Ni_{12}(CO)_{21}]^{2-}$: the individual Ni—Ni distances for octahedral holes containing H are 0.02—0.07 Å longer than those for holes without H[2b].

There are ten terminal, one symmetrically bridging and four asymmetrically bridging carbonyl groups in the cluster. The $[(Ph_3P)_2N]^+$ cation is in the usual bent form[8], with a P—N—P angle of 142.9(4)°.

We now return to the observation which originally attracted us to $[HCo_6(CO)_{15}]^-$: the anomalous ^{1}H-NMR chemical shift of $\delta = 23.2$[3b]. This signal (a moderately broad singlet) is observable at −100 °C in acetone, when the solution is prepared at low temperature, or in dichloromethane. At −70 °C, a broad signal is present, but at −50 °C no signal could be observed. The signal reappears by cooling again to −100 °C. The finding that the signal is absent when the compound is dissolved in [D$_6$]acetone would suggest that, in solution, the H atom may leave the cluster and exchange with the solvent. Further evidence that the H atom may quite easily enter and leave its "metal cage" is provided by the simple protonation of $[Co_6(CO)_{15}]^{2-}$, and the converse reaction of $[HCo_6(CO)_{15}]^-$ observed on simple dissolution in solvents such as water, methanol or even tetrahydrofuran[9]. This borderline ability to accommodate the interstitial hydride observed between solid state and solution is in fair agreement with the predicted trend that decreasing the number of interstitial holes present in the cluster leads to decreased stability of the hydride[3b]. It should be noted that $[HRu_6(CO)_{18}]^-$, which is suspected from X-ray analysis to contain an interstitial H atom[10], also shows a ^{1}H-NMR signal with similar downfield shift ($\delta = 16.4$), whereas the signals of the larger interstitial clusters $[HNi_{12}(CO)_{21}]^{3-}$ ($\delta = -24.0$), $[H_2Ni_{12}(CO)_{21}]^{2-}$ ($\delta = -18.0$)[2b], $[H_2Rh_{13}(CO)_{24}]^{3-}$ ($\delta = -26.7$), and $[H_3Rh_{13}(CO)_{24}]^{2-}$ ($\delta = -29.3$)[2c, 2d] are all found at the expected high-field positions. It is clear that more results, both spectroscopic and crystallographic, will be needed before we can successfully correlate structural information with the NMR chemical shifts of atoms embedded within metal clusters.

Received: October 30, 1978 [Z 125 IE]
German version: Angew. Chem. 91, 86 (1979)

[1] a) *W. M. Mueller, J. P. Blackledge, G. G. Libowitz:* Metal Hydrides. Academic Press, New York 1968; b) *F. Reidinger, J. J. Reilly, R. W. Stoenner* in *G. D. Mahan, W. J. Roth:* Superionic Conductors. Plenum Press, New York 1976, p. 427.

[2] a) *A. Simon*, Z. Anorg. Allg. Chem. *355*, 311 (1967); b) *R. W. Broach, L. F. Dahl, G. Longoni, P. Chini, A. J. Schultz, J. M. Williams*, Adv. Chem. Ser. *167*, 93 (1978); c) *V. G. Albano, A. Ceriotti, P. Chini, G. Ciani, S. Martinengo, W. M. Anker*, J. Chem. Soc. Chem. Commun. *1975*, 859; *S. Martinengo, B. T. Heaton, R. J. Goodfellow, P. Chini, ibid. 1977*, 3.

[3] a) *P. Chini*, J. Chem. Soc. Chem. Commun. *1967*, 29; b) *P. Chini, G. Longoni, S. Martinengo, A. Ceriotti*, Adv. Chem. Ser. *167*, 1 (1978).

[4] *H. D. Kaesz, R. B. Saillant*, Chem. Rev. *72*, 231 (1972).

[5] *H. A. Hodali, D. F. Shriver, C. A. Ammlung*, J. Am. Chem. Soc. *100*, 5239 (1978).

[6] $R(F) = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $R(wF) = \{\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o^2\}^{1/2}$; $R(F^2) = \Sigma|F_o^2 - |F_c|^2|/\Sigma F_o^2$; $R(wF^2) = \{\Sigma w(F_o^2 - |F_c|^2)^2/\Sigma wF_o^4\}^{1/2}$. Weights (w) were taken inversely proportional to the estimated variance for each reflection.

[7] *V. Albano, P. Chini, V. Scatturin*, J. Organometal. Chem. *15*, 423 (1968). However, it should be pointed out that the different arrangement of carbonyl groups in $[Co_6(CO)_{15}]^{2-}$ and $[HCo_6(CO)_{15}]^-$ may account for part of the difference in Co—Co bond lengths in the two anions.

[8] See references in *R. D. Wilson, R. Bau*, J. Am. Chem. Soc. *96*, 7601 (1974).

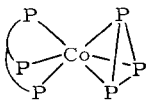
[9] *D. W. Hart, R. G. Teller, C. Y. Wei, R. Bau, G. Longoni, S. Campanella, P. Chini, T. F. Koetzle*, unpublished.

[10] *C. R. Eady, B. F. G. Johnson, J. Lewis, M. C. Malatesta, P. Machin, M. McPartlin*, J. Chem. Soc. Chem. Commun. *1976*, 945.

[(triphos)Co(δ-P$_3$)Cr$_2$(CO)$_{10}$]: A Trinuclear Heterometal Complex Containing *cyclo*-Triphosphorus as μ$_3$-Ligand

By *Stefano Midollini, Annabella Orlandini*, and *Luigi Sacconi*[*]

The first sandwich metal complex of *cyclo*-triphosphorus *(1)*[11] contains a central cobalt atom bound to six phosphorus atoms, three of which belong to the η^3-P$_3$ unit and three to the tridentate tritertiary phosphane $CH_3C(CH_2PPh_2)_3$(triphos). We have found that this complex possesses Lewis base properties due to the three donor phosphorus atoms of the P$_3$ unit. Indeed *(1)* reacts with Cr(CO)$_6$ in the molar ratio 1:1 or 1:2 to give the binuclear *(2)* and the trinuclear complex *(3)*.



(1)

$\xrightarrow[h\nu]{Cr(CO)_6}$ (triphos)Co(η^3-P$_3$)Cr(CO)$_5$ *(2)*

(triphos)Co(η^3-P$_3$)Cr$_2$(CO)$_{10}$ *(3)*

Even on treating *(1)* with an excess of Cr(CO)$_6$, it was not possible to isolate any compound containing more than two Cr(CO)$_5$ groups. This is probably due to the bulkiness of these coordination units.

A complete X-ray structure analysis performed on the complex *(3)* (Fig. 1) shows the structure of the donor complex

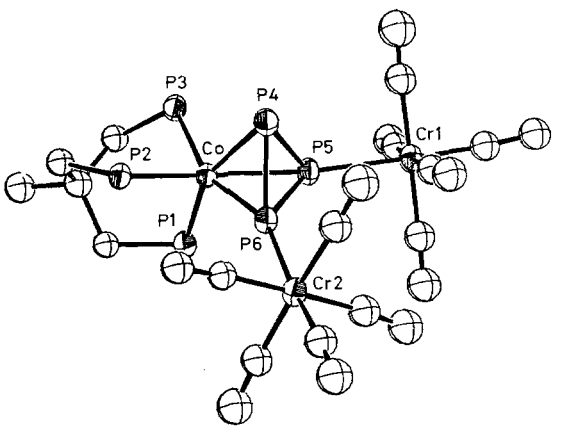


Fig. 1. Inner skeleton of *(3)* [ORTEP diagram]. Monoclinic, space group C2/c, $a = 36.48(2)$, $b = 13.45(1)$, $c = 26.59(1)$ Å, $\beta = 105.0(1)°$, $Z = 8$. Data collection: Philips PW 1100 automatic diffractometer, refined from 3725 observed reflections with $I \geq 3\sigma(I)$ to $R = 0.08$. Bond lengths: P—P(ring) = 2.14, Cr—P = 2.42 Å (av.). Bond angles: Cr1—P5—P6 = 132.8°, Cr1—P5—P4 = 123.3°, Cr1—P5—Co = 165.4°, Cr2—P6—P5 = 138.1°, Cr2—P6—P4 = 129.6°, Cr2—P6—Co = 157.1°.

(1) to be almost unchanged on bonding to the two Cr(CO)$_5$ groups. Each Cr atom is six-coordinate and is bound to a P atom and to five CO groups in a distorted octahedral geometry. The values of the CrPCo and CrPP angles, which range from 123.3 to 165.4°, show that the Cr—P bonds lie out of the plane of the P$_3$ ring. The Cr—P distances, 2.42 Å, are equal to the Cr—P distance in the complex $Ph_3PCr(CO)_5$[12]. This suggests that the coordination properties of the P atoms in the *cyclo*-P$_3$ unit are similar to those of the phosphorus in triphenylphosphane.

[*] Prof. Dr. L. Sacconi, Dr. S. Midollini, Dr. A. Orlandini
Istituto di Chimica Generale e Inorganica, Università, Laboratorio CNR
Via J. Nardi 39, I-50132 Florence (Italy)

The IR spectra in $CHCl_3$ solution of the complexes *(2)* and *(3)* in the CO region are essentially similar. The 2058 w, 1990 vw, 1945 s, and 1917 m cm^{-1} bands (attributable to A_1^1, B_1, E, A_1^2 modes, respectively, in the complex *(2)*) are those expected for a $LCr(CO)_5$ complex in which the local symmetry is reduced by the lower symmetry of the L group[3].

While the cobalt atom formally accepts three electrons from the three phosphorus atoms of the μ_3-bonded P_3 unit, each chromium atom receives an electron pair from one P atom. Thus each metal atom in the trinuclear complex has a closed-shell electronic structure with consequent diamagnetism.

Procedure

A solution of *(1)* (300 mg, 0.39 mmol) in THF (40 ml) is added under nitrogen to solid $Cr(CO)_6$ (600 mg, 2.7 mmol) in a quartz vessel. The mixture is refluxed under UV light for 4 h. The red-brown solution is then evaporated and the unreacted $Cr(CO)_6$ removed by sublimation. The residue is dissolved in THF and mixed with dibutyl ether. After concentration, 150 mg of *(3)* is obtained. If only 87 mg (0.39 mmol) of $Cr(CO)_6$ is employed, compound *(2)* is obtained.

Received: July 31, 1978
in abbreviated form: September 6, 1978 [Z 70 IE]
German version: Angew. Chem. *91*, 93 (1979)

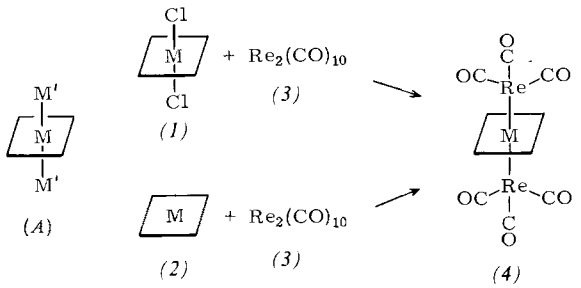
[1] *M. Di Vaira, C. A. Ghilardi, S. Midollini, L. Sacconi*, J. Am. Chem. Soc. *100*, 2550 (1978).
[2] *H. J. Plastas, J. M. Stewart, S. O. Grim*, Inorg. Chem. *12*, 265 (1973).
[3] *G. R. Dobson, I. W. Stolz, R. K. Sheline*, Adv. Inorg. Chem. Radiochem. *8*, 1 (1966).

Preparation of a New Series of Trinuclear Metallophthalocyanines and -porphyrins

By *Shinzi Kato, Ippei Noda, Masateru Mizuta*, and *Yuji Itoh*[*]

Polynuclear metalloporphyrin complexes are well known[1], whereas the corresponding phthalocyanine complexes, have so far never been described in the literature. We report here on the synthesis of novel trinuclear metallophthalocyanines and -porphyrins of the type (A), M, M' = metal.

The compounds *(4a)* and *(4d)* listed in Table 1 where obtained on reaction of dichloro(phthalocyaninato)tin(IV) *(1a)*, $Sn(Pc)Cl_2$, or dichloro(5,10,15,20-tetraphenylporphyrinato)tin(IV) *(1d)*, $Sn(TPP)Cl_2$ with decacarbonyldirhenium *(3)* at 180 °C. It is interesting that reaction of *(3)* with complexes possessing no axial ligands such as Zn(Pc) *(2b)* or Mg(TPP) *(2f)* likewise leads to the trinuclear compounds *(4)*.



The structures proposed for *(4a)*—*(4g)* are in accord with the results of elemental analysis and UV/VIS, IR and Raman spectroscopic data. The UV/VIS absorption spectra contain characteristic bands or a Soret band; the maxima are very similar to those of the starting complexes *(1)* or *(2)*, thus suggesting the presence of the phthalocyaninato- or porphyrinatometal moiety. In the mass spectra, no chloride ion was detected. The infrared spectra of the complexes in the solid state show characteristic intense bands in the region of the metal carbonyl stretching bands and resemble quite closely those of $TPP[Re(CO)_3]_2$[2]; this would suggest the presence of two $Re(CO)_3$ groups, one located above and the other below the plane of the Pc- or TPP-ligand. No characteristic absorption bands appear in the FIR region of 150—250 cm^{-1}, in which the metal-metal stretching vibrations of tin-transition metal complexes are to be observed[3].

Though the existence of metal-metal bonds in the complexes *(4)* could not be proven, we assign the structures[4] of type (A) to these compounds on the basis of the spectral data mentioned above, and the results of an X-ray structure analysis on the complex $[Sn(TPP)\{Re(CO)_3(C)\}_2]$[5], obtained according to a similar procedure at 160—165 °C.

Experimental

A mixture of *(1a)* (70.2 mg, 0.1 mmol) and *(3)* (326 mg, 0.5 mmol) in *o*-dichlorobenzene (6 ml) was heated at 180 °C for 7 h. Two characteristic bands in the VIS spectrum at 631 and 696 nm (in CH_2Cl_2) disappeared and new bands appeared at 644 and 712 nm (in CH_2Cl_2). After removal of solvent *in vacuo* and subsequent vacuum sublimation of excess

Table 1. Trinuclear metallophthalocyanine and -porphyrin complexes *(4)*; L = $Re(CO)_3$. All complexes melt above 300 °C.

Complexes		Yield [%]	UV/VIS Solvent	UV/VIS λ_{max} [nm]	IR, Raman [a]	IR, Raman [a] ν(C≡O) [cm^{-1}]
(1a)→*(4a)*	$Sn(Pc)L_2$	68	CH_2Cl_2	644, 712	KBr	2000, 1995, 1980, 1940 sh, 1905
(2b)→*(4b)*	$Zn(Pc)L_2$	56	$1\text{-}C_{10}H_7Cl$	613, 648, 679	KBr	2050, 1995, 1920
(2c)→*(4c)*	$Mg(Pc)L_2$	37	$o\text{-}Cl_2C_6H_4$	615, 644, 661, 698	CH_2Cl_2	2000, 1995, 1930
(1d)→*(4d)*	$Sn(TPP)L_2$	23	CH_2Cl_2	436 sh, 446 (Soret), 576, 620	CH_2Cl_2	2000, 1995, 1920, 2280 [a], 2200 [a]
(2e)→*(4e)*	$Zn(TPP)L_2$	48	$CHCl_3$	424 sh, 440 (Soret), 468, 510, 602, 653	KBr	2000, 1995, 1990
(2f)→*(4f)*	$Mg(TPP)L_2$	63	CH_2Cl_2	400 sh, 409 (Soret), 458, 511, 658	CH_2Cl_2	2000, 1995, 1930, 2256 [a], 2194 [a]
(2g)→*(4g)*	$Co(TPP)L_2$	45	CH_2Cl_2	418 (Soret), 479 sh, 653	KBr	2050, 1995, 1920, 2235 [a], 2175 [a]

[a] Raman in $CHCl_3$.

[*] Prof. Dr. S. Kato [+], I. Noda, Prof. Dr. M. Mizuta, Y. Itoh
Department of Chemistry, Faculty of Engineering, Gifu University
Kagamihara, Gifu 504 (Japan)
[+] Author to whom correspondence should be addressed.

(3), column chromatographic purification (Sephadex LH-20, CH_2Cl_2) of the resulting residue gave 79.2 mg (68%) of phthalocyaninato[bis(tricarbonylrhenium)]tin *(4a)* as dark green microcrystals.

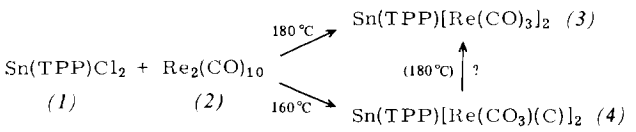
Received: October 10, 1978 [Z 129a IE]
German version: Angew. Chem. *91*, 84 (1979)

[1] a) *J. W. Buchler* in *K. M. Smith*: Porphyrins and Metalloporphyrins. Elsevier, New York 1974, p. 157; b) *W. R. Scheidt*, Acc. Chem. Res. *10*, 339 (1977).
[2] a) *C. P. Hrung*, Dissertation, Texas A & M University 1975; b) *M. Tsutsui, C. P. Hrung, D. Ostfeld, T. S. Srivastava, D. L. Cullen, E. F. Meyer, Jr.*, J. Am. Chem. Soc. 97, 3952 (1975).
[3] *U. Kunze, S. B. Sastrawan*, J. Organomet. Chem. *154*, 223 (1978).
[4] Crystals suitable for an X-ray structure analysis have still not been obtained.
[5] *I. Noda, S. Kato, M. Mizuta, N. Yasuoka, N. Kasai*, Angew. Chem. *91*, 85 (1979); Angew. Chem. Int. Ed. Engl. *18*, 83 (1979).

A Metalloporphyrin Containing Carbyne-like Carbido Carbon: 5,10,15,20-Tetraphenylporphyrinato[bis(μ-carbidotricarbonylrhenium)]tin(IV)[**]

By *Ippei Noda, Shinzi Kato, Masateru Mizuta, Noritake Yasuoka*, and *Nobutami Kasai*[*]

The green 5,10,15,20-tetraphenylporphinato[bis(tricarbonylrhenium)]tin(IV) *(3)*[1] is formed on reaction of the dichloro compound *(1)* with decacarbonyldirhenium *(2)* at 180°C. Interestingly, however, we have found that the same reaction at 160–165°C affords a dark red complex *(4)*, showing similar IR spectroscopic data to those of *(3)*. An X-ray structure analysis[3] of *(4)*, revealed it as being, to our knowledge, the first metalloporphyrin containing carbido-carbon ligands.



The compound *(4)* was prepared by a procedure similar to that used previously[2], from *(1)* and *(2)* by 240 hours' heating at 160–165°C [$\lambda_{max}(CH_2Cl_2)$: 402 sh, 420 (Soret), 512, 552, 591 and 628 nm; ν(C≡O) (KBr): 2000, 1995, and 1920 cm^{-1}]. Small single crystals of *(4)* for X-ray crystallographic analysis were obtained on allowing a solution of the complex in *o*-dichlorobenzene to stand for several weeks. As shown in Figure 1 the centrosymmetric molecule contains two $Re(CO)_3$ groups, one located above and one below the plane of the porphyrin ring which is centered by the tin atom. Surprisingly, the tin and rhenium atoms are linked by a carbido-carbon atom, which is bound carbyne-like to the rhenium atom. The Re—C1 length (1.75 Å) is close to the Re≡C distance (1.747 Å) which might be predicted from the sum of the covalent radii [using half the Re≡Re distance (1.145 Å) in $Re_2Cl_5 \cdot \{MeS(CH_2)_2SMe\}_2$[4] and half the C≡C

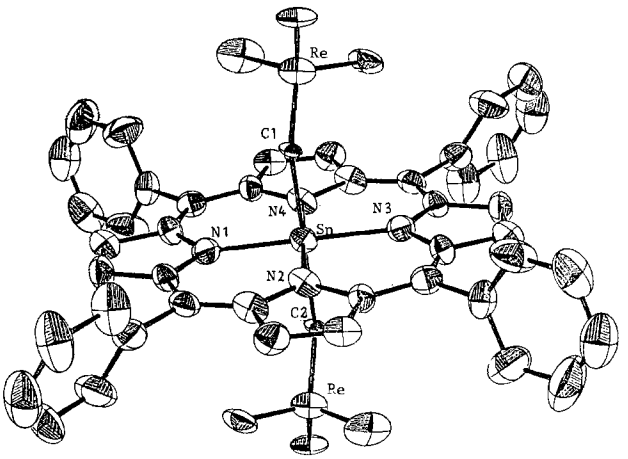


Fig. 1. Structure of the carbido complex *(4)* [3].

distance (0.603 Å)[5] in common acetylene compounds]. The Sn—C1 length (2.14 Å) is in good agreement with the length of the Sn—C single bonds in $Me_2ClSnSC(S)NMe_2$[6] [2.17(5) and 2.20(5) Å]. Further, it is interesting that the Sn—C1≡Re angle is 138.5(8)°. Thus, the Sn—C≡Re linkage is nonlinear. We connot as yet offer a reasonable explanation for this finding. The angles N1—Sn—C1 and N2—Sn—C1 are 89.4(5) and 90.6(5)°, respectively. The porphyrin ring is planar within 0.7 Å; Sn, N1, N2, N3 and N4 lie in a plane. Two Sn—N lengths [2.07(2) Å] are equal, the N—Sn—N angles are 89.3(6) and 90.1(6)°, and the other bond lengths and angles also have values in the usual range. At the present time, it is unclear whether *(4)* is converted into *(3)* or not on heating to 180°C[7].

Received: October 10, 1978 [Z 129b IE]
German version: Angew. Chem. *91*, 85 (1979)

[1] *S. Kato, I. Noda, M. Mizuta, Y. Itoh*, Angew. Chem. *91*, 84 (1979); Angew. Chem. Int. Ed. Engl. *18*, 82 (1979).
[2] *M. Tsutsui, C. P. Hrung, D. Ostfeld, T. S. Srivastava, D. L. Cullen, E. F. Meyer, Jr.*, J. Am. Chem. Soc. 97, 3952 (1975).
[3] The structure was solved by the heavy-atom method and refined to convergence ($R = 0.084$) using anisotropic temperature factors for all non-hydrogen atoms: Sn(TPP)[Re(CO)$_3$(C)]$_2$ 2*o*-$C_6H_4Cl_2$, space group $P2_1/n$ (No. 14), $a = 10.44(2)$, $b = 13.48(1)$, $c = 20.19(2)$ Å, $\beta = 110.8(1)°$, $Z = 2$, $\rho_{exp} = 1.92$, $\rho_{calc} = 2.02$ g cm^{-3}, $\mu(Mo) = 61.6$ cm^{-1}. Diffractometer with graphite-monochromatized Mo-Kα radiation, ω scan technique. *A. Ashida*, The Universal Crystallographic Computing Program System-Osaka, the Computer Center, Osaka University (1973).
[4] *M. J. Bennett, F. A. Cotton, R. A. Walton*, J. Am. Chem. Soc. *88*, 3866 (1966).
[5] *L. Pauling*: The Nature of the Chemical bond. 3rd Edit. Cornell University Press, Ithaca 1960.
[6] *N. Yasuoka, N. Kasai, M. Kakudo*, Bull. Chem. Soc. Jpn. *43*, 1601 (1970).
[7] We have confirmed spectroscopically the conversion of *(4)* into *(3)* on heating at 180°C under excess of $Re_2(CO)_{10}$.

Carbonylation of Lithium Dialkylamides to Give Carbamoyllithiums

By *Valentin Rautenstrauch* and *Michel Joyeux*[*]

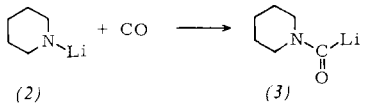
Authentic acyl anions would be useful as reagents in organic synthesis[1] and as models for the study of acyl-transition

[*] Prof. Dr. S. Kato [+], I. Noda, Prof. Dr. M. Mizuta
Department of Chemistry, Faculty of Engineering, Gifu University
Kagamihara, Gifu 504 (Japan)
Prof. Dr. N. Kasai [+], Prof. Dr. N. Yasuoka
Department of Applied Chemistry, Faculty of Engineering, Osaka University
Yamadakami, Suita, Osaka 565 (Japan)
[+] Authors to whom correspondence should be addressed.

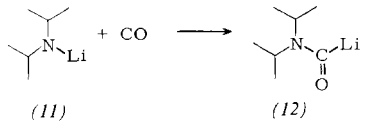
[**] We wish to thank Professor Dr. *A. Nakamura* and Dr. *K. Miki* of Osaka University and Professor Dr. *T. Ashida* and Prof. Dr. *T. Sakabe* of Nagoya University for useful comments.

[*] Dr. V. Rautenstrauch [+], Dr. M. Joyeux
Firmenich SA, Laboratoire de Recherche
b.p. 239, CH-1211 Genève 8 (Switzerland)
[+] Author to whom correspondence should be addressed: on leave at the Department of Chemistry, Stanford University, Stanford, Calif. 94305 (USA).

metal compounds. Only certain carbamoyllithiums (CAL-s) with presumably ionic, bent structures appear to be largely persistent in solution[2–5] and thus represent an unexplained "island of stability" in the area of acyl anions. Of the reported modes of formation—namely (A) the addition of carbon monoxide to lithium dimethylamide[2a] or *tert*-butylamide[2b, 6], (B) the transmetalation between butyllithium and bis(diethylcarbamoyl)mercury[3], and (C) the lithiation of dialkylformamides with lithium diisopropylamide[4] or *tert*-butyllithium[5]—the simplest, method (A), has been the least studied, with contradictory results (cf. [2]). We have investigated method (A) in detail and report typical findings with two lithium dialkylamides[6].

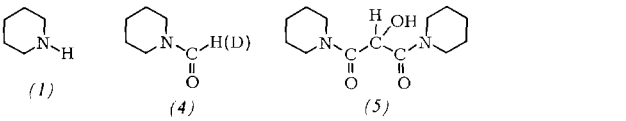


(2) *(3)*

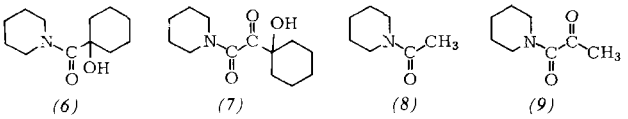


(11) *(12)*

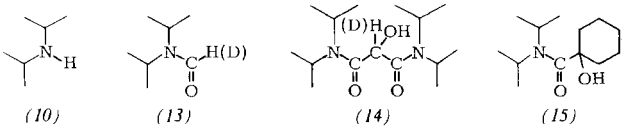
Passing CO into a *ca.* 0.6 M solution of lithium piperidide *(2)* in 1,2-dimethoxyethane (DME)/tetrahydrofuran(THF)/hexane at *ca.* −75 °C under standard conditions [Procedure (PR)] affords a solution of the corresponding CAL *(3)*, detectable by trapping reactions. Hydrolysis leads to the formamide *(4)* [yield based on *(2)* 20—30 %[7a]], hydrolysis with D_2O and workup with H_2O to the labeled formamide $[D_1]$-*(4)* along with small amounts of *(4)* [85:15 to 90:10[7b]]. Reaction with cyclohexanone (0.6 equiv., PR) and hydrolysis gives the hydroxycarboxamide *(6)* [m.p. 121—122 °C] and in addition the hydroxy(oxo)carboxamide *(7)* [m.p. 116—117 °C; molar ratio ≈4:1, yield *(6)* + *(7)* *ca.* 85 %[8a]]. Similarly, reaction with methyl iodide (PR) and hydrolysis affords the acetamide *(8)* and the α-oxopropionamide *(9)* [≈1:1, yield *(8)* + *(9)* *ca.* 65 %[8a]]. Reaction with *(8)* instead of methyl iodide under otherwise the same conditions and subsequent hydrolysis likewise leads to *(9)*: addition of *(3)* to *(8)* thus competes with the methylation of *(3)*; protonation of the secondary adduct leads to cleavage to give *(9)* and *(1)*. *(7)* (and *(1)*) must be formed analogously, by addition of *(3)* to the initially formed alkoxide of *(6)*, protonation of the secondary adduct, and cleavage. *(3)* apparently does not react further with the secondary adducts.



(1) *(4)* *(5)*



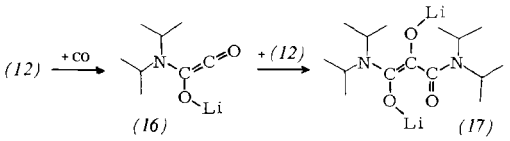
(6) *(7)* *(8)* *(9)*



(10) *(13)* *(14)* *(15)*

Passing CO into a solution of lithium diisopropylamide *(11)* at *ca.* −75 °C (PR) analogously affords a solution of the corresponding, hindered CAL *(12)*. On reaction with cyclohexanone, the secondary addition is suppressed, and after hydrolysis *(15)* is obtained [m.p. 137–138 °C, yield *ca.* 50 %[8a, b]]. Hydrolysis affords the formamide *(13)* [yield based on *(11)* 20—40 %[7a]]; hydrolysis with D_2O and workup with H_2O gives the labeled formamide $[D_1]$-*(13)* along with small amounts of *(13)* [84:16 to 98:2[7b, 9]].

Both on prior (partial) trapping of *(3)* and *(12)* with cyclohexanone and subsequent hydrolysis [→ *(6)* + *(7)* and → *(15)*] and on direct hydrolysis, the hydroxymalonamides *(5)*[8c] [m.p. 81—82 °C] and *(14)* [m.p. 102—103 °C; yield based on *(11)* or *(10)* (stoichiometry: 2 *(10)* + 3 CO → *(14)*, 10—20 %[7a]] are isolated[10] along with the formamides *(4)* and *(13)*. When CAL *(12)* is generated *via* method (C), without introduction of CO, *via* the equilibrium *(11)* + *(13)* ⇌ *(10)* + *(12)*, in concentrations comparable with those obtained here on carbonylation (starting from *ca.* 0.5 M solutions of *(11)* and *(13)*) and in the same medium, none of *(14)* is found on hydrolysis after leaving the reaction mixtures for 5 min *(4b)* to 4 h[9] at *ca.* −75 °C. This suggests that the anionic precursors of *(14)* and *(5)* are formed by twofold addition of the CAL-s *(12)* and *(3)* to CO: the yield of *(14)* [*ca.* 35 % together with 20 % of *(13)*] indeed increases when more CO is introduced (PR, introduction of CO for 9 instead of 4 h)[11]. For this reason we have not attempted to convert the lithium amides *(2)* and *(11)* completely. Even more *(14)* [yield *ca.* 40 %] is isolated when the carbonylation is carried out at *ca.* 5 °C (otherwise according to PR). *(12)* presumably reacts with CO to give a short-lived adduct *(16)*, which rapidly adds *(12)* to give the dianion *(17)* of *(14)* (formation of the dianion of *(5)* analogous). Hydrolysis with D_2O[9] and workup with H_2O indeed leads to labeled $[D_1]$-*(14)*[12].



(12) *(16)* *(17)*

Most lithium dialkylamides should react analogously with CO to give CAL-s. Their synthetic utility is primarily limited by 1) the reaction of the CAL-s with CO; 2) the incomplete conversions of the amides [in part due to 1]; 3) the secondary additions of unhindered CAL-s to primary adducts.

Procedure

20 mmol of *n*-butyllithium (1.5—1.6 M) in hexane is added to 20 mmol of *(1)* or *(10)* in DME (10 ml) and THF (10 ml)[13] at *ca.* −75 °C under an inert gas and after 5 min CO is passed (*ca.* 3 l/h) at *ca.* −75 °C for 4 h through the stirred solution. Hydrolysis: the solution (*ca.* −75 °C) is poured into *ca.* 100 ml of H_2O (*ca.* 22 °C). Hydrolysis with D_2O[9]: 3 ml of D_2O (*ca.* 22 °C) is added at once to the stirred solution (*ca.* −75 °C) and the resulting mixture is diluted with H_2O. Reaction with cyclohexanone or methyl iodide: 0.6 mol of the substrates per mol of *(1)* or *(10)* is added at *ca.* −75 °C, and the resulting mixtures are stirred for 3 h ($C_6H_{10}O$) or 1 h (CH_3I) at −75 °C and finally for 1 h at *ca.* 5 °C; hydrolysis as above. Isolation: The hydrolysates are diluted to *ca.* 250 ml with H_2O and continuously extracted with ether for 48 h. The extracts are concentrated and roughly fractionated. Pure substances are obtained by gas chromatography and/or recrystallization.

Received: May 22, 1978 [Z 72a IE]
German version: Angew. Chem. *91*, 72 (1979)

[1] *D. Seebach* in *R. Scheffold:* Modern Synthetic Methods 1976. Sauerländer, Aarau 1976; in *D. Seyferth:* New Applications of Organometallic Reagents in Organic Synthesis. Elsevier, Amsterdam 1976.

[2] a) *P. Longi, R. Montagna, R. Mazzocchi*, Chim. Ind. (Milan) *47*, 480 (1965); b) *P. Jutzi, F. W. Schröder*, Angew. Chem. *83*, 334 (1971); Angew. Chem. Int. Ed. Engl. *10*, 339 (1971).

[3] *U. Schöllkopf, F. Gerhart*, Angew. Chem. 79, 819 (1967); Angew. Chem. Int. Ed. Engl. 6, 805 (1967). Method (B) is an indirect variant of method (A), since bis(diethylcarbamoyl)mercury is generated from Hg^{II}-acetate, diethylamine and CO: *U. Schöllkopf, F. Gerhart, ibid. 78*, 675 (1966), and *5*, 252 (1966).

[4] a) *B. Bánhidai, U. Schöllkopf*, Angew. Chem. *85*, 861 (1973); Angew. Chem. Int. Ed. Engl. *12*, 836 (1973); b) *R. R. Fraser, P. R. Hubert*, Can. J. Chem. *52*, 185 (1974); c) *U. Schöllkopf, H. Beckhaus*, Angew. Chem. *88*, 296 (1976); Angew. Chem. Int. Ed. Engl. *15*, 293 (1976); cf. also d) *H. Bredereck, F. Effenberger, R. Gleiter, ibid. 77*, 964 (1965), and *4*, 951 (1965).

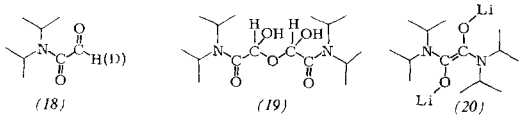
[5] *A. S. Fletcher, K. Smith, K. Swaminathan*, J. Chem. Soc. Perkin Trans. I *1977*, 1881.

[6] For the carbonylation of lithium monoalkylamides according to [2b] see *V. Rautenstrauch, M. Joyeux*, Angew. Chem. *91*, 73 (1979); Angew. Chem. Int. Ed. Engl. *18*, 85 (1979).

[7] a) Several runs. The variations in the yields are probably caused by variations in the CO flow and by incomplete extraction (PR). b) Several runs. Control experiments with $[D_1]$-*(4)* and $[D_1]$-*(13)* show that no D/H exchange takes place during the isolation; *(4)* and *(13)* are probably formed *via* method (C), on incomplete lithiation of the amines *(1)* and *(10)*.

[8] a) Yield not optimized. – b) The hydrolysate contains *(13)* and cyclohexanone, which probably reacts in part with unconsumed *(11)* to give the enolate. – c) Yield not determined, of the same order as that of *(14)*.

[9] On hydrolysis of the solutions of *(12)* with a relatively small amount of H_2O or D_2O (PR, hydrolysis with D_2O) the glyoxylamides *(18)* and $[D_1]$-*(18)*, respectively (cf. [4d]) [yield up to 15% based on *(11)*; only partially survives the extraction (PR)] or their readily formed hemihydrates *(19)* and $[D_2]$-*(19)* [m.p. 103–106°C (loss of water to give *(18)* and $[D_1]$-*(18)*, *meso*-form)] are obtained in varying yields, which long confused us: control experiments show that *(18)* (and/or *(19)* and/or the hydrate of *(18)*) is formed after the addition of H_2O or D_2O in the two-phase system consisting of the aqueous phase and the cold (*ca.* –75°C) DME/THF/hexane solution, which contains *(11)*, *(12)* (?), *(10)*, *(13)* and LiOH. *(18)* is *not* formed when the solutions are poured into a large excess of H_2O (PR, hydrolysis); it is also not formed in method (C), *via* addition of *(12)* to *(13)*. Thus *(18)* is neither derived from *(16)*, nor from a dimer *(20)* of *(12)*.



(18) *(19)* *(20)*

[10] Two further, not fully identified compounds are found in the hydrolysate of the solution containing *(3)*.

[11] Without further passage of CO, the CO still present in the solution reacts slowly with *(11)* and *(12)* on standing for 20–48 h at *ca.* –75°C (yield of *(13)* after hydrolysis *ca.* 20%, of *(14)* 20–40% [7a]; hydrolysis with D_2O gives $[D_1]$-*(13)*:*(13)* ≈ 97:3). We do not know whether the carbonylations under these conditions are reversible, as is the case at elevated temperatures: *J. C. Powers, R. Sneider, T. G. Parsons*, Tetrahedron Lett. *1965*, 1713.

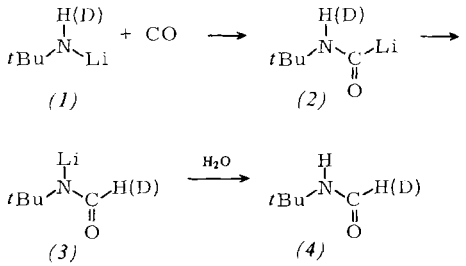
[12] 50–80% $[D_1]$-*(14)* several runs, 50–20% *(14)*; $[D_1]$-*(14)* apparently undergoes partial H/D exchange during isolation.

[13] With THF alone a jelly is formed which is converted into a normal solution by addition of DME.

Carbonylation of Lithium Monoalkylamides to Give *N*-Lithio(alkyl)formamides

By *Valentin Rautenstrauch* and *Michel Joyeux*[*]

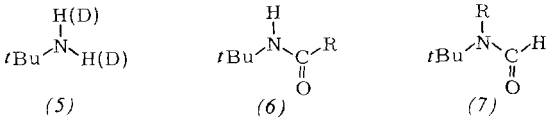
We report that the carbamoyllithium *(2)* which formed when carbon monoxide is passed into solutions of lithium *tert*-butylamide *(1)*[1] rearranges rapidly to give the *N*-lithioformamide *(3)*, as expected on the basis of the pK_a values of *(2)*.



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

Passing CO into *ca.* 0.6 M solutions of lithium dialkylamides in 1,2-dimethoxyethane/tetrahydrofuran/hexane at *ca.* –75°C under standard conditions affords the corresponding carbamoyllithiums[3] which are persistent in solution; hydrolysis leads to the *N*,*N*-dialkylformamides, hydrolysis with D_2O and workup with H_2O to the labeled $[D_1]$-formamides[3].

Reaction of the lithium monoalkylamide *(1)* with CO under these conditions (Procedure[3]) and subsequent hydrolysis also affords the *N*-alkylformamide *(4)* [yield based on *(1)* *ca.* 30%], but hydrolysis with D_2O and workup with H_2O leads to unlabeled *(4)* [yield *ca.* 50%[4]]. Analogous carbonylation of the labeled amide $[D_1]$-*(1)*—prepared from labeled *tert*-butylamide ($[D_2]$-*(5)*, $[D_1]$-*(5)*, *(5)*)[5], contaminated with *(1)*—and hydrolysis yields the labeled formamide



(5) *(6)* *(7)*

R = $SiMe_3$, $GeMe_3$, $PbMe_3$

$[D_1]$-*(4)* (91%) and a small amount of *(4)* (9%; yield of $[D_1]$-*(4)* + *(4)* *ca.* 15%[4, 5]). The ratios $[D_1]$-*(1)*:*(1)* and $[D_2]$-*(5)*:$[D_1]$-*(5)*:*(5)* were not determined independently, because D/H exchange is difficult to avoid during manipulation and analysis; $[D_1]$-*(1)*:*(1)* can at best have been ≥ 96:4[5] and may have dropped to ≥ 91:9 by D/H exchange. These experiments alone afford proof—which is more convincing when contrasted with the corresponding experiments with authentic carbamoyllithiums[3]—that *(2)* and $[D_1]$-*(2)* are shortlived primary products and rearrange to give *(3)* and $[D_1]$-*(3)*, respectively. This result can be generalized as formulated in the title. The derivatives described in [1] therefore did not have structures of type *(6)* most likely are the structures of type *(7)*[5].

Received: May 22, 1978 [Z 72b IE]
German version: Angew. Chem. *91*, 73 (1979)

[*] Dr. V. Rautenstrauch [+], Dr. M. Joyeux
Firmenich SA, Laboratoire de Recherche
b.p. 239, CH-1211 Genève 8 (Switzerland)

[+] Author to whom correspondence should be addressed; on leave at the Department of Chemistry, Stanford University, Standford, Calif. 94305 (USA).

[1] *P. Jutzi, F. W. Schröder*, Angew. Chem. *83*, 334 (1971); Angew. Chem. Int. Ed. Engl. *10*, 339 (1971).

[2] pK_a of R_2NCHO *ca.* 38 (*R. R. Fraser, P. R. Hubert*, Can. J. Chem. *52*, 185 (1974)), of $RNHCHO$ *ca.* 18 (*J. Z. Zabicky*: The Chemistry of Amides. Wiley-Interscience, New York 1970, p. 188–197).

[3] *V. Rautenstrauch, M. Joyeux*, Angew. Chem. *91*, 72 (1979); Angew. Chem. Int. Ed. Engl. *18*, 83 (1979).

[4] The variations in the yields are probably caused by variations in the CO flow, by incomplete extraction, and in the case of $[D_1]$-*(1)* by inaccurate weighing of ($[D_2]$-*(5)*, $[D_1]$-*(5)*, *(5)* [5]).

[5] *(5)* and D_2O were mixed in a molar ratio of 4:96; the mixture ([D_2]-*(5)*, [D_1]-*(5)*, *(5)*) formed by exchange was distilled into the reaction flask under argon and lithiated to give a mixture of [D_1]-*(1)* and *(1)* as, in [2] but with excess butyllithium so as to convert any entrained D_2O, HOD, H_2O into LiOD and LiOH. On complete exchange with the D_2O, without D/H exchange during distillation, and neglecting kinetic isotope effects in the lithiation [D_1]-*(1)* and *(1)* should have been formed in a molar ratio of 96:4.

[6] *L. Birkofer, A. Ritter*, Angew. Chem. 77, 414 (1965); Angew. Chem. Int. Ed. Engl. 4, 417 (1965); *L. Birkofer, H. Dickopp*, Chem. Ber. *101*, 3579 (1968).

BOOK REVIEWS

Optoacoustic Spectroscopy and Detection. Edited by *Yoh-Han Pao*. Academic Press, New York—London 1977. xi, 244 pp., numerous figs., and tables, bound, $ 19.00.

Optoacoustic or photoacoustic spectroscopy is one of the most recent procedures in instrumental analysis, although the underlying physical phenomenon was reported as long ago as 1880 by *Alexander Graham Bell*. It is a variant of classical absorption spectroscopy in the UV/visible and IR regions, in which a microphone is used as the detector. This combination of optics with acoustics has led to the designation optoacoustic or photoacoustic spectroscopy. In this, the first monograph on the new procedure nine authors, including *L. B. Kreuzer* and *A. Rosencwaig* who are accounted pioneers in the field, report on the physical principles, design of the apparatus, and the possible applications, in eight independent chapters each with its own bibliography.

An introductory chapter on signal production and detection is followed by sections on energy transfer, the principles underlying the optoacoustic spectrometer, on tunable light sources in the UV/visible and the IR region, and on the optoacoustic spectroscopy of gases and solids.

The individual chapters are very clearly written and are provided with a wealth of illustrations. The literature review is probably the most complete that exists at present for this field. The book can be recommended to all who are interested in this new process of instrumental analysis and are active in teaching and research or in the application of this area of absorption spectroscopy.

Egon Fahr [NB 438 IE]

Principles of Colloid and Surface Chemistry. By *P. C. Heimenz*. Undergraduate Chemistry: A Series of Textbooks, Vol. 4. Marcel Dekker, New York—Basel 1977. 1st edit., xi, 516 pp., bound, SFr. 64.00.

Important aspects of the extensive field of colloid chemistry are treated in eleven chapters with the physical considerations placed in the foreground.

After the introduction of the important experimental values, Chapters 1—4 give an extensive treatment of viscosity, sedimentation, and diffusion (the fundamental mathematical derivations are given in every case), and a discussion of osmotic phenomena. Chapter 5 discusses light scattering theoretically and with numerous experimental examples. There follow chapters on surface tension and adsorption from the liquid phase, starting consistently with the Gibbs equation. The description of adsorption isotherms is placed as the central point of Chapter 8, which deals with adsorption from the gas phase. Unfortunately, this chapter is confined to physisorption, whereas in view of the demanding title of the book at least a brief illustration of the very important area of chemisorption could have been expected. Chapter 9 is devoted to electrochemistry (electrode processes, Debye-Hückel and Gouy-Chapman theory), while van der Waals interaction and its significance for flocculation phenomena of colloidal particles are treated in Chapter 10. The final chapter contains information on electrophoresis and other electrokinetic phenomena.

All in all, the book covers an astonishingly wide field and offers many details; it is forcefully and clearly written, but also includes strict mathematical derivations wherever these are necessary. It is designed for chemists who wish to enter the field of colloid chemistry, though specialists too will find the occasional useful detail.

Klaus Christmann [NB 439 IE]

Methodische Fortschritte im medizinischen Laboratorium (Progress in Methods used in the Medical Laboratory). Vol. 3: **Akute Syndrome** (Acute Syndromes). Edited by *A. Englhardt* and *H. Lommel*. Verlag Chemie, Weinheim—New York 1978. 1st edit., viii, 288 pp., 35 figs., 138 tables, plastic, DM 62.00.

It is unfortunate that the subtitle "Laboratory diagnostics of acute internal diseases" does not appear on the cover, for what is the uninformed or even just the curious reader to make of an "acute syndrome"? Certainly not a "group of related acute symptoms" as given in textbooks and dictionaries.

In their foreword the editors indicate that the plan of the book was based on the following concepts:

1. All modern methods of an emergency laboratory are to be treated.
2. The book should be a reference work for acute situations that call for rapid treatment.
3. Detailed references should provide a review of clinical symptoms, diagnoses, and differential diagnoses.
4. Clearly laid out tables should give side by side clinical pictures and laboratory investigations.

The book contains the following chapters, written by a number of individual authors: acute endogenous intoxications, acute exogenous intoxications, acute cerebral processes: apoplexy and its differential diagnosis, acute disturbances of the cardiovascular system, acute disturbances of hemostatis: acute bleeding, acute disturbances in the abdominal region: the acute abdomen, acute inflammatory organ disorders, acute disturbances of the defense system against infections, acute hemolytic crisis.

It must be emphasized that the clinicochemical part determines the value of the book. All essential data on methods are described in detail or references are given to customary test methods. In view of the progress in the field of clinical chemistry this method of presentation will soon make necessary a supplementary volume or even a new edition.

The book contains a section (p. 281) on "Enzyme immunoassays for the detection of drugs in serum and urine", but the keyword "Enzyme immunoassay" does not appear in the index. There are many similar cases. This is indeed a pity, since a book on emergency medicine is naturally only as good as its index.

The clinician will regret particularly the omission of, *inter alia*, the following signs of acute pictures: diarrhea, unconsciousness due to lactacidosis, coma paraproteinaemicum, and pulmonary embolism.

The strength of the book lies in the emphasis on laboratory diagnostics, so that it can be recommended particularly to users in this field.

Friedrich Willig [NB 436 IE]

Structure Reports. Edited by *J. Trotter* for the International Union of Crystallography. Bohn, Scheltema & Holtema, Utrecht. Vol. 40B (part 1+2) for 1974. Organic Section. Publ. 1976, 1227 pp., bound, fl. 272.00; Vol. 41A for 1975, Metals and Inorganic Section. Publ. 1977, 477 pp., bound, fl. 127.50; 60-Year Structure Index 1913—1973. A. Metals and Inorganic Compounds. Publ. 1976, 229 pp., bound, fl. 68.00; Supplement for 1974—1975. Publ. 1977, 47 pp., bound fl. 10.00; 60-Year Structure Index 1913—1973. B. Organic and Organometallic Compounds. Publ. 1976, 437 pp., bound, fl. 161.50; Strukturbericht (Structure Report). Cumulative Index for Vol. 1—7 (1913—1939). Publ. 1976, 91 pp., bound, fl. 42.50 (Price to Subscribers).

X-Ray structure determinations enable the most extensive statements to be made about the structure of chemical compounds and are used increasingly because of the enormous development of automatic measuring procedures and of elegant methods of calculation. The volume of the results is increasing accordingly, but only their technically correct collection and ease of retrieval enable them to be rationally evaluated by the many potential users, be they crystallographers, chemists, biologists, mineralogists, physicists, metallurgists, or others.

Therefore, in 1956, the International Union of Crystallography continued as "Structure Reports" the "Strukturberichte" begun in 1931 by *P. P. Ewald* and *C. Hermann*; with the volumes listed above it was possible to catch up with the current literature, insofar as this is ever possible in a traditional abstracts publication.

Whereas at the beginning of the series each paper of "structural interest" was abstracted critically and in detail, the data have had to be reduced to the core of the structural information: chemical formula, name of the substance, literature citation (with reference to older papers), unit cell, space group, conditions of measurement, description of structure (sometimes with illustration), atomic distances and bond angles (selected values), and atomic coordinates (only for the simpler structures). Nowadays each volume contains the structures published in the year specified, provided that the data named above can be taken from the paper.

In the volumes of series A the structures are arranged in order of increasing complexity but with regard to the chemical relationships (*e.g.* alloys, sulfides, oxides, phosphates, silicates). In the volumes of series B a division into classes has been attempted (*e.g.* aliphatic amines, N-heterocycles, metal complexes (N-ligand)). Structures for which the data are incomplete are collected in a table.

The reader obtains a stimulating review, the user is thrown back on the indexes: author's name index, substance name index (rational and mineral names), and the molecular formula index. Since the year of publication is second in importance for the purposes of a structure search, the new 60-year indexes are a very considerable help to the owner of all the volumes. An attempt to increase the usefulness has been made by means of a classified index. In Part A the index for some classes is according to the molecular formula, for others according to the periodic system. In addition, this volume contains an alphabetical index of mineral names and a structure-type index after *Pearson* for metallic substances. Part B contains, besides the usual molecular formula index a classifying molecular formula index, sorted according to organic-chemical classes and according to compounds of the transition metals.

Since further structural information was provided in the first volumes of the series (Strukturbericht 1—7), these volumes have additionally their own collective index, which contains special subject and substance indexes taken from the original indexes after modernization and translation into English.

The value of a collection of abstracts must be measured by the criteria of completeness, reliability, variety of entry points, and the period covered. Although the yearly volumes are a great help and often make it unnecessary to go to the original literature, yet in the important 60-year indexes many things can be sought in vain. Many molecular formulas given in the individual indexes are lost. In the classifying indexes the compounds are entered only once, but one does not know where. For instance, "tricarbonyl(hexaethylborazine)chromium(0)" is found among the metal-π-complexes (arenes) but not among boron compounds. In the more detailed classifying index of inorganic compounds the variable nomenclature makes searching still more of a problem. Thus, $Cu_2In_2O_5$ occurs not among the indates, like *e.g.* $CdIn_2O_4$, but among cuprates as "copper indium oxide"; $CuAl_2O_4$ not among the aluminates, like *e.g.* $NiAl_2O_4$, but among cuprates as "copper(II) aluminate". No one should be deceived by the simple, apparently obvious division into classes (nitrates, tellurides, *etc.*) into thinking that the chemical relations are completely reproduced. Search for compounds containing several relevant components requires great care; one finds the Roussin compounds $CsFe_4S_3(NO)_7(H_2O)$ among sulfides, $Fe_4(NO)_4S_4$ among nitrosyls, and $(C_2H_5)_2(Fe_2(NO)_4S_2)$ in the organic part among metal complexes with a sulfur ligand.

To aid a search for crystal structures of organic and organometallic compounds better indexes are available; for metals and inorganic compounds the present book is, in spite of its failings, currently the most complete work of reference. Particularly noteworthy is the structure-type index (after *Pearson*), containing nearly 2000 compounds.

That the problem of finding and displaying large quantities of data can also be handled in a modern way is shown by the work "Molecular Structure and Dimensions"[*].

Günter Bergerhoff [NB 440a IE]

Liquid Fuels from Coal. Edited by *R. T. Ellington*, Academic Press, New York—London, 1977. 1st edit., xvii, 273 pp., numerous figs. and tables, bound, $ 14.50.

A great deal of R & D work has been done in the USA on the liquefaction of coal in the past few years, and the subject was discussed in detail at the 172nd National Meeting of the American Chemical Society in 1976. This book contains 17 studies, each preceded by a short introductory note by the editor. The following topics are discussed:

Dissolution and liquefaction of coal: effect of the solvent; liquefaction with mixtures of H_2 and CO; influence of various catalyst-carriers and of the mineral fraction of coal.

Kinetics of various reactions: hydrogenation over Co/Mo

[*] Cf. Angew. Chem. Int. Ed. Engl. *17*, 872 (1978).

catalysts; general criteria for catalyst development; regeneration and abrasion of the catalyst in the H-coal process; kinetics of coal hydrodesulfurization; solubility of hydrogen and the kinetics of the hydrogenation of coal; short contact time liquefaction of coal.

Separation of solid products: modification of the particle size of inorganic coal components in the liquid product; coagulation and filtration of the ash components in the Synthoil process.

Analytical methods: separation procedures and development of methods for product analysis; application of high-pressure liquid chromatography; petrographic classification of solid residues.

The experimental equipment is generally described accurately and the results are detailed in tables and diagrams. The book is well worth recommending. The results are of interest not only for the liquefaction of coal, but also for the processing of heavy petroleum residues.

K. Hedden [NB 434 IE]

Ullmanns Encyklopädie der technischen Chemie. Edited by *E. Bartholomé, E. Biekert, H. Hellmann, H. Ley* (deceased), and *W. M. Weigert* (deceased). Volume 13: Hormone bis Keramik (Hormones to Ceramics). Verlag Chemie, Weinheim—New York 1977. 4th Edit., xv, 735 pp., bound DM 380.00.—Volume 14: Keramische Farben bis Kork (Ceramic Colors to Cork). Verlag Chemie, Weinheim—New York 1977. 4th Edit., xv, 717 pp., bound DM 380.00.

Volumes 13 and 14 of "Ullmann" continue the series of alphabetically arranged volumes of the new edition of this reference work.

Among the many keywords of Volume 13, the following ones catch the eye, partly on account of the size of the corresponding entries: Hormones (71 pages), insecticides (65 pages), ion exchangers (68 pages), rubber (129 pages). The last-named article impressively underlines the comprehensive and thorough treatment typical of "Ullmann". The entry is subdivided into five sections entitled: Introduction and natural rubber; synthetic rubber; rubber chemicals and additives; processing and regeneration; testing. Each of these sections is preceded, like every other entry, by a clear list of contents which reveals, for example, that the wealth of industrial and technical information presented is also accompanied by purely chemical material. In this case, for instance, the chemical composition of latex is considered under the heading "natural rubber".

Mention should be made of the following organic intermediates dealt with in Volume 13: hydroquinone (4 pages); aliphatic hydroxy- and keto carboxylic acids (9 pages); aromatic hydroxy carboxylic acids (6 pages); imidazole (3 pages); isocyanates (12 pages); isoprene (10 pages). Topics from inorganic chemistry include: hydrazine (13 pages); hydrides (25 pages); the elements indium (10 pages), iodine (8 pages), and potassium (66 pages), including their compounds; electrical insulators (19 pages), chalk (12 pages), ceramics (25 pages). Dyes are represented by the keywords indigo and indigoid dyes (5 pages), indicator dyes (14 pages), and cationic dyes (10 pages), and pharmaceuticals by cough medicines (12 pages), interferons (4 pages), and the article on hormones mentioned above. Various other keywords not assignable to specific substances also warrant attention: hydrogenation and dehydrogenation (13 pages); natural isotopes and isotope separation (31 pages); heterogeneous catalysis and catalysts (53 pages); and the keyword ion exchangers, in which there unfortunately appears to be some slight lack of coordination between the various authors. A further remark is also called for here: the so-called liquid ion exchangers are used not only in uranium recovery but also for the enrichment of other metals such as copper on an industrial scale (see also Volume 2, p. 571).

Volume 14 is dominated by two keywords which have become highly topical: nuclear engineering (167 pages) and coal and coal refining (282 pages). The article on nuclear engineering is largely devoted to the numerous chemical problems of this field; however, a well-balanced survey of the entire field is also given, as follows from the individual section headings: Historical and introduction; power reactors, general; thermal reactors (converters); breeders; fuel cycle; nuclear fusion. Of particular interest to the chemist is the section on the fuel cycle which could also contribute important factual material for restoring the current public discussion of nuclear power stations to a less emotional level. Precisely this keyword of nuclear engineering beautifully illustrates the way in which the presentation of a large field of study in the new Ullmann becomes a terse monograph in the best sense of the word. The same can be said of the keyword coal and coal refining. A preliminary general section considers, *inter alia*, the origin, occurrence, chemical structure, mining and processing of coal; methods of refining coal are also surveyed before being considered in separate sections: Fischer-Tropsch synthesis; gas production; hydrogenation; carbonization and coking of lignite; carbonization and coking of coal. The section on gas production considers not only gasification of coal but all other processes for the production of gas containing CO and H_2, as well as synthetic natural gas, *i.e.* processes using petroleum fractions (naphtha, heavy oil) and natural gas as raw materials. Thus all the problems connected with the production of these gases, which are of interest both as chemical raw materials and as energy sources, are surveyed in a comprehensive manner, as are purification operations.

Other large entries in Volume 14 include: adhesives and dispersions (42 pages), carbon (57 pages), hydrocarbons (62 pages, including the section on their separation). Furthermore, the keywords ketenes (9 pages), aliphatic ketones (31 pages), aromatic ketones (4 pages), and carboxylic esters (3 pages) represent organic intermediates, while inorganic materials include cobalt (18 pages), carbon dioxide (13 pages), and carbon monoxide (68 pages), and color chemistry is represented by ceramic colors (12 pages).

Summarizing, it may be said that the two volumes live up to the high standard already set by previous volumes with regard to quality of presentation and production.

Ulfert Onken [NB 445 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Catalysis in Coal Conversion. *By J. A. Cusumano, R. A. Dalla Betta,* and *R. B. Levy.* Academic Press, New York 1978. xiii, 272 pp., bound, $ 21.00.—ISBN 0-12-199935

Einführung in die Atom- und Molekülphysik. By *P. Zimmermann.* Akademische Verlagsgesellschaft, Wiesbaden 1978. 115 pp., paper, DM 16.80.—ISBN 3-400-00400-6

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 2
February 1979
Pages 91–172

Structure and Bonding in Cyclic Sulfur-Nitrogen Compounds

By Herbert W. Roesky[*]

The coordination number of sulfur is used in this review as a classification principle; cyclic sulfur-nitrogen compounds in which the sulfur is di-, tri-, and tetracoordinated are discussed. Compounds with sulfur (and nitrogen) of coordination number 2 are electron-rich combinations of elements whose π-electrons are extensively delocalized. A correlation between the coordination number and the bond length can be observed in certain compounds containing tri- and tetracoordinated sulfur.

1. Introduction

As a rule, the formal oxidation number of the sulfur atom is used for the description of sulfur compounds[1]. However, in many cases this formalism does not correctly reflect reality; thus, for S_4N_4 a mean oxidation number of +3 is obtained for the sulfur. As an alternative to the oxidation number, which cannot be measured, one can consider the coordination number, which is an observable.

2. Concept for the Description of Cyclic Sulfur-Nitrogen Compounds

Solely on the basis of the coordination numbers of two, three, and four there are 13 possible arrangements of the sulfur atom in ring systems (Table 1).

A graph-type notation can be selected to distinguish between these varieties[2]. For example, the six-membered ring *(1)*, which contains three sulfur atoms of type *a*, can be described by (*aaa*). Correspondingly, for the derivative *(2)* we obtain the notation (*kkk*). The notation (*abl*) corresponds to six-membered sulfur-nitrogen rings *(3)* with three types of sulfur

Table 1. Sulfur atoms as ring members with coordination numbers of two, three, and four. The 13 possibilities are indicated by lower-case letters.

Coordination number		
2	3	4
a	d	j
b	e	k
c	f	l
	g	m
	h	
	i	

[*] Prof. Dr. H. Roesky
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt/Main 50 (Germany)

(1) (aaa)

(2) (kkk)

atoms[3]. The sulfur-sulfur bonds in such rings are indicated by a bar placed over the corresponding identifying letters, *e.g.* ($\bar{a}\bar{e}b$) for the S_3N_2 derivative *(4)*.

The range of sulfur-nitrogen compounds is wide, since by starting with the 13 basic building blocks more than 100 chemically reasonable six-membered rings can be constructed. Only a few of these possibilities have so far actually been synthesized.

(3) (abl)

(4) ($\bar{a}\bar{e}b$)

It now becomes easy to understand that a useful nomenclature for sulfur-nitrogen compounds can be achieved in terms of coordination number alone.

Assuming the feasibility of classifying sulfur-nitrogen compounds by the coordination number, is it also possible to correlate chemical and physical properties with the coordination number? Before attempting to establish such relationships with the aid of examples, we shall describe certain representative syntheses of these types of compounds.

3. Selected Processes for the Synthesis of Sulfur-Nitrogen Compounds

In general, sulfur-nitrogen compounds are prepared from sulfur-halogen compounds and ammonia. A large variety of products is usually formed in such reactions. Some of the redox reactions involved, such as those in the synthesis of S_4N_4, are still not fully understood[4]. The best yield is obtained in the case of S_4N_4 when the S and the Cl are used in the ratio of 1:3; this can be accomplished by addition of elemental chlorine to SCl_2[5, 11]:

$$4SCl_2 + 2Cl_2 + 16NH_3 \rightarrow S_4N_4 + 12NH_4Cl$$

S_4N_4 (see Fig. 9) is a key compound for the preparation of SN-rings[6]. Reaction of S_2Cl_2 with NH_4Cl or urea affords $S_3N_2Cl^+Cl^-$ in good yield[7, 8].

What happens when the relatively stable N—H bond in the NH_3 molecule ($D^{298} = 390\,kJ\,mol^{-1}$) is replaced by the substantially weaker Sn—N bond in $N[Sn(CH_3)_3]_3$ ($D^{298} = 167\,kJ\,mol^{-1}$ in $(CH_3)_3SnN(CH_3)_2$)? In place of S_4N_4

$$4\ S_2Cl_2 + 4\ N[Sn(CH_3)_3]_3 \longrightarrow$$

$$\left[\begin{array}{c} CH_3 \\ N\text{–}Sn\text{–}CH_3 \\ S \quad | \\ N\text{–}S \end{array}\right]_2 + 2\ (CH_3)_4Sn + 1/2\ S_8 + 8\ (CH_3)_3SnCl$$

(5)

we obtain the tin compound *(5)* with two-coordinate sulfur and nitrogen atoms (see Fig. 1).

Depending on the temperature, S_4N_4 reacts with $N[Sn(CH_3)_3]_3$ to give the sulfur diimide *(6)* and sulfur:

$$S_4N_4 + 2N[Sn(CH_3)_3]_3 \rightarrow 3(CH_3)_3Sn\text{—}N{=}S{=}N\text{—}Sn(CH_3)_3 + {}^1/_8S_8$$

(6)

At higher temperatures the sulfur obtained acts as a nucleophilic reagent; the tin compound *(5)* is again formed[9, 10]:

$$2(6) + {}^1/_4S_8 \rightarrow (5) + 2(CH_3)_4Sn$$

Sulfur diimide *(6)* is an ideal starting material for the preparation of linear and cyclic SN compounds with a low coordination number of the sulfur, since the tin-nitrogen bond can very easily be cleaved by halides.

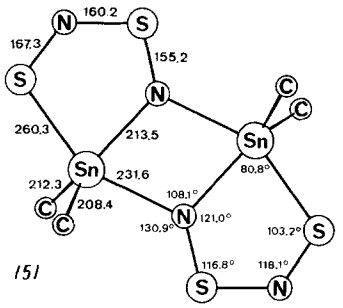


Fig. 1. Structure of dimeric $S_2N_2Sn(CH_3)_2$ *(5)*. Bond lengths in pm [25].

X-ray structure analysis of *(5)* (Fig. 1) reveals that the molecule is dimeric and planar in the solid state. The molecule consists of two five-membered rings and one four-membered ring, with fivefold-coordinated tin; coordination takes place *via* nitrogen and not *via* sulfur. Molecular-weight determinations reveal that the dimer is also present in solution[11].

The tin atom in compound *(5)* can easily be replaced. Thus, COF_2 will react to form cyclic ketone *(7)* (Fig. 2), while with SOF_2 the five-membered sulfur-nitrogen oxide S_3N_2O *(4)* is obtained, in which the sulfur atoms have coordination numbers of two or three.

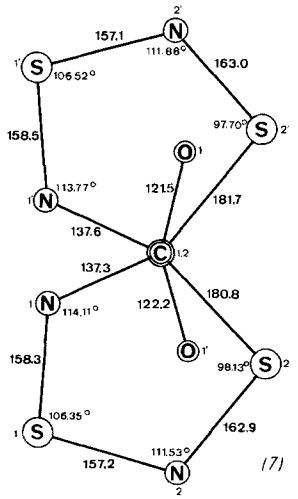
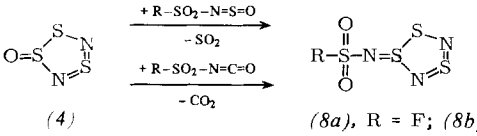


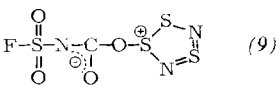
Fig. 2. Structure of S_2N_2CO *(7)* [27]. The molecules are arranged in pairs. Bond lengths in pm.

The ketone *(7)* is a yellow, crystalline solid that sublimes without decomposition in a vacuum; on UV irradiation it liberates CO to form S_4N_4. S_3N_2O *(4)* is a red, oily liquid which does not wet glass and which forms a plastic noncrystalline solid at low temperatures. S_3N_2O can be prepared very easily by hydrolysis of $S_3N_2Cl^+Cl^-$ with anhydrous formic acid[8]. On reaction of S_3N_2O *(4)* with iminosulfur oxides or isocyanates, SO_2 or CO_2 respectively is evolved and substituted sulfur-nitrogen five-membered rings of type *(8)* are obtained provided that the groups R are electron-attracting substituents.



(4) *(8a)*, R = F; *(8b)*, R = CF_3
(8c), R = n-C_4F_9

The above-mentioned reactions lead to the conclusion that the S_3N_2 ring structure is preserved during the reaction. When FSO_2NCO reacts with *(4)* an adduct is first formed, to which the structure *(9)* has been assigned on the basis of its IR spectrum. This suggests that compounds of type *(8)* may



(9)

also be obtained by cleavage of SnN or SiN bonds with $S_3N_2Cl^+Cl^-$[12–14].

Amides react with $S_3N_2Cl^+Cl^-$ with liberation of hydrogen chloride. While $CF_3SO_2NH_2$ gives rise to the five-membered ring *(8b)*, sulfamide ($H_2N—SO_2—NH_2$) gives the eight-membered ring $S_4N_4O_2$ (see Fig. 11)[8]. This reaction first made $S_4N_4O_2$ ready accessible; like S_4N_4 (see Fig. 9), it can react with a variety of reagents to give new ring systems. $S_4N_4O_2$ is a key compound for the preparation of SN rings with variously coordinated sulfur atoms[3].

However, S_4N_4 is still important in the synthesis of SN compounds with low coordination numbers of the ring atoms. Thus, its reaction with tetraalkylammonium azides[15] gives $N_3S_3^-$, while with the Lewis acid SbF_5 it gives the cation $S_4N_4^{2+}$[16]. From S_4N_4 and trifluoromethanesulfonic acid anhydride or AsF_5 we can isolate the radical-cation $N_2S_3^+$ in the form of a salt, so that its crystal structure can be determined (see Fig. 5c)[17, 18]. Since most reactions with SN compounds are of a radical nature, $N_2S_3^+$ is very important as an intermediate.

4. Sulfur-Nitrogen Compounds with Sulfur and Nitrogen of Coordination Number Two

Sulfur and nitrogen have very similar radius-to-charge ratios, assuming that both elements have a coordination number of two. The Mullikan electronegativity[19] of sulfur in its s^2p^4 valence state is 2.28, and that of nitrogen in its s^2p^3 valence state is also 2.28. An SN bond system of this type can be regarded as largely nonpolar. The six valence electrons of sulfur in such an SN unit can formally be classified as follows: two electrons are shared in σ-bonds, two form the lone pair, and two are left over for the formation of π-bonds. In nitrogen, one π-electron is left over. The number of π-electrons in the molecule can be increased systematically by adding further sulfur and nitrogen atoms. If the electron density within an SN rings is not too high, we can always expect to find planar rings with delocalized electrons. The electron density can be diminished by transforming the neutral molecule into the cation. These relationships will be demonstrated for rings of various sizes in the remaining part of this article.

4.1. Four-Membered Rings

The smallest SN ring known at present with coordination number 2 at the sulfur and nitrogen atoms is S_2N_2 (Fig. 3)[20, 21], which has a 6 π-electron structure.

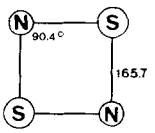


Fig. 3. Molecular structure of S_2N_2. Bond lengths in pm.

As expected, this molecule has SN bonds of approximately the same length and is square-planar. The bonding can be described by a four-center π-electron system. According to a simple Hückel MO treatment, the molecule has one pair of bonding π-electrons, four electrons are in nonbonding π-orbitals, while the π*-orbital is unoccupied (Fig. 4). S_2N_2 is isoelectronic with the planar S_4^{2+} cation[22, 23].

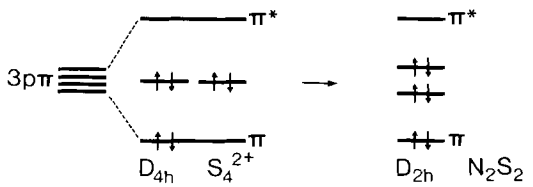


Fig. 4. Distribution of the four 3pπ atomic orbitals in S_2N_2; compare with S_4^{2+}.

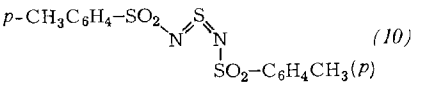
The square-planar D_{4h} symmetry of the S_4^{2+} ion is lowered to the D_{2h} symmetry of S_2N_2. With $SbCl_5$, S_2N_2 forms a 1:2 adduct; this implies an exchange interaction with the nonbonding π-electrons. From this we may conclude that the S—N bonds are not lengthened in the adduct. Molecular structure analysis confirms this assumption[24].

For the so far unknown $S_2N_2^{2+}$, isoelectronic with the P_4 molecule, we can postulate in advance a tetrahedral or planar structure with two localized double bonds.

4.2. Five-Membered Rings

What changes in bonding can be expected on going from four-membered to five-membered SN rings? Here we must consider whether the fifth member of the ring participates in the π-bonding. If we examine the bond lengths and angles in a series of five-membered rings with different atoms or groups X, comparison of the numerical values (Table 2) reveals no immediately obvious relationship. The atoms or groups X have no significant influence upon the S—N bond lengths. The mean bond lengths ($\overline{SN}$) in all three sulfur-nitrogen compounds are approximately constant. Evidently in the S_2N_2

part there is an electron-density distribution reminiscent of "electron billiards", as a consequence of slight differences in energy levels. Even the cations $N_2S_3^+$ (Fig. 5c) and $N_2S_3Cl^+$, in which the electron density is very much lower, give $\overline{SN}$ values that scarcely deviate from those of the neutral molecules. Further numerical values are given in Figure 5a.



(10)

favorable[30]. Both the *cis,trans*[31] and the *trans,trans* configuration[32] are known in complexes. However, besides the N-

Table 2. Bond lengths [pm] and angles [°] in five-membered SN rings with S_2N_2X skeleton.



Cpd.	>X	S1N1	S1N2	S2N2	$\overline{SN}$	∢N1	∢N2	∢S1	∢S2	Ref.
(5) [a]	$>Sn(CH_3)_2$	155.2	160.2	167.3	160.9	121.0	118.1	116.8	103.2	[25]
(8d) [b]	$>S^+-NR$	157.3	154.0	162.8	158.0	119.7	117.6	109.7	97.8	[25]
	$>S^+Cl$	161.7	154.3	161.5	159.1	118.0	120.7	106.3	95.5	[26]
(7) [c]	$>C^+-O$	158.3	157.2	162.9	159.4	114.1	111.5	106.3	98.1	[27]
[d]	$>S^+$	155.5	157.5	161.7	158.2	119.8	119.9	107.2	96.4	[18, 25]

[a] Dimer, cf. Fig. 1. [b] Cf. Fig. 5b. [c] Cf. Fig. 2. [d] Cf. Fig. 5c.

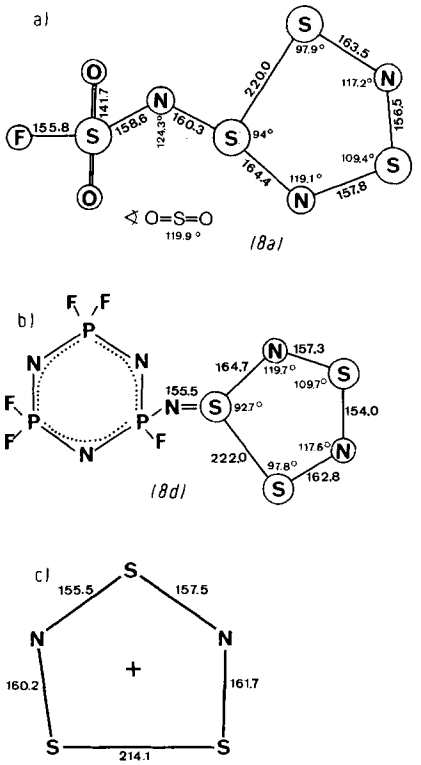


Fig. 5. Molecular structure of a) $S_3N_3SO_2F$ *(8a)*, b) $S_3N_3P_3N_3F_5$ *(8d)* obtained from the PN-ring with $N[Sn(CH_3)_3]_2$ substituents and $S_3N_2Cl^+Cl^-$, c) $S_3N_2^+$ [18, 25]. Bond lengths in pm.

All of the above five-membered rings can be described as 6 π-electron systems[28, 29]; they are almost planar.

4.3. Six-Membered Rings

Of the six-membered rings that contain sulfur and nitrogen with a coordination number of two, the sulfur diimide derivatives are very suitable for comparison purposes since they provide several well-investigated examples.

According to quantum-mechanical calculations, the *cis,trans* form of bis(*p*-tolylsulfonyl)sulfur diimide *(10)* is the most

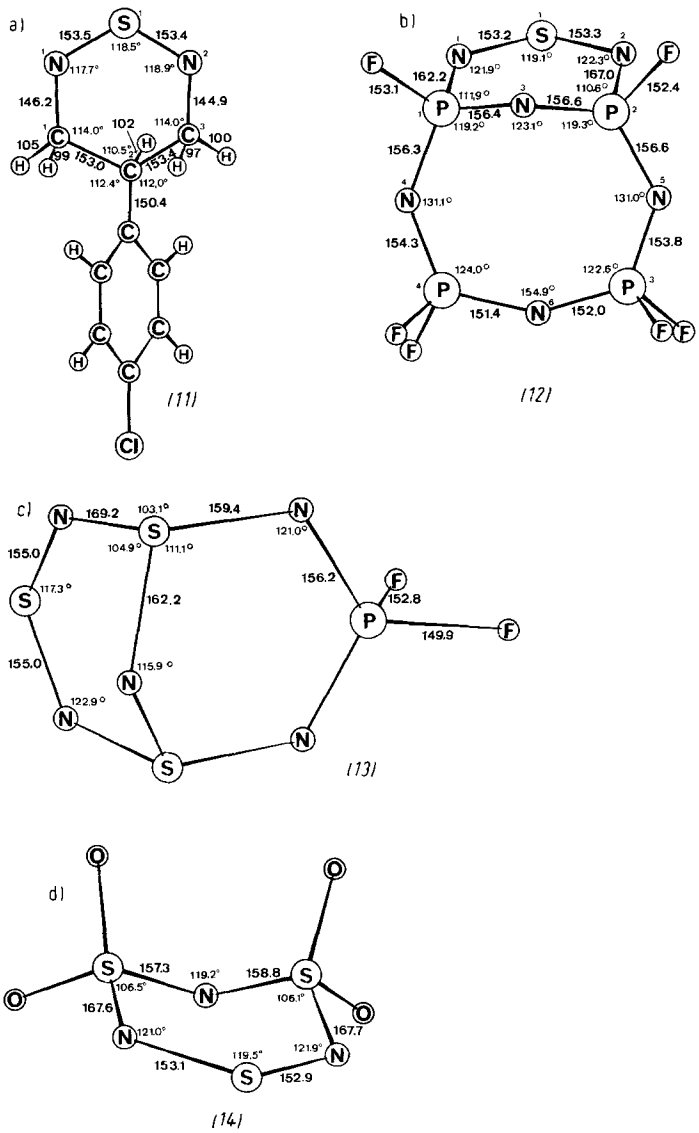
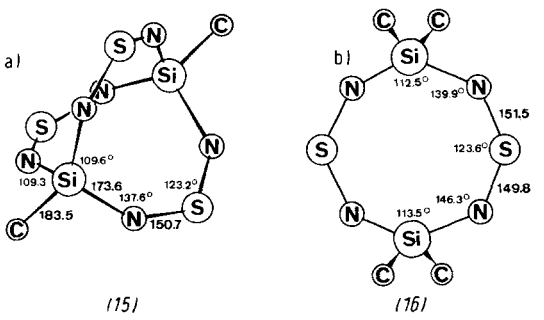


Fig. 6. Molecular structures of a) 4-(4-chlorophenyl)-4,5-dihydro-3*H*-1λ^4,2,6-thiadiazine *(11)* [34], b) $SN_2N_4P_4F_6$ *(12)* [35, 38], c) $S_3N_5PF_2$ *(13)* [37], d) $S_3N_3O_4^-$ *(14)* [36]. Bond lengths in pm.

atoms, the sulfur atom of the sulfur diimide can also act as a coordination site; examples of this are provided by the pentacarbonyl complexes of chromium and tungsten[33]. The *cis,cis* arrangement is attained in sulfur diimides by cyclization[34-42].

We shall consider the compounds *(11)*–*(14)* as representative examples, in which the sulfur diimide group is bound to tetracoordinated carbon[34], tetracoordinated phosphorus[35,38], or tri- or tetracoordinated sulfur[36,37] (Fig. 6). (The last two of these compounds do not, strictly speaking, belong in this section.)

The common feature of all the above-mentioned substituents on the nitrogen atoms of the SN_2 system in *(11)*–*(14)* is that they show no π-exchange interaction with this system. The substituents act as barriers to full conjugation with the 4 π-electron skeleton; only hyperconjugation is conceivable. This accounts for the almost identical S—N bond lengths and angles, which are not influenced even by a negative charge as in $S_3N_3O_4^-$ (Fig. 6d)[36] or by the electron-attracting action of fluorine atoms (Figs. 6b and 6c). Furthermore, it can be deduced that the S—N bond lengths are independent of the substituent so long as no π-interactions take place. The sulfur diimide group, including also the neighboring atoms, is planar. The nitrogen atoms of the SN_2 groups have bond angles of approximately 120° in all the compounds. On the basis of these results it is to be expected that the S—N bond will be shorter when the electron density between S and N is increased by an increase of the angle at the nitrogen or at the sulfur. In fact, we find that in both of the silicon-bridged SN_2 derivatives *(15)* and *(16)*[25,43-45] the S—N bonds are shortened to 150 pm (Fig. 7).



(15) *(16)*

Fig. 7. Molecular structure of a) $(CH_3)_2Si_2N_6S_3$ *(15)*, b) $(CH_3)_4Si_2N_4S_2$ *(16)*. Bond lengths in pm.

Compound *(16)* contains the shortest known bond between sulfur and nitrogen of coordination number two (149.8 pm). The reason for this shortening may be an alteration of the electron density in the σ-skeleton; this effect is known to occur with silicon atoms[46]. As expected, the Si—NSN—Si structure in *(15)* and *(16)* is planar. The bonding in cyclic SN_2 compounds can best be described if, in addition to the sulfur-nitrogen σ-bonds, one assumes a 3-center-4-electron π-bonding. Of the 16 valence electrons, 6 are σ-electrons, 4 are π-electrons, and 6 are nonbonding electron pairs.

4.4. Larger Rings

Gleiter[47] investigated the symmetry properties of a planar eight-membered ring with a D_{4h} configuration. Figure 8 shows the HMO diagram for a planar S_4N_4 ring.



Fig. 8. HMO diagram for planar S_4N_4.

Assuming that each nitrogen and each sulfur atom in S_4N_4 has a lone pair and that the SN units are linked to one another by σ-bonds, 12 π-electrons are left over. These will be distributed in such a way that two are in each of the five lowest orbitals (a_{2u}, e_g, b_{2u}, b_{1u}), while each e_g orbital will have one electron, with parallel spin, according to Hund's rule. There results a triplet ground state for a molecule with D_{4h} configuration. The degeneracy of the two highest occupied orbitals will be eliminated by Jahn-Teller distortion. The desired splitting is obtained on considering interactions between opposite sulfur atoms; this is how the cage-like structure of S_4N_4 comes about (Fig. 9). The D_{2d} structure with two S—S σ-bonds is thus preferred, since calculations show it to yield the lowest total electron energy for the singlet ground state of S_4N_4[48].

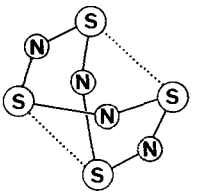


Fig. 9. Molecular structure of S_4N_4.

Taking the MO diagram for planar S_4N_4 as a starting point, and using $S_4N_4 \cdot SbCl_5$ as an example, *Gleiter* has shown that Lewis acids can exert a decisive influence on the structure of S_4N_4. To a first approximation we can assume that the electron-attracting effect of Lewis acids acts only on a single atom. This eliminates the degeneracy of the two highest occupied orbitals. It is not necessary to have exchange interactions between opposite atoms in order to obtain a singlet ground state. The 10 π-electron system $S_4N_4^{2+}$ actually has a planar configuration[16]. However, the resonance stabilization for the planar arrangement cannot be very important, since in other S_4N_4 derivatives, *e.g.* $[S_4N_4][SbCl_6]_2$, a distorted, nonplanar form has been found. These examples show that slight alterations of the ring electron density can have a drastic influence

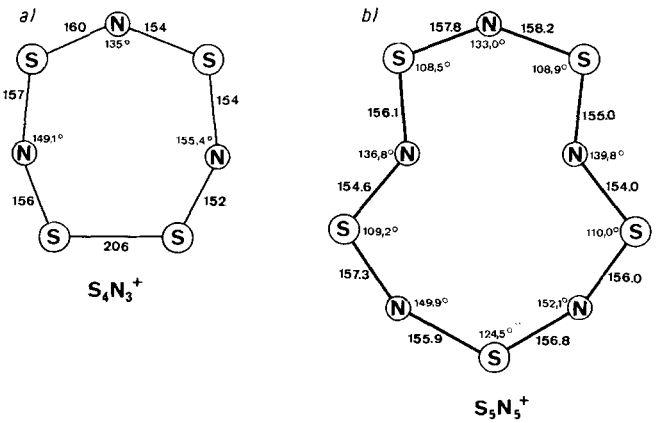


Fig. 10. Molecular structures of a) $S_4N_3^+$ and b) $S_5N_5^+$. Bond lengths in pm.

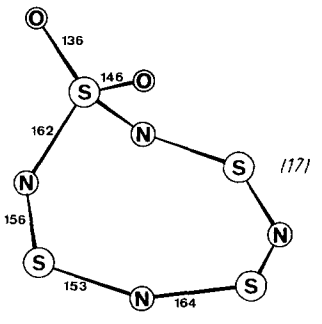
on the structure. The structures of $S_4N_4 \cdot SbCl_5$ or $S_4N_4 \cdot SO_3$ can be considered as transitions between the $S_4N_4^{2+}$ ring and the S_4N_4 cage. The cations $S_4N_3^+$ and $S_5N_5^+$ also have planar structures (Fig. 10).

$S_4N_3^+$ can be described as a 10π-, and $S_5N_5^+$ as a 14π-electron system. In $S_5N_5^+$, apart from the azulene-like structure (Fig. 10b), a heart-shaped structure is known. Comparison of the six possible $S_5N_5^+$ structures on the basis of MO considerations shows that the azulene structure should be preferred[49].

The deviation of the angle at the nitrogen from the angles in the corresponding regular polygon can be regarded as characteristic of the cyclic delocalized π-electron systems under discussion. Thus, the angle at the nitrogen has the following mean values: in $S_3N_2^+$ (Fig. 5c, Table 2) 120° (instead of 108°); in $S_4N_3^+$ (Fig. 10a) 146.5° (instead of 129°), and in $S_5N_5^+$ (Fig. 10b) 142.5° (instead of 144°). The size of the angle at the sulfur will not be further discussed here, since it is known that in carbon-sulfur compounds an increase of the angle at doubly-coordinated sulfur from 65.8 to 113° produces no change in the bond length[50, 51]. The essential information concerning this class of compounds can be summarized as follows: sulfur-nitrogen rings in which both elements have a coordination number of two can be classified as cyclic, delocalized, π-electron systems; as a rule they are planar when they comprise six, ten, or fourteen π-electrons and so obey the Hückel rule. The number of ring members and the size of the angles have little effect upon the S—N distances. The most favorable energy state is attained by an optimal electron distribution. Planar structures can also be found in compounds that do not obey the Hückel rule, *e.g.* in the 8π-electron system $S_4N_4O_2Sn_2(CH_3)_6$.

5. Sulfur-Nitrogen Compounds with Higher Coordination Numbers of the Sulfur

We have already discovered for $S_3N_3O_4^-$ *(14)* (Fig. 6d) that higher coordination numbers of the sulfur impede electron delocalization. This is also evident in $S_4N_4O_2$ *(17)* (Fig. 11).

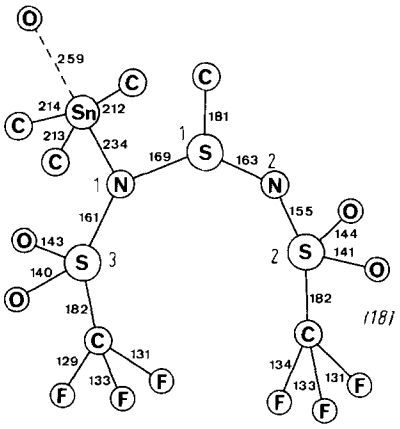


(17)

Fig. 11. Molecular structure of $S_4N_4O_2$ *(17)*. Bond lengths in pm.

Whereas the S_3N_2 moiety is planar, the NSO_2N group assumes a tetrahedral configuration. The tetracoordinated sulfur and the neighboring nitrogens are pulled out of the plane of the ring. This sulfur atom no longer contributes to electron delocalization.

There is an obvious correlation in compound *(18)*—a noncyclic derivative—between the bond lengths and the coordination numbers of the atoms involved (Fig. 12)[52]. At the shortest S—N distance, (S2—N2: 155 pm), the sulfur has a coordination number of four and the nitrogen a coordination number of two. This is not surprising, since the increase in the coordination number will give rise to a contraction of the orbital; this leads to better overlapping which, in turn, strengthens the bond. Concomitantly, the increase in the coordination number (CN) at N1 leads to a lengthening of the S3—N1



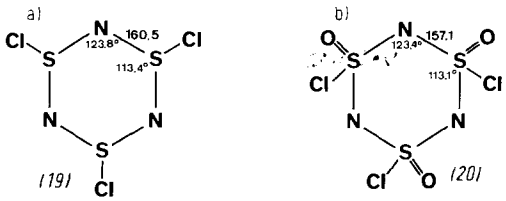
(18)

Fig. 12. Molecular structure of $(CF_3SO_2N)_2Sn(CH_3)_3SCH_3$ *(18)*. Bond lengths in pm.

distance, to 161 pm. By analogy, the S1—N2 distance is found to be shorter than the S1—N1, so that the following sequence of increasing bond lengths is obtained:

$$S(CN=4)—N(CN=2) < S(CN=4)—N(CN=3) \approx$$
$$S(CN=3)—N(CN=2) < S(CN=3)—N(CN=3)$$

For a comparison of the S—N bond lengths as functions of the coordination numbers, we turned our attention to the cyclic compounds $N_3S_3Cl_3$ *(19)* and $N_3S_3O_3Cl_3$ *(20)* (Fig. 13).



(19) *(20)*

Fig. 13. Molecular structure of a) $N_3S_3Cl_3$ *(19)* and b) $N_3S_3O_3Cl_3$ *(20)*. Bond lengths in pm.

In accordance with the above considerations, the S—N bond in *(20)* [S(CN=4)—N(CN=2)], 157.1 pm, is shorter than that in *(19)* [S(CN=3)—N(CN=2)], 160.5 pm, as expected.

The alternance of S—N bond lengths (154 and 166 pm) in $N_4S_4F_4$ fits this scheme perfectly, since the mean value is as large as the S—N distances in $N_3S_3F_3$[1, 5, 53]. The rule is also obeyed by the molecules NSF and NSF_3. The S—N distance in NSF (144.6 pm) is—as expected—longer than that in NSF_3 (141.6 pm). The rule no longer applies when a nitrogen atom is substituted by a system capable of conjugation, since in this case the electron density distribution, and with it the separation, are modified.

These conclusions make it clear that one can speak of neither "single" nor "double" bonds, and that there is little

point in comparing bond lengths in sulfur-nitrogen compounds unless the coordination number is taken into account[54]. These phenomena should also apply to combinations of other elements.

My thanks go first to my associates who took part in the preparation of this review, and also to my colleagues Prof. B. Krebs, Dr. A. Gieren, and Prof. A. Simon, who allowed me to use their unpublished results. I am indebted to the Fonds der Chemischen Industrie, Hoechst AG, and the Deutsche Forschungsgemeinschaft for generous support, which made these studies possible in the first place.

Received: August 31, 1977;
revised: June 21, 1978 [A 255 IE]
German version: Angew. Chem. *91*, 112 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] *O. Glemser*, Angew. Chem. *75*, 697 (1963); Angew. Chem. Int. Ed. Engl. *2*, 530 (1963).
[2] *I. Haiduc*, Chemistry of Inorganic Heteroatom Ring Systems. Madrid, June 22–26, 1977.
[3] *H. W. Roesky, M. Witt*, unpublished results.
[4] *M. Goehring*: Ergebnisse und Probleme der Chemie der Schwefel-Stickstoff-Verbindungen. Akademie-Verlag, Berlin 1957.
[5] *O. Glemser, R. Mews*, Adv. Inorg. Chem. Radiochem. *14*, 333 (1972).
[6] *H. W. Roesky*, Chem.-Ztg. *98*, 121 (1974).
[7] *W. L. Jolly, K. D. Maguiere, D. Rabinovich*, Inorg. Chem. *2*, 1304 (1963).
[8] *H. W. Roesky, W. Schaper, O. Petersen, T. Müller*, Chem. Ber. *110*, 2695 (1977).
[9] *H. W. Roesky, H. Wiezer*, Angew. Chem. *85*, 722 (1973); Angew. Chem. Int. Ed. Engl. *12*, 674 (1973).
[10] *H. W. Roesky, H. Wiezer*, Chem. Ber. *107*, 3186 (1974).
[11] *H. W. Roesky*, Z. Naturforsch. *B 31*, 680 (1976).
[12] *H. W. Roesky, E. Janssen*, Chem.-Ztg. *98*, 260 (1974).
[13] *H. W. Roesky, E. Janssen*, Chem. Ber. *108*, 2531 (1975).
[14] *M. Montenarh, R. Appel*, Z. Naturforsch. *B 31*, 902 (1976).
[15] *J. Bojes, T. Chivers*, J. Chem. Soc. Chem. Commun. *1977*, 453.
[16] *R. J. Gillespie, D. R. Slim, J. D. Tyrer*, J. Chem. Soc. Chem. Commun. *1977*, 253.
[17] *H. W. Roesky, A. Hamza*, Angew. Chem. *88*, 226 (1976); Angew. Chem. Int. Ed. Engl. *15*, 226 (1976).
[18] *R. J. Gillespie, P. R. Ireland, J. E. Vekris*, Can. J. Chem. *53*, 3147 (1975).
[19] *J. Hinze, H. H. Jaffé*, J. Am. Chem. Soc. *84*, 540 (1962).
[20] *M. J. Cohen, A. F. Garito, A. J. Heeger, A. G. MacDiarmid, C. M. Mikulski, M. S. Saran, J. Kleppinger*, J. Am. Chem. Soc. *98*, 3844 (1976).
[21] *C. M. Mikulski, P. J. Russo, M. S. Saran, A. G. MacDiarmid, A. F. Garito, A. J. Heeger*, J. Am. Chem. Soc. *97*, 6353 (1975).
[22] *R. J. Gillespie, J. Passmore, P. K. Ummat, O. C. Vaidya*, Inorg. Chem. *10*, 1327 (1971).
[23] *R. Steudel*, Angew. Chem. *87*, 683 (1975); Angew. Chem. Int. Ed. Engl. *14*, 655 (1975).
[24] *R. L. Patton, K. N. Raymond*, Inorg. Chem. *8*, 2426 (1969).
[25] *K. Krebs et al.*, unpublished results.
[26] *A. Zalkin, T. E. Hopkins, D. H. Templeton*, Inorg. Chem. *5*, 1767 (1966).
[27] *H. W. Roesky, E. Wehner, E. J. Zehnder, H. J. Deiseroth, A. Simon*, Chem. Ber. *111*, 1670 (1978).
[28] *A. W. Cordes, R. F. Kruh, E. K. Gordon*, Inorg. Chem. *4*, 681 (1965).
[29] *A. J. Banister*, Nature Phys. Sci. *237*, 92 (1972); *239*, 69 (1972).
[30] *A. Kalman, B. Duffin, A. Kucsman*, Acta Crystallogr. *B 27*, 586 (1971).
[31] *R. T. Kops, E. van Aken, H. Schenk*, Acta Crystallogr. *B 29*, 913 (1973).
[32] *J. Kuyper, K. Vrieze*, J. Chem. Soc. Chem. Commun. *1976*, 64.
[33] *R. Meij, J. Kuyper, D. J. Stufkens, K. Vrieze*, J. Organomet. Chem. *110*, 219 (1976).
[34] *A. Gieren, F. Pertlik*, Angew. Chem. *88*, 852 (1976); Angew. Chem. Int. Ed. Engl. *15*, 782 (1976).
[35] *A. Gieren, B. Dederer, H. W. Roesky, E. Janssen*, Angew. Chem. *88*, 853 (1976); Angew. Chem. Int. Ed. Engl. *15*, 783 (1976).
[36] *H. W. Roesky, W. Grosse Böwing, I. Rayment, H. M. M. Shearer*, J. Chem. Soc. Chem. Commun. *1975*, 735.
[37] *J. Weiss, I. Ruppert, R. Appel*, Z. Anorg. Allg. Chem. *406*, 329 (1974).
[38] *H. W. Roesky, E. Janssen*, Angew. Chem. *88*, 24 (1976); Angew. Chem. Int. Ed. Engl. *15*, 39 (1976).
[39] *I. Rayment, H. M. M. Shearer*, Acta Crystallogr. *A 31*, 62 (1975).
[40] *O. J. Scherer, R. Wies*, Z. Naturforsch. *B 25*, 1486 (1970).
[41] *O. J. Scherer, R. Wies*, Angew. Chem. *84*, 585 (1972); Angew. Chem. Int. Ed. Engl. *11*, 529 (1972).
[42] *R. Steudel, F. Rose, R. Reinhardt, H. Bradaczek*, Z. Naturforsch. *B 32*, 488 (1977).
[43] *H. W. Roesky, H. Wiezer*, Chem.-Ztg. *97*, 661 (1973).
[44] *G. Ertl, J. Weiss*, Z. Naturforsch. *B 29*, 803 (1974).
[45] *H. W. Roesky, H. Wiezer*, Angew. Chem. *86*, 130 (1974); Angew. Chem. Int. Ed. Engl. *13*, 146 (1974).
[46] *H. Bock, W. Ensslin*, Angew. Chem. *83*, 435 (1971); Angew. Chem. Int. Ed. Engl. *10*, 404 (1971).
[47] *R. Gleiter*, J. Chem. Soc. *A 1970*, 3174.
[48] *P. Cassoux, J.-F. Labarre, O. Glemser, W. Koch*, J. Mol. Struct. *13*, 405 (1972).
[49] *R. Bartetzko, R. Gleiter*, Inorg. Chem. *17*, 945 (1978).
[50] *A. F. Wells*: Structural Inorganic Chemistry. Oxford University Press, London 1967.
[51] *M. Rouault, G. Gallagher*, Phys. Rev. *75*, 1319 (1949).
[52] *H. W. Roesky, M. Diehl, H. Fuess, J. W. Bats*, Angew. Chem. *90*, 73 (1978); Angew. Chem. Int. Ed. Engl. *17*, 58 (1978).
[53] *B. Krebs, S. Pohl*, Chem. Ber. *106*, 1069 (1973).
[54] The "single" and "double" bonds in the structures are shown for the sake of comparison.

Empirical Parameters of Solvent Polarity as Linear Free-Energy Relationships

By Christian Reichardt[*]

Although the effect of solvent on the rate and the position of equilibrium of chemical reactions has been known since the last century, there are still no reliable and exact methods for a quantitative description and prediction of such solvent effects. Empirical parameters of solvent polarity are of great value in this respect and can be derived with the aid of the principle of "linear relationships between free energies" (LFE relationships). The present article deals with the possibilities of establishing reaction and absorption series using solvent-dependent standard reactions or standard absorptions of organic compounds. Particular attention is merited by the summary of the 24 most important empirical parameters of solvent polarity and the table of $E_T(30)$ values for 151 solvents. In addition to examples of the application of these values, attempts to improve the LFE correlations of singular empirical parameters of solvent polarity with the aid of multiparametric equations are described.

1. Introduction

When a chemist wishes to carry out a specific liquid-phase chemical reaction in the laboratory, he not only has to prepare the intended reagents and select a suitable reaction vessel and appropriate temperature but must also decide on a reaction medium, the correct choice being of major importance to the success of the planned reaction. The effect of solvents on chemical reactivity has been known for over a hundred years[**]; every chemist is therefore well aware that solvents can exert a considerable influence on reaction rates and on the position of chemical equilibria. Since at present there are some three hundred solvents in common use[3] (quite apart from the infinite number of possible solvent mixtures), a chemist requires not just experience and intuition but also qualitative rules (*e.g.* "like dissolves like") and quantitative data (*e.g.* boiling point, dielectric constant, refractive index) to enable him to make this generally difficult choice.

One of the most important selection criteria in this connection is a property of solvents generally known as "solvent polarity". Although the expression "polarity of a solvent" is often used, it is in fact not easy to define this property precisely, and it is still more difficult to assess it quantitatively. The simplicity of electrostatic solvation models has resulted in the effect of the dielectric constant (ε) and the permanent dipole moment (μ) being given prominence over other factors and ascribed a special role as parameters of solvent polarity. In fact, however, the dielectric constant describes only the change in the electric field intensity that occurs between the plates of a condenser when the latter is removed from vacuum and placed in a solvent. This induces a dipole moment in apolar solvent molecules (displacement polarization) and the now dipolar molecules are aligned (orientation polarization). The dielectric constant therefore describes the ability of a solvent to separate electrical charges and orient its dipolar molecules. However, the total sum of the interactions between the solute and solvent molecules is much more extensive and complicated: in addition to the nonspecific coulombic, directional, inductive, and dispersion interactions, there are also specific hydrogen bond, electron pair donor (EPD)/electron pair acceptor (EPA), and solvophobic interactions. Hence from a practical point of view it would seem expedient to take "solvent polarity" to mean the over-all solvation ability of a solvent, this in turn being determined by the sum of all the molecular properties responsible for the interactions between the solvent and the solute. It stands to reason that solvent polarity as thus defined cannot generally be described quantitatively by a single physical parameter (ε, μ, *etc.*). This fact and the difficulty of calculating rates and equilibrium positions of chemical reactions in solution with such physical data have led to the parameters of solvent polarity being determined by purely empirical means. The procedure is to start with well known, easily measured, and strongly solvent-dependent processes, which are investigated as reference processes in the greatest possible number of solvents: the rate or the position of equilibrium of a carefully selected model reaction or the spectral absorption of a suitable standard dye. From the rate or equilibrium constants or the absorption maxima thus obtained it is then possible to derive empirical parameters of solvent polarity which generally provide a more comprehensive measure of the over-all solvation ability of the solvent than individual physical data (cf. [1, 2, 4–10] for reviews). The model processes selected can be compared with probes to determine the effect of the solvent in the molecular-microscopic region.

This approach is characteristic of the experimental chemist, but it is regarded with mistrust rather than goodwill by theoreticians. However, organic chemistry has since its very beginning made use of the qualitative, empirical rule that similar compounds react in similar ways and that similar changes in the structure and the reaction medium produce similar changes in the reactivity of the compounds. As the application of this rule and the selection of suitable model reactions naturally leaves room for subjective decisions, the rather derisory remark that organic chemistry is not a science but an art would appear to be not wholly unfounded[11].

[*] Prof. Dr. C. Reichardt
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg (Germany)

[**] The effect of the solvent on the rate of chemical reactions was first described in 1862 by *Berthelot* and *Saint-Gilles* in connection with their studies on the esterification of acetic acid with ethanol. The effect of the solvent on the position of the chemical equilibrium was established in 1896 when the keto-enol tautomerism of 1,3-dicarbonyl compounds was discovered (cf. [1, 2]).

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0170 $ 01.00/0*

The principle of "linear free-energy relationships" (LFE relationships) occupies a position of central importance in the mathematical description and theoretical interpretation of empirical observations[12-14]. In what follows it will first be demonstrated that the empirical parameters of solvent polarity can be understood as the result of such LFE relationships. A table summarizing the most important solvent parameters known at present and their application and expansion in the form of multiparametric equations complete the review. A more detailed description will be found in an earlier monograph[2].

2. Linear Free-Energy Relationships

Consideration of a series of reactions (*i.e.* a group of reactions in each of which one of the reaction partners has its molecular structure changed slightly in one detail or in which the reaction medium is changed while the functional group—the reaction center—remains unchanged), often reveals that the rate or equilibrium constants k_i of a reaction series A correlate with the corresponding constants of a related reaction series B in which the structure of the reaction partners or the medium was changed in the same way as in series A. This correlation is generally, although not necessarily, linear and can be described by Eq. (1),

$$\lg k_i^B = m \cdot \lg k_i^A + c \tag{1}$$

in which the subscript i stands for the same structural or solvent-determined variation in the two reaction series. However, the prerequisite is that all the other experimental conditions such as the second reaction partner, pressure, temperature, reaction mechanism, *etc.* are kept constant while one parameter is systematically varied.

As the logarithm of the equilibrium constant K of a chemical reaction is proportional to the change in the free energy of reaction ΔG^0 in accordance with Eq. (2),

$$\lg K = -\frac{\Delta G^0}{2.3 \times R \times T} \tag{2}$$

and the logarithm of the rate constant k, according to *Eyring*'s theory of absolute reaction rates, is proportional to the free energy of activation ΔG^* (Eq. (3)),

$$\lg\left(\frac{k}{R \cdot T/N \cdot h}\right) = -\frac{\Delta G^*}{2.3 \times R \times T} \tag{3}$$

Eq. (1) in fact describes a linear relationship between free energies. If one relates the rate constants or the equilibrium constants within a series of reactions to a standard reaction (with standard substituent or standard solvent; subscript o), Eq. (1) becomes Eq. (4):

$$\lg(k_i^B/k_o^B) = m \cdot \lg(k_i^A/k_o^A) \tag{4}$$

LFE relationships of this type are useful in two respects. On the one hand the LFE correlation of experimental data from a new reaction series with those of a known series documents a mechanistic similarity between the two series, which can be useful in explaining reaction mechanisms[15]. On the other hand, LFE relationships can be used to predict the rate and equilibrium constants that will be produced by changes in the reactant structure or in the reaction medium.

If one looks at a reaction between a substrate S and a reagent R[*] in a medium M, which leads *via* an activated complex to the product P,

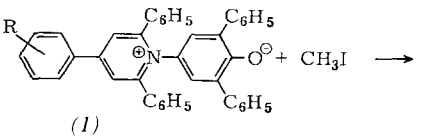
$$(S)_M + (R)_M \rightleftarrows [S \ldots R]^{\ddagger}_M \rightarrow (P)_M \tag{5}$$

then a reaction series can be established in three ways by making small changes:

a) *Variation of the substrate S by the introduction of substituents.* In the case of substituted benzene derivatives this results in the well-known Hammett equation (6)[16],

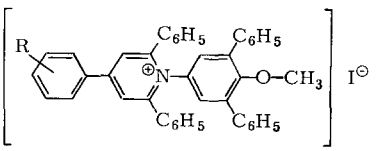
$$\lg k_X - \lg k_o = \sigma \cdot \rho \tag{6}$$

in which k_X is the rate or equilibrium constant of *meta*- or *para*-substituted aromatic substrates, σ is the substituent constant, and ρ is the reaction constant[**]. Eq. (6) describes



(1)

(1a), R = H



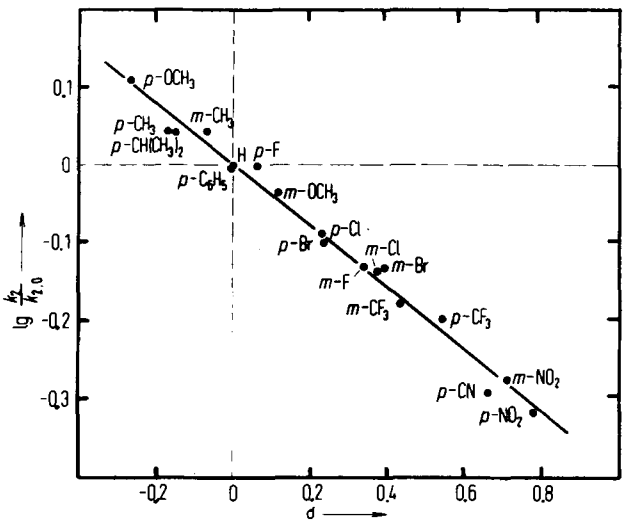


Fig. 1. Hammett correlation of the substituent constants σ with the logarithms of the relative rate constants $\lg(k_2/k_{2,o})$ of the S_N2 alkylation of substituted pyridiniophenolates of type *(1)* with methyl iodide in chloroform at 25°C [17]: $\lg(k_2/k_{2,o}) = -0.40 \cdot \sigma$ (number of value pairs $n = 18$; correlation coefficient $r = -0.993$).

[*] The designation of one reactant as the *substrate* and of the other as the *reagent* is not entirely arbitrary. In general the substrate is structurally varied in a reaction series while the reagent remains unchanged. A catalyst is always regarded as a reagent.

[**] $\rho = 1$ applies for the standard equilibrium reaction

$$C_6H_5{-}CO_2H + H_2O \rightleftarrows C_6H_5{-}CO_2^{\ominus} + H_3O^{\oplus}$$

in water at 25°C.

the effect of *meta*- and *para*-substituents on the rates and the equilibria of reactions in the side chain of benzene derivatives. A typical Hammett correlation is shown in Figure 1[17].

As was to be expected, and as documented by the negative sign of ρ, electron-attracting substituents reduce the rate of the S_N2-alkylation of pyridiniophenolates of type *(1)* while electron-releasing substituents increase this rate.

b) *Variation of the reagent R.* An example of this is the catalysis relationship of *Brønsted* and *Pedersen*, according to which the effectiveness of a catalyst in a generally acid- or base-catalyzed reaction is proportional to its acid or base strength[18]. This quantitative relationship, formulated already in 1924, was the first example of an LFE relationship[11-14].

c) *Variation of the medium M.* Finally, variation of the reaction medium while all the other reaction conditions are kept constant yields the desired empirical parameters of solvent polarity, provided that the standard reaction selected, whose rate or position of equilibrium is determined in various solvents, is sufficiently solvent-dependent. If one regards the solvent molecules of the solvation shell surrounding the substrate and the reagent as loosely bound substituents, then the analogy between the modification of the chemical reactivity of the substrate produced by the introduction of substituents and the modification produced by changing the reaction medium is particularly striking. While substituents can change the chemical reactivity of a substrate only discontinuously, a variation of the medium (particularly when solvent mixtures are used) makes it possible to produce a virtually continuous effect on substrate reactivity[19].

If one develops the concepts of "chemical reaction" and "reagent" further, then it is also possible to formulate the "reaction" of a photon $h \cdot \nu$ with a substrate S, dissolved in medium M, in a similar way to Eq. (5):

$$\underset{\text{ground state}}{(S)_M} + h \cdot \nu \rightleftharpoons \underset{\text{excited state}}{(S)_M^*} \qquad (7)$$

LFE relationships can therefore be derived not only in the form of relationships between rate or equilibrium constants but also with the aid of spectroscopic studies of members of a reaction series in different spectral regions (UV/VIS[20], IR[20], NMR[21a], *etc.*). On the basis of Eq. (7) a reaction series (or better an absorption series) can be established in two ways:

a) *Variation of the substrate S by the introduction of substituents.* This procedure results in a spectroscopic Hammett equation which is most expediently formulated for the spectral excitation of substituted dyes in the UV/VIS region according to a suggestion by *Kosower*, *Wallenfels*, and *Hoffmann* as follows[21b]:

$$\frac{E_{T,R} - E_{T,0}}{2.3 \times R \times T} = \sigma \times \rho_A \qquad (8)$$

$E_{T,R}$ and $E_{T,0}$ are the transition energies (kcal/mol or kJ/mol) of the compound substituted by R or the reference compound (generally R = H), R is the gas constant, T is the absolute temperature, σ is the usual Hammett substituent constant, and ρ_A is the absorption constant[22,23]. The difference between the transition energies is divided by $2.3RT$ to bring it into the same order of magnitude as the Hammett substituent constants, which were obtained primarily from equilibrium or rate constants. In addition, ρ_A is then a dimensionless number, just like the reaction constant ρ [Eq. (6)]. The absorption constant ρ_A is a measure of the susceptibility with which the position of the absorption band of a dye reacts to a change in the substituent R. A typical example of such a UV/VIS spectroscopic Hammett correlation is shown in Figure 2[23] (for further examples cf. [20, 22, 24, 25]).

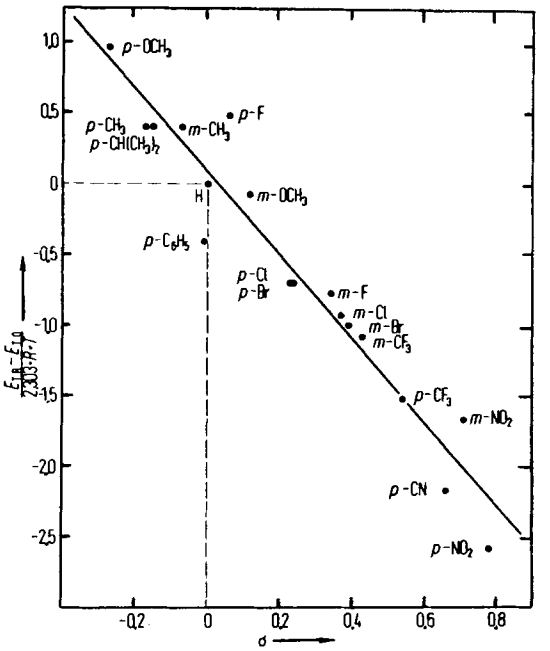


Fig. 2. Hammett correlation of the substituent constants σ with the modified transition energies $(E_{T,R} - E_{T,0})/2.3 \cdot R \cdot T$ of the longest-wavelength π-π^*-absorption band of substituted pyridiniophenolates of type *(1)* in methanol at 25 °C [23]: $(E_{T,R} - E_{T,0})/2.3 \cdot R \cdot T = -2.97 \cdot \sigma + 0.08$ ($n = 18$; $r = -0.962$).

In accordance with the negative sign of the absorption constant ρ_A in the case of pyridiniophenolates of type *(1)*, electron-attracting substituents produce a bathochromic shift in the longest-wavelength π-π^* band (which can be regarded as an intramolecular charge transfer band[*]), while electron-releasing substituents give rise to a hypsochromic shift. A value of $\rho_A < 0$ should always be maintained if a lower π-electron density is present in the electron ground state at the absorption center[**] than in the first excited state[23].

If the substrate is kept constant in Eq. (7), a series of reactions can also be produced by introducing substituents into the solvent M, for example by varying R in the homologous series of aliphatic alcohols R—OH which interact with the substrate (*e.g.* by hydrogen bonding). An example of this can be found in [23].

b) *Variation of the medium M.* If the absorption band of a standard substrate S is sufficiently solvatochromic (*i.e.* if its position depends on the solvent), a systematic variation of the solvent makes it possible to introduce empirical param-

[*] The excitation of π-electrons corresponding to the longest-wavelength absorption band of pyridiniophenolates of type *(1)* is accompanied by a reduction of the permanent dipole moment of approximately 30×10^{-30} C m (*ca.* 9 D), which corresponds to an intramolecular charge transfer from the phenolate to the pyridinium group [26].

[**] By "absorption center" is meant that atom of the molecular skeleton with which the perturbation in the π-electron system of the dye caused by the substituent R is associated.

eters of solvent polarity spectroscopically. The UV/VIS absorption spectrum of a negatively solvatochromic standard dye of this type is shown in Figure 3[27-29]. The longest-wavelength absorption maximum of pyridiniophenolate *(1a)* is shifted hypsochromically by 357 nm when the solvent is changed from diphenyl ether to water, this corresponding to a change in the electron transition energy by 28 kcal/mol (117 kJ/mol). The transition energies E_T calculated according to Eq. (9) can be used either directly as empirical parameters of solvent polarity

$$E_T\,[\text{kcal/mol}] = hc\tilde{\nu}N = 2.859 \times 10^{-3} \times \tilde{\nu}\,[\text{cm}^{-1}] \qquad (9)^{[*]}$$

or in the form of a relative measure of solvent polarity *RPM* (relative polarity measure) defined by Eq. (10), as suggested by *Dähne et al.*[30]

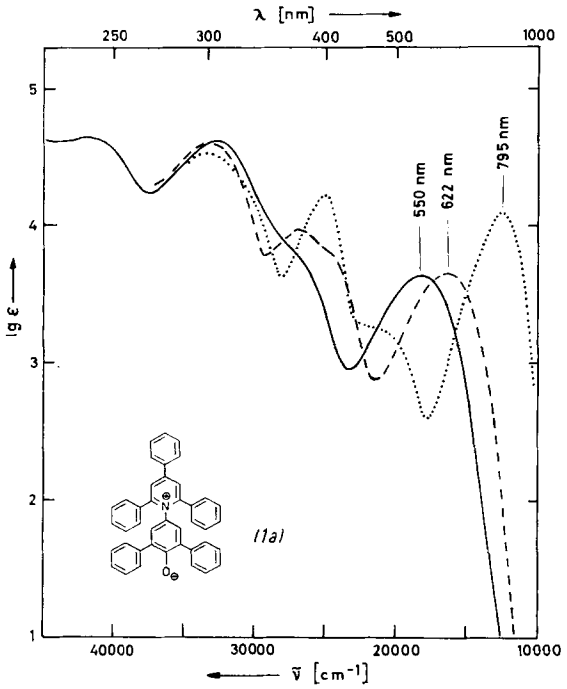


Fig. 3. UV/VIS absorption spectrum of 2,6-diphenyl-4-(2,4,6-triphenyl-1-pyridinio) phenolate *(1a)* in ethanol (——), acetonitrile (- - - - -), and 1,4-dioxane (.....) at 25°C [27, 28].

$$RPM = \frac{E_T(n\text{-hexane}) - E_T}{E_T(n\text{-hexane})} \qquad (10)$$

One of the advantages of using the dimensionless *RPM* values of Eq. (10) is that spectroscopic polarity parameters obtained with various solvatochromic standard substrates can more readily be compared with one another. Regardless of the nature of the indication of the solvent polarity, the *RPM* value of *n*-hexane (as the least polar solvent) is always equal to zero. Positively solvatochromic standard dyes yield positive *RPM* values and negatively solvatochromic dyes negative *RPM* values; however, for correlation analyses it is sufficient to use absolute |*RPM*| values. The choice of an *n*-hexane solution instead of the gas phase as the reference state within a reaction series is made for experimental reasons: because of the low volatility of solvatochromic dyes, their absorption spectra cannot usually be recorded in the gas phase. The relative polarity function *RPM* is not only applicable to solvent-determined band shifts in the UV/VIS absorption region; it can also be used for other wavelength regions (IR, NMR, ESR).

When substituent or solvent effects as described above are interpreted with the aid of model processes that yield the same or similar effects, the thermodynamic parameters that are compared are generally free energies. However, the empirical and generally linear LFE relationships obtained are not derived from the laws of formal thermodynamics and are therefore also referred to as "extrathermodynamic relationships"[19]. These relationships are obtained by combining molecular-microscopic detailed model reactions with the formal parameters of thermodynamics and hence are also not as rigorous as macroscopic thermodynamic laws. Since LFE-relationships are not restricted to correlations between thermodynamic parameters, but can also encompass other physicochemical properties (*e.g.* optical excitation energies), their use is often also referred to more generally as "correlation analysis"[13, 14].

3. Empirical Parameters of Solvent Polarity

Table 1 gives a selection of empirical parameters of solvent polarity that have been obtained by determining solvent-dependent equilibrium constants, rate constants, or absorption maxima (in the UV/VIS, IR, NMR, or ESR region) within a series of reactions in which only the solvent was systematically varied. A more comprehensive description of *all* the empirical solvent parameters known at present is given in a monograph[2].

Negatively and positively solvatochromic dyes are particularly suitable as standard substances for the determination of empirical solvent parameters[*], and of these, by virtue of the exceptionally large extent of its solvatochromism, the negatively solvatochromic pyridiniophenolate *(1a)* (cf. Fig. 3) is especially suitable[27-29]. Its $E_T(30)$ values have so far been determined for 151 pure solvents[27, 58] and for many binary solvent mixtures[28, 63-66][**]. Table 2 summarizes all the $E_T(30)$ values known at present, including the dimensionless relative polarity measure calculated from them according to Eq. (10).

The position of the longest-wavelength absorption maximum of this pyridiniophenolate *(1)* depends not only on the solvent (solvatochromism) but also on temperature (ther-

[*] The units [kcal/mol] were selected for E_T so that the latter could be compared directly with free reaction energies and free activation energies. As E_T values have already found wide application in the literature, we decided not to convert them into kJ/mol in this review in order to avoid confusion. In the SI system the following applies instead of Eq. (9):

$E_T\,[\text{kJ/mol}] = 1.196 \times 10^{-2} \times \tilde{\nu}\,[\text{cm}^{-1}]$.

[*] With increasing solvent polarity the solvent-dependent absorption band is shifted bathochromically in the case of positively solvatochromic dyes and *vice versa*. For the theoretical interpretation of the solvatochromism of organic compounds that in most cases belong to the group of merocyanine dyes see also [59—62].

[**] Further $E_T(30)$ values of organic solvents were recently determined by *J. Hormadaly* and *Y. Marcus*, J. Phys. Chem., in press. The author is indebted to Prof. *Marcus*, Hebrew University, Jerusalem, for sending in still unpublished results.

Table 1. Empirical parameters of solvent polarity.

Symbol (name)	Physical quantity measured	Solvent-dependent standard process	n [a]	Ref.
From equilibrium measurements				
L (desmotropic constant)	equilibrium constant	keto-enol tautomerism equilibrium of ethyl acetoacetate at *ca.* 20 °C	13	[31]
$-\Delta G^0_{OCH_3}$	free energy of the reaction in standard state	conformation equilibrium between *cis*- and *trans*-2-isopropyl-5-methoxy-1,3-dioxane at 25 °C	17	[32]
$-\Delta G^0$	free energy of the reaction in standard state	NH/OH tautomerism equilibrium of Schiff bases of pyridoxal-5'-phosphate at 25 °C	8	[33]
DN (donor number)	reaction enthalpy $-\Delta H_{EPD\cdot SbCl_5}$	1:1 adduct formation between antimony(V) chloride as standard EPA and EPD solvents in 1,2-dichloroethane at 25 °C	40	[10, 34]
From measurements of reaction rates				
Y	relative rate constant k_1	S_N1 solvolysis of *tert*-butyl chloride at 25 °C	11	[35, 36]
$\lg k_1$, $\lg k_{ion}$ W [b]	rate constant k_1	solvolysis of 2-(4-methoxyphenyl)-2-methylpropyl tosylate at 75 °C	15	[37, 36]
X	relative rate constant k_2	S_E2 reaction of tetramethyltin with bromine at 20 °C	7	[38]
$\mathscr{S}$ ($\lg k_2$)	rate constant k_2	S_N2 Menshutkin reaction between tri-*n*-propylamine and methyl iodide at 20 °C	78	[39, 40]
Ω	*endo*-/*exo*-product ratio	Diels-Alder $[\pi 4_s + \pi 2_s]$ cycloaddition of cyclopentadiene to methyl acrylate at 30 °C	14	[41, 42]
From spectroscopic measurements				
Z	molar transition energy	charge-transfer absorption of 1-ethyl-4-methoxycarbonyl-pyridinium iodide at 25 °C	46	[43]
E_T, $E_T(30)$ [c]	molar transition energy	π-π*-absorption of pyridiniophenolate (*1a*) at 25 °C (cf. Fig. 3)	151	[27—29]
χ_R	molar transition energy	π-π*-absorption of a positively solvatochromic undecamethinemerocyanine dye at 25 °C	58	[44]
χ_B	molar transition energy	π-π*-absorption of a negatively solvatochromic nonamethinemerocyanine dye at 25 °C	12	[44]
E_T, PM [d]	molar transition energy	π-π*-absorption of 5-dimethylamino-2,4-pentadienal		[30]
$\Phi(F)$	wave number difference	n-π*-absorption of saturated aliphatic ketones	23	[45]
E_K	molar transition energy	d-π*-absorption of tetracarbonyl [*N*-(2-pyridylmethylene) benzylamino]molybdenum(0)	40	[46]
E_T^{SO}	molar transition energy	n-π*-absorption of *N*,*N*-dimethylthiobenzamide *S*-oxide	35	[47]
π^*	absorption wave number	π-π*-absorption of several compounds, particularly nitro-substituted arenes (*e.g.* 4-nitroanisole (1-methoxy-4-nitrobenzene))	70	[48]
S	equilibrium constant, rate constant, molar transition energy	mixed parameter, calculated from various solvent-dependent processes	47	[49]
G	relative wave number difference	IR stretching vibration absorption of X=O and X—H···B groups (X=C, S, N, O, or P, B=solvent) in the gas phase and in solution	20	[50]
B	wave number difference	IR stretching vibration absorption of O—D and O—H groups in CH_3OD or C_6H_5OH in the gas phase and in solution	55 [51] 198 [52]	[8] [51, 52]
$\mathscr{A}_N$	splitting constant a^{14N}	^{14}N-HFS splitting in the ESR spectra of three dialkylaminyl oxide radicals	31	[53, 54]
P	relative ^{19}F-NMR chemical shift	^{19}F-NMR absorption of 1-fluoro-4-nitrosobenzene	52	[55, 56]
AN (acceptor number)	relative ^{31}P-NMR chemical shift	^{31}P-NMR absorption of triethylphosphane oxide	34	[10, 57]

[a] Number of pure solvents for which the empirical parameter was obtained. [b] "W" stands for "Winstein's parameter", following the proposal by *P. D. Bartlett*, J. Am. Chem. Soc. *94*, 2161 (1972). [c] Since the standard dye (*1a*) was numbered 30 in [27], its molar transition energies were designated by $E_T(30)$. [d] Cf. Eq. (10).

mosolvatochromism)[67], on external pressure (piezosolvatochromism)[68], and on the substituent in the 4-phenyl ring (Fig. 2)[23]. The chemical reactivity of this molecule with respect to alkylating reagents is also affected by both substit-

Table 2. Empirical parameters of solvent polarity $E_T(30)$ derived from the longest-wavelength UV/VIS absorption band of negatively solvatochromic pyridiniophenolate (*1a*) at 25°C and 1 bar (cf. Eq. (9) and Fig. 3) [27—29, 58].

Solvent	$E_T(30)$ [a, b] [kcal/mol]	*RPM* [c]
1,1,1,3,3,3-Hexafluoro-2-propanol	69.3 [d]	−1.243
Water	63.1	−1.042
2,2,2-Trifluoroethanol	59.5	−0.926
2,2,3,3-Tetrafluoro-1-propanol	59.4	−0.922
1,2,3-Propanetriol (glycerol)	57.0 [e]	−0.845
Formamide	56.6	−0.832
1,2-Ethanediol (glycol)	56.3	−0.822
Methanol	55.5	−0.796
1,3-Propanediol	54.9 [f]	−0.777
1,2-Propanediol	54.1 [e]	−0.751
N-Methylformamide	54.1	−0.751
Diethylene glycol	53.8	−0.741
Ethanol/water (80:20 vol-%)	53.7	−0.738
Triethylene glycol	53.5	−0.731
1,3-Butanediol	52.8 [e]	−0.709
2-Propyn-1-ol (propargyl alcohol)	52.5 [d]	−0.699
2-Methoxyethanol	52.3	−0.693
2-Propen-1-ol (allyl alcohol)	52.1	−0.686
N-Methylacetamide	52.0 [g]	−0.683
Ethanol	51.9	−0.680
2-Aminoethanol	51.8	−0.676
Acetic acid	51.2 [d]	−0.657
Benzyl alcohol	50.8	−0.644
1-Propanol	50.7	−0.641
1-Butanol	50.2	−0.625
2-Hydroxymethylfuran (furfuryl alcohol)	50.0 [d]	−0.618
2-Phenylethanol	49.5 [h]	−0.602
1-Pentanol	49.1	−0.589
2-Methyl-1-propanol (isobutyl alcohol)	49.0	−0.586
1-Hexanol	48.8	−0.579
2-Propanol	48.6	−0.573
3-Phenyl-1-propanol	48.5 [h]	−0.570
1-Heptanol	48.5 [h]	−0.570
1-Octanol	48.3	−0.563
Cyclopentanol	47.7	−0.544
1-Decanol	47.6 [h]	−0.540
2,6-Dimethylphenol (2,6-xylenol)	47.6	−0.540
2-Butanol	47.1	−0.524
3-Methyl-1-butanol (isoamyl alcohol)	47.0	−0.521
Cyclohexanol	46.9	−0.518
1-Dodecanol	46.7 [h]	−0.511
1-Phenylethanol	46.7 [h]	−0.511
Acrylonitrile	46.7	−0.511
4-Methyl-1,3-dioxolan-2-one (propylene carbonate)	46.6	−0.508
2-Pentanol	46.5	−0.505
Nitromethane	46.3	−0.498
Acetonitrile	46.0	−0.489
3-Pentanol	45.7	−0.479
Dimethyl sulfoxide	45.0	−0.456
Methyl acrylate	44.5	−0.440
Aniline	44.3	−0.434
Tetra-*n*-hexylammonium benzoate	44.3	−0.434
Tetrahydrothiophene 1,1-dioxide (sulfolane)	44.0	−0.424
2-Methyl-2-propanol (*tert*-butyl alcohol)	43.9 [g]	−0.421
Acetic anhydride	43.9 [i]	−0.421
N,*N*-Dimethylformamide	43.8	−0.417
N,*N*-Dimethylacetamide	43.7	−0.414
Propionitrile	43.7	−0.414
Nitroethane	43.6	−0.411
Trimethyl phosphate	43.6	−0.411
Butyronitrile	43.1	−0.395
Benzyl cyanide	42.9	−0.388
N-Methylaniline	42.5	−0.375
1-Methyl-2-pyrrolidinone	42.2	−0.366
Acetone	42.2	−0.366
Benzonitrile	42.0	−0.359
Nitrobenzene	42.0	−0.359
1,2-Diaminoethane	42.0	−0.359
1,2-Dichloroethane	41.9	−0.356
2-Chloropyridine	41.9 [k]	−0.356
2-Methyl-2-butanol (*tert*-pentyl alcohol)	41.9	−0.356
Triethyl phosphate	41.7	−0.350
Glycerol triacetate (triacetin)	41.6	−0.346
5-Acetyl-5-methyl-1,3-dioxane	41.5	−0.343
2-Butanone	41.3	−0.337
Acetophenone	41.3	−0.337
2-Pentanone	41.1 [h]	−0.330
Dichloromethane	41.1	−0.330
Dimethyl carbonate	41.1	−0.330
Tetramethylurea	41.0	−0.327
Morpholine	41.0	−0.327
Hexamethylphosphoric acid triamide	40.9	−0.324
3-Methyl-2-butanone (isopropyl methyl ketone)	40.9 [h]	−0.324
Ethyl formate	40.9	−0.324
Cyclohexanone	40.8	−0.320
Dimethyl phthalate	40.7	−0.317
Tri-*n*-propyl phosphate	40.5	−0.311
Cyclopentanone	40.3 [h]	−0.304
Pyridine	40.2	−0.301
2-Hexanone	40.1 [h]	−0.298
Methyl acetate	40.0	−0.294
Tri-*n*-butyl phosphate	39.6	−0.282
4-Methyl-2-pentanone (isobutyl methyl ketone)	39.4 [h]	−0.275
1,1-Dichloroethane	39.4	−0.275
Quinoline	39.4	−0.275
3-Pentanone	39.3	−0.272
N,*N*,*N*',*N*'-Tetramethylguanidine	39.3	−0.272
Chloroform	39.1	−0.265
Deuteriochloroform	39.0	−0.262
3,3-Dimethyl-2-butanone (*tert*-butyl methyl ketone)	39.0	−0.262
4-Heptanone	38.9	−0.259
Triethylene glycol dimethyl ether	38.9	−0.259
2,4-Dimethyl-3-pentanone (diisopropyl ketone)	38.7	−0.252
Diethylene glycol dimethyl ether	38.6	−0.249
2-Methylpyridine (2-picoline)	38.3	−0.239
1,2-Dimethoxyethane	38.2	−0.236
Fluorobenzene	38.1	−0.233
o-Dichlorobenzene	38.1	−0.233
Ethyl acetate	38.1	−0.233
Vinyl acetate	38.0	−0.230
2,6-Dimethyl-4-heptanone (diisobutyl ketone)	38.0	−0.230
N,*N*-Dimethylaniline	38.0	−0.230
Iodobenzene	37.9	−0.227
Bromoethane	37.6	−0.217
n-Propyl acetate	37.5	−0.214
Diethylene glycol diethyl ether	37.5	−0.214
Bromobenzene	37.5	−0.214
Chlorobenzene	37.5	−0.214
Tetrahydrofuran	37.4	−0.210
1-Chloropropane	37.4	−0.210
Methoxybenzene (anisole)	37.2	−0.204
m-Dichlorobenzene	37.0 [h]	−0.197
2-Amino-2-methylpropane (*tert*-butylamine)	36.8	−0.191
2,6-Dimethylpyridine (2,6-lutidine)	36.7	−0.188
2-Methyltetrahydrofuran	36.5	−0.181
Ethoxybenzene (phenetole)	36.4	−0.178
Diethyl carbonate	36.2 [h]	−0.172
1,1,1-Trichloroethane	36.2	−0.172
1,4-Dioxane	36.0	−0.165
Trichloroethylene	35.9	−0.162
Piperidine	35.5	−0.149
Diethylamine	35.4	−0.146
Diphenyl ether	35.3 [g]	−0.142
Diethyl ether	34.6	−0.120
Benzene	34.5	−0.117
o-Xylene	34.3 [h]	−0.110
Diisopropyl ether	34.0	−0.100
1,8-Cineol (1,8-epoxy-*p*-menthane)	34.0 [h]	−0.100
Toluene	33.9	−0.097
tert-Butylbenzene	33.7	−0.091
p-Xylene	33.5 [h]	−0.084
Di-*n*-butyl ether	33.4	−0.081

Diisopropylamine	33.3	−0.078
Triethylamine	33.3	−0.078
m-Xylene	33.3 [h]	−0.078
1,3,5-Trimethylbenzene (mesitylene)	33.1	−0.071
Carbon disulfide	32.6	−0.055
Carbon tetrachloride	32.5	−0.052
Tetrachloroethylene	31.9	−0.032
Cyclohexane	31.2	−0.010
n-Hexane	30.9	−0.000

[a] Standard dye: 2,6-diphenyl-4-(2,4,6-triphenyl-1-pyridinio) phenolate (*1a*). Since its formula was numbered 30 in [27], its molar transition energies were designated as $E_T(30)$ values. [b] Conversion to SI units gives 1 kcal/mol = 4.184 kJ/mol. [c] *RPM* (relative polarity measure) = $[E_T(n\text{-hexane}) - E_T]/E_T(n\text{-hexane})$; cf. Eq. (10). [d] Calculated on the basis of the linear correlation between $E_T(30)$ and Z from Kosower's Z values, using $Z = 1.41 \cdot E_T(30) + 6.92$ [58]. [e] *E. M. Kosower, H. Dodiuk*, J. Am. Chem. Soc. *98*, 924 (1976). [f] *E. M. Kosower, H. Dodiuk, K. Tanizawa, M. Ottolenghi, N. Orbach*, J. Am. Chem. Soc. *97*, 2167 (1975). [g] Value at 30 °C. [h] This $E_T(30)$ value was determined by *G. Collier* (personal communication from *J. Shorter* of June 21, 1978). The author wishes to thank *G. Collier* and *J. Shorter*, University of Hull (England), for communication of their unpublished results. Cf. also *A. G. Burden, N. B. Chapman, H. F. Duggua, J. Shorter*, J. Chem. Soc. Perkin Trans. II *1978*, 296. [i] From the corresponding Z-value calculated by *T. G. Beaumont, K. M. C. Davis*, J. Chem. Soc. *B1968*, 1010. [k] *W. Jeblick, K. Schank*, Justus Liebigs Ann. Chem. *1977*, 1096.

uents and by the solvent (Fig. 1)[17]. Hence it was possible, with *one and the same* standard substrate, to establish no less than three LFE relationships (cf. Figs. 1—3). The extreme sensitivity with which pyridiniophenolates of type *(1)* react to slight changes in the surrounding medium can be compared to the behavior of *Hans Christian Andersen*'s "princess and the pea"[69].

Although the empirical parameters of solvent polarity shown in Table 1 were obtained with very different standard processes, there are satisfactory linear relationships between most of them, particularly when solvents with highly specific interaction capabilities (*e.g.* protic solvents) are correlated separately[2, 4, 29, 70]. Nevertheless, the use of individual solvent parameters to predict solvent effects should be limited in the first approximation to largely analogous processes (reactions, absorptions), since only then is the proportion of intermolecular forces in the interaction between the solvent and the substrate roughly the same as in the interaction between the solvent and the standard substrate. Even when the Hammett equation (6) is used different σ-scales are often selected depending on whether, for example, one is concerned with the effect of the substituent on reactions of substituted aromatic substrates (σ, σ^+, σ^-, σ^0) or aliphatic compounds (σ^*, Taft equation)[13, 14].

Hence the empirical Koppel-Pal'm solvent parameter B shown in Table 1 and defined according to Eq. (11) should be primarily a measure of the Lewis basicity of the solvent against CH_3OD as the standard substrate[8, 51, 52].

$$B = \Delta\tilde{\nu}_{OD} = \tilde{\nu}^0_{CH_3OD} - \tilde{\nu}_{CH_3OD\cdot B} \qquad (11)$$

$\tilde{\nu}^0_{CH_3OD}$ and $\tilde{\nu}_{CH_3OD\cdot B}$ are the wave numbers of the O—D stretching vibration band in the IR spectrum of monomeric CH_3OD, measured in the gas phase ($\tilde{\nu}^0_{CH_3OD} = 2720\,cm^{-1}$[51]) and in a solvent B. EPD solvents reduce $\tilde{\nu}_{CH_3OD\cdot B}$; the wave number difference $\Delta\tilde{\nu}_{OD}$ is proportional to the strength of the HBD/EPD interaction[*].

[*] EPD = electron pair donor; EPA = electron pair acceptor; HBD = H-bond donor; HBA = H-bond acceptor. HBA solvents are also EPD solvents, HBD solvents correspond to protic solvents.

Of particular importance to the determination of the Lewis basicity or nucleophilicity of a solvent are the donor numbers *DN* introduced by *Gutmann et al.*[10, 34], defined according to Eq. (12) as the negative enthalpies of the reaction of EPD solvents with antimony(v) chloride as the standard acceptor in a highly diluted 1,2-dichloroethane solution.

$$\text{EPD} + SbCl_5 \xrightleftharpoons[\text{in } Cl{-}CH_2CH_2{-}Cl]{25\,^\circ C} \text{EPD} \rightarrow SbCl_5$$

$$DN \equiv -\Delta H_{\text{EPD}\cdot SbCl_5}\,[\text{kcal/mol}] \qquad (12)$$

The donor number is a molecular property that reflects the entire interaction of an EPD solvent with the electron pair acceptor and is of particular significance in predicting coordination-chemical reactions in solution[10, 71].

In protic solvents the $E_T(30)$ values of Table 2 should reflect above all their HBD properties and hence the electrophilicity or Lewis acidity of these solvents. In the electron ground state the pyridiniophenolate *(1a)* with the phenolate oxygen has a strongly basic, anionic HBA center, while the positive charge is delocalized over the pyridine ring and screened by the phenyl groups. Since the electron excited state is much less dipolar owing to intramolecular charge transfer absorption[26], the molecule will only exhibit extra stabilization by protic solvents compared with aprotic solvents in the electron ground state. Hence the $E_T(30)$ values of protic solvents are generally greater than those of comparable dipolar aprotic solvents (cf. Table 2).

Similarly, the electrophilic properties of solvents can be characterized by the acceptor number *AN* (cf. Table 1), which is defined according to Eq. (13) as the relative ^{31}P chemical shift of triethylphosphane oxide[10, 57].

$$(Et_3P{=}O \leftrightarrow Et_3P^{\oplus}{-}O^{\ominus}) + \text{EPA} \rightleftharpoons Et_3P^{\delta\oplus}\cdots O^{\delta\ominus} \rightarrow \text{EPA}$$

$$AN \equiv \frac{\delta_{corr}}{\delta_{corr}(Et_3PO{-}SbCl_5)} \cdot 100 = \delta_{corr} \cdot 2.348 \qquad (13)$$

δ_{corr} is the solvent-dependent ^{31}P chemical shift of triethylphosphane oxide extrapolated to infinite dilution, referred to *n*-hexane, and corrected for the difference between the volume susceptibilities of *n*-hexane and the solvent in question. The ^{31}P chemical shift of the 1:1 adduct $Et_3PO{-}SbCl_5$ dissolved in 1,2-dichloroethane is used as the reference state within this series; it is set arbitrarily as equal to 100. The acceptor numbers of organic solvents lie accordingly between 0 (*n*-hexane) and 100 ($Et_3PO{-}SbCl_5$). As was to be expected, they give a satisfactory linear relationship with the $E_T(30)$ values of Table 2[57]: $AN = 1.56 \times E_T(30) - 48.9$ ($n = 29$; $r = 0.940$)[58].

In 1976 *Kamlet* and *Taft*[72] established an α-scale of solvent HBD acidities and a β-scale of solvent HBA basicities by a UV/VIS spectroscopic method they called the solvatochromic comparison method. To determine the β values the absorption wave number shifts of 4-nitroaniline relative to *N,N*-diethyl-4-nitroaniline were measured in a series of HBA solvents. Both standard compounds are capable of acting as H-bond acceptors (*via* the oxygen atoms in the nitro group) in protic HBD solvents, but only 4-nitroaniline can also act as an H-bond donor in HBA solvents (*via* the amino group). Taking the $\Delta\Delta\tilde{\nu}$-value of 2800 cm^{-1} measured in hexamethyl-

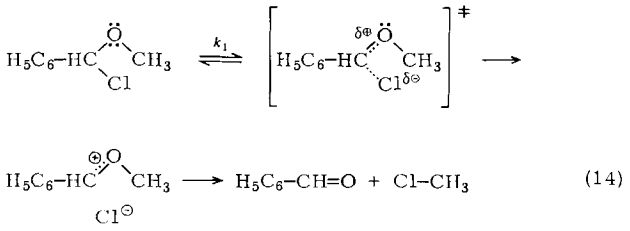
phosphoric acid triamide (a particularly strong HBA solvent) as a reference point ($\beta_1 = 1.000$) it was possible to obtain an LFE scale of HBA basicities (=Lewis basicities) for 30 HBA solvents. By the same principle, using 4-nitroanisole (1-methoxy-4-nitrobenzene) and the pyridiniophenolate *(1a)* (Fig. 3), an α-scale of the HBD acidities for eleven protic solvents was derived[72].

Owing to the peculiarities of the selected standard processes, the above-mentioned parameters are no longer true characteristics of general solvent polarity but rather ones of the electrophilic and nucleophilic properties of organic solvents (cf. Section 5).

4. Applications

The application of empirical parameters of solvent polarity will be demonstrated with the aid of three examples. Many other correlation analyses can be found in [2, 10, 29].

The first-order thermolysis of α-chlorodialkyl ethers gives rise in aprotic solvents only to aldehyde and alkyl halide, but not, as in the gas phase, to HCl-elimination products[73]. Concerted one- and two-stage mechanisms proceeding *via* a cyclic, isopolar, activated complex, a radical mechanism,



(14)

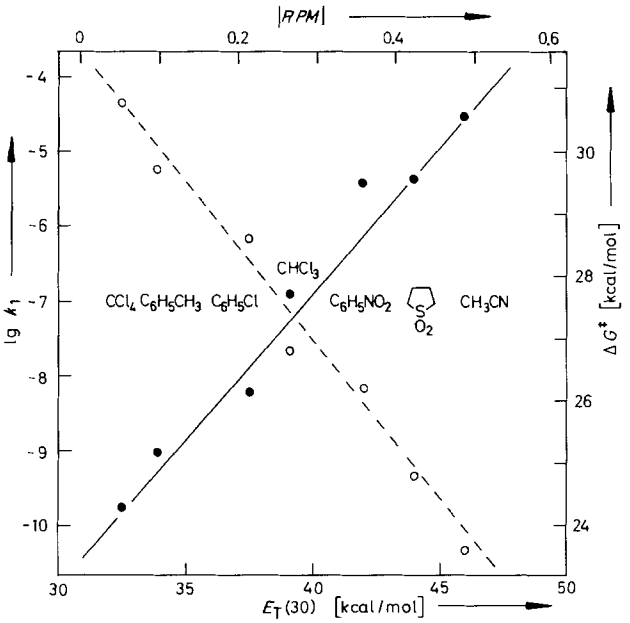


Fig. 4. Correlation between $E_T(30)$ and $\lg k_1$ (●) and $\Delta G^{\neq}$ (○) of the thermolysis of α-chlorobenzyl methyl ether in aprotic solvents at 25 °C in accordance with Eq. (14) [73]:

$\Delta G^{\neq} = -0.51 \cdot E_T(30) + 47.4$ ($n = 7$; $r = -0.991$).

and an ion-pair mechanism with a dipolar activated complex have been suggested for the reaction in solution[73].

The exceptionally marked acceleration of the reaction obtained during the thermolysis of α-chlorobenzyl methyl ether with increasing solvent polarity ($k_1(CH_3CN)/k_1(CCl_4) = 1.7 \times 10^5$; $\Delta\Delta G^{\neq} = 7.2$ kcal/mol) and the linear correlation between the logarithms of the rate constants or the free activation energies of this reaction and the $E_T(30)$ values (cf. Fig. 4) indicate beyond all doubt a reaction taking place *via* a dipolar, cryptoionic activated complex as shown in Eq. (14)[73].

Figure 5 shows the correlation between $E_T(30)$ values and the differences between the transition energies $\Delta E_T'$ of sodium 4-nitrophenolate and 4-nitroanisole measured in 21 solvents[74]. To increase the solubility of the sodium salts in nonpolar solvents the cryptand [15]crown-5-ether was added in all cases as a cation solvator. The longest-wavelength solvatochromic absorption band of the 4-nitrophenolate ion is ascribable to a π-π^* transition with intramolecular charge transfer character. Because of the same type of solvation of the 4-nitrophenyl part of the molecule, 4-nitroanisole was used as the reference substance. A striking satisfactory correlation is then found between $E_T(30)$ values and $\Delta E_T'$, although two different straight lines with opposing slopes are obtained for protic and aprotic solvents, indicative of different solvation mechanisms in the two solvent series. Protic solvents are good anion solvators, which solvate the 4-nitrophenolate ion specifically *via* H-bridges, the intensity of their action increasing with increasing HBD character of the protic solvents used. Accordingly an increasing hypsochromic shift of the longest-wavelength absorption band of the 4-nitrophenolate ion relative to that of 4-nitroanisole ($\hat{=}$ reduction of $\Delta E_T'$) is observed in the solvent series $(CH_3)_3COH$ < i-C_3H_7OH < n-C_3H_7OH < C_2H_5OH < $HOCH_2CH_2OH$ < CH_3OH ≈ H_2O (cf. also the α-scale of HBD acidities in [72]). Aprotic solvents, in contrast, are poor anion solvators, and in these solvents the effect of the solvent on the longest-wavelength absorption band of sodium 4-nitrophenolate must be interpreted by increasing dissociation of the ion pair and the resultant steady reduction of the cation-anion interaction, which gives rise to a bathochromic shift[74]. Results of this type are also of significance to the solvent-determined varying chemical reactivity of ambident phenolate ions to alkylating agents[75].

Finally, it should be mentioned that a linear correlation can even be found between $E_T(30)$ values and the molecular ellipticities $[\theta]$ taken from CD spectra of a solution of 2-benzoylbenzoic acid and (−)-(*R*)-amphetamine in eleven solvents (cf. Fig. 6)[76].

The achiral 2-benzoylbenzoic acid in benzene has an absorption band at 322 nm ($\varepsilon = 111$) which is due to the n-π^*-absorption of the carbonyl group. The addition of an equimolar amount of (−)-(*R*)-amphetamine induces more strongly positive circular dichroism in the region of the n-π^*-absorption, its magnitude depending on the solvent: as the solvent polarity increases, the induced circular dichroism is reduced (from $[\theta] = +1320$ in CCl_4 to $[\theta] = 0$ in CH_3OH). The cause of this induced circular dichroism is assumed to be the formation of a 1:1 salt *(2)*, which is initially present in nonpolar solvents as a (possibly H-bonded) ion pair. With increasing solvent polarity *(2)* dissociates *via* solvent-separated ion pairs into free solvated ions, in which the contact between the γ-keto acid and the chiral gegenion is virtually lost and hence also

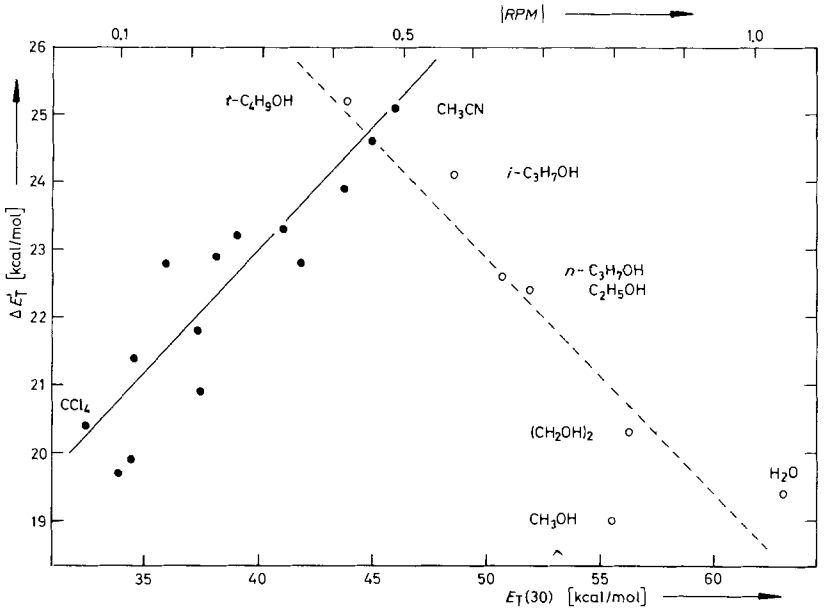
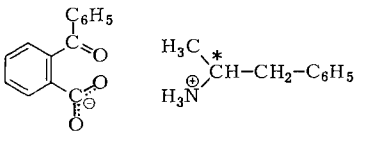


Fig. 5. Correlation between $E_T(30)$ and the difference between the transition energies ΔE_T^* of sodium 4-nitrophenolate and 4-nitroanisole, measured in protic (○) and aprotic (●) solvents in the presence of [15]crown-5-ether [74].



(2)

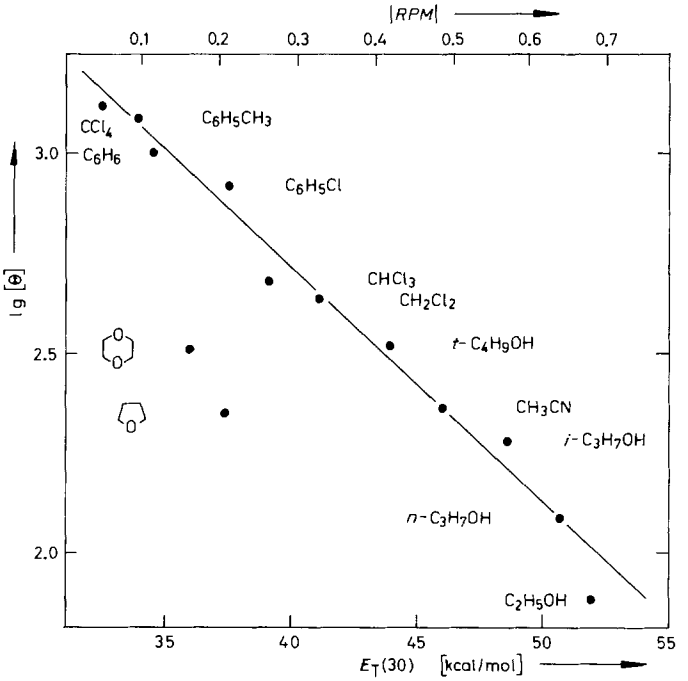


Fig. 6. Correlation between $E_T(30)$ and the logarithms of the molecular ellipticities $[\theta]$ of the 1:1 salt (2) from 2-benzoylbenzoic acid and (−)-(*R*)-amphetamine, measured in dilute solution (*ca.* 10^{-3} M) at 25°C [76]: $\lg[\theta] = -0.06 \cdot E_T(30) + 5.1$ ($n = 11$; $r = -0.989$).

the induced circular dichroism[76]. The deviation of the points for the ethereal solvents 1,4-dioxane and tetrahydrofuran from the straight correlation lines can easily be explained by competitive H-bridge formation between the γ-keto acid and the HBA solvent.

5. Multiparametric Equations

Despite the large number of very good to satisfactory LFE correlations between the empirical parameters of solvent polarity given in Table 1 and numerous other solvent-dependent processes, there is an at least equal number of examples where no such simple correlation can be found. The simple definition of "solvent polarity" as a solvent characteristic that can be universally determined and applied with the aid of singular empirical parameters is obviously too great a simplification. The solvation of solute molecules by the solvent, generally classified somewhat arbitrarily into specific and nonspecific solvation, is the result of very diverse and complex interactions and is therefore as a rule more complicated than, for example, the interaction between substrate and substituent. It is therefore truly amazing that despite the multiplicity of possible substrate-solvent interactions reasonable correlations can be obtained in so many cases with singular empirical solvent parameters. However, with a view to assessing several aspects of the substrate-solvent interaction there has recently been no shortage of attempts to establish LFE relationships in the form of multiparametric equations like Eq. (15).

$$A = A_0 + b \times B + c \times C + d \times D + \cdots \qquad (15)$$

A stands for a solvent-dependent, physicochemical parameter ($\lg K$, $\lg k$, E_T, *etc.*), determined for a specific reaction or absorption in a series of solvents, A_0 is the corresponding parameter in the gas phase or in an inert solvent taken as the reference state. The terms *B*, *C*, *D*,... represent independent but complementary solvent parameters that can be used as quantitative characteristics for different substrate-solvent inter-

actions; b, c, d, ... are regression coefficients that describe the susceptibility of A to the respective substrate-solvent interactions and have the significance of statistical weighting factors. Naturally, it is only possible to obtain such multiparametric correlation for a solvent-dependent process if measurements are available for a sufficiently large number of solvents and suitable statistical evaluation methods are used[5, 14]. A statistical method suitable for this purpose is factor analysis, in which reciprocal relationships between a large number of variables can be calculated in the form of multiparametric equations. A review of the principles and applications of factor analysis in organic chemistry can be found in[77]. The separation of solvent polarity into several interaction parameters as implied in Eq. (15) is initially purely formal and does not necessarily even have a theoretical basis, since the intermolecular interactions are coupled with one another, *i.e.* cannot be independent. Nevertheless, in a factor analysis the aim is in a second step to identify the initially still abstract factors B, C, D, ... and to determine their relationships to known parameters, thereby obtaining information about the proportion of the total solvent effect accounted for by individual interactions. Multiparametric equations of type (15) designed to provide a better quantitative description of the solvent effect on chemical reactions and light absorptions have been established over the last few years in particular by *Katritzky et al.*[78], *Koppel* and *Pal'm*[5, 8, 79], *Fawcett* and *Krygowski*[80], *Dougherty*[81], *Kamlet* and *Taft*[48], and *Mayer*[81a]. In this context we shall merely mention that efforts have also been made to improve the description of the effect of substituents on chemical reactivity with the aid of multiparametric equations[13, 82].

Katritzky et al.[78] tried out several multiparametric equations consisting of linear combinations of available empirical solvent parameters. The most successful proved to be a two-parameter combination of $E_T(30)$ values and functions of the dielectric constant or the refractive index. A more recent example of this is the S_N2 reaction between benzyl chloride and aniline, studied in twelve solvents, the solvent-dependent rate constant being found to correlate best in statistical terms with $E_T(30)$ values and the Kirkwood parameter $(\varepsilon-1)/(2\varepsilon+1)$ according to Eq. (16)[83]:

$$\lg k_2 = 0.0865 \times E_T(30) + 10.87 \times (\varepsilon-1)/(2\varepsilon+1) - 13.125 \qquad (16)$$

On the basis of a separation of specific and nonspecific substrate-solvent interactions, *Koppel* and *Pal'm*[5, 8, 79] suggested the four-parameter equation (17):

$$A = A_o + y \times Y + p \times P + e \times E + b \times B \qquad (17)$$

Here A and A_o have the same meaning as in Eq. (15). The nonspecific parameters Y and P are parameters for the polarization and polarizability of the solvent in accordance with classical dielectric theory, and E and B are specific parameters for the Lewis acidity (electrophilic solvation ability) and Lewis basicity (nucleophilic solvation ability) of the solvent. The dielectric constant ε is the basis for the polarization parameter Y and is used in the form of the Kirkwood functions $(\varepsilon-1)/(2\varepsilon+1)$ or $(\varepsilon-1)/(\varepsilon+2)$. The corresponding function $(n_D^2-1)/(n_D^2+2)$ of the refractive index n_D is used as a solvent polarizability parameter P. The parameters used for the Lewis acidity E are the $E_T(30)$ values of pyridiniophenolate *(1a)* (Fig. 3), although these were corrected to take account of nonspecific interactions by subtracting the polarization term $(y \times Y)$ and the polarizability term $(p \times P)$ according to Eq. (18) (using $E=0$ for the gas phase):

$$\begin{aligned} E &= E_T(30) - E_T^0(30) - y \times Y - p \times P \\ &= E_T(30) - 25.37 - 14.39 \times Y - 9.08 \times P \end{aligned} \qquad (18)[*]$$

By definition, in Eq. (17) $e=1$ stands for the basic reference process, *i.e.* the π-π^*-absorption of pyridiniophenolate *(1a)*. The parameters used for the Lewis basicity B were the wavenumber differences of the OD-stretching vibration band of monomeric CH_3OD defined in Eq. (11) (using $B=0$ for the gas phase). By definition, in Eq. (17) $b=1$ then stands for this reference process.

By way of example, the S_N1 solvolysis of *tert*-butyl chloride studied in 23 protic and aprotic solvents at 25°C correlates well according to Eq. (19) with the terms Y, P, and E of Eq. (17) (multiple correlation coefficient $R=0.982$), the E-term being predominant[8]:

$$\lg k_1 = -19.89 + 13.89 \times Y + 13.46 \times P + 0.378 \times E \qquad (19)$$

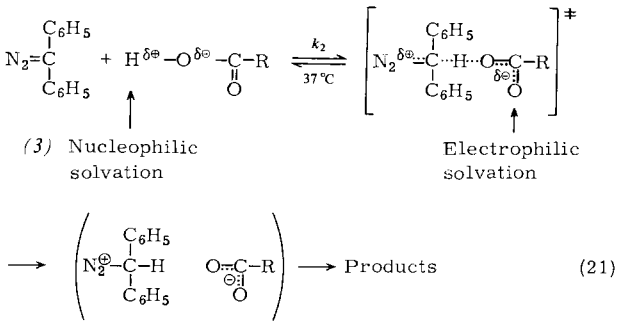
The relative contribution of the individual terms of Eq. (19) to the total solvent effect, as determined by the regression coefficients y, p, and e, reflects quantitatively the high sensitivity of this S_N1 reaction to a change in polarity (expressed by $Y=(\varepsilon-1)/(2\varepsilon+1)$, in the polarizability (P), and in the electrophilicity (E) of the solvent. In contrast, the nucleophilic properties of the solvents used can be totally disregarded (absence of the $b \times B$ term in Eq. (19) because $b=0$), as one would expect for an S_N1 reaction. The positive value of y is consistent with the increasing charge separation during the transition from the neutral starting molecule to the dipolar activated complex $[Me_3C^{\delta+}\ldots Cl^{\delta-}]^{\neq}$. The sign of e is also positive, and this indicates an additional stabilization of the activated complex relative to Me_3C—Cl by electrophilic solvation in protic solvents (by H-bond formation in accordance with $[Me_3C^{\delta+}\ldots Cl^{\delta-}\ldots H\text{—}S]^{\neq}$). Finally, the positive sign of p indicates that the activated complex of this S_N1 reaction would have a higher polarizability than the starting compound[8].

As more recent examples of correlation analysis with the aid of the Pal'm-Koppel equation (17) we shall mention only the second-order reactions between benzenesulfonyl chloride and imidazole[85], between benzaldehyde and aniline[85a], and between carboxylic acids and diazodiphenylmethane *(3)* in aprotic solvents[86]. In the last case there is a significant correlation between $\log k_2$ (determined in 43 aprotic solvents) and all four parameters of Eq. (17) in accordance with Eq. (20) $(R=0.979)$[86]:

$$\lg k_2 = -3.190 + 4.463 \times Y + 12.330 \times P + 0.210 \times E - 0.0181 \times B \qquad (20)$$

The finding that in Eq. (20) b has a negative sign and e a positive one can be best explained by nucleophilic stabilization of the carboxylic acid used and electrophilic stabilization of the activated complex in accordance with the simplified reaction scheme (21)[86].

[*] On the basis of more recent $E_T(30)$ values Eq. (18) and the E-scale of Lewis acidity defined by it were expanded and improved in 1974 [84].



(21)

A much simpler but equally successful two-parameter equation (22) was proposed by *Fawcett* and *Krygowski*[80]:

$$A = A_0 + \alpha \times E_T(30) + \beta \times DN \qquad (22)^{[*]}$$

According to this, all it is necessary to know to describe the effect of a solvent on the parameter A is the solvent's Lewis acidity (assessed with the aid of the $E_T(30)$ values; Table 2) and Lewis basicity (measured by the donor numbers DN; cf. Eq. (12) and Table 1). The regression coefficients α and β accordingly describe the relative dependence of A on the electrophilic or nucleophilic properties of the solvent in which A is measured. As the $E_T(30)$ and the DN values for a specific solvent series do not vary numerically to the same extent, the α and β values are normalized using partial regression coefficients α' and β' according to Eqs. (23a) and (23b):

$$\bar{\alpha} = 100 \times \alpha'/(\alpha' + \beta') \qquad (23a)$$
$$\bar{\beta} = 100 \times \beta'/(\alpha' + \beta') \qquad (23b)$$

$\bar{\alpha}$ and $\bar{\beta}$ can then be interpreted as the percentage contribution of solvent acidity and solvent basicity to the total solvent effect obtained. Some results of the application of Eq. (22) to solvent-dependent processes (including processes used to establish singular empirical solvent parameters) are summarized in Table 3.

predominantly by the Lewis acidity of the solvent ($\bar{\alpha} = 88$ or 85%). The corresponding α-coefficient according to Eq. (22) has a negative sign in both cases, which represents a reduction of the reaction rate with increasing Lewis acidity of the solvent. The azide ion is evidently more highly stabilized as an H-bond acceptor in protic solvents than the anionic activated complex, in line with the smaller charge density of the latter. The linear relationship between the ^{23}Na-NMR chemical shifts of $NaClO_4$ solutions and the donor number DN found by *Popov et al.*[89] is consistent with the higher $\bar{\beta}$-value of 93%, which indicates that it is predominantly the nucleophilic properties of the solvent that determine cation solvation.

Many further applications of the two-parameter Eq. (22)—including the solvent-dependent solvent activity coefficients, ionic solvation enthalpies, standard reduction potentials of organic molecules, molar heats of solution, *etc.*—can be found in [80].

Another semiempirical multiparametric equation (24) for calculating the solvent dependence of chemical reactions using the donor numbers DN[10, 34] and the acceptor numbers AN[10, 57] was published recently by *Mayer*[81a]:

$$\Delta G^S - \Delta G^R = a \cdot (DN^S - DN^R) + b \cdot (AN^S - AN^R) + c \cdot (\Delta G_{tp}^{oS} - \Delta G_{tp}^{oR}) \qquad (24a)$$

$$\Delta\Delta G = a \cdot \Delta DN + b \cdot \Delta AN + c \cdot \Delta\Delta G_{tp}^{o} \qquad (24b)$$

ΔG is the free standard reaction energy or the free activation energy ($\Delta G^{\neq}$), and ΔG_{tp}^{o} represents the free standard vaporization energy in a solvent S and a reference solvent R. The coefficients a and b are then related to the donor and acceptor strengths of the reaction participants relative to the reference compounds $SbCl_5$ and $(C_2H_5)_3PO$. Some of the successful applications of Eq. (24) have been in calculating the solubilities of alkali metal halides in several solvents, the solvent dependence of complex formation and ion association equilibria, and the solvent dependence of an S_NAr reaction[81a].

Table 3. Application of the complementary Lewis acid/base description of solvent effects according to Eq. (22) [80].

Solvent-dependent process	n [a]	$\bar{\alpha}$	$\bar{\beta}$	R [b]	Ref.
S_N1 solvolysis of *tert*-butyl chloride (Y)	5	80	20	0.909	[35, 36]
S_N1 solvolysis of 2-(4-methoxyphenyl)-2-methylpropyl tosylate ($\lg k_{ion}$)	13	99	1	0.908	[37]
S_N2 reaction $N_3^- + n$-C_4H_9Br	10	88	12	0.905	[87]
S_NAr reaction $N_3^- + 4$-NO_2—C_6H_4F	11	85	15	0.969	[88]
Diels-Alder cycloaddition cyclopentadiene + methyl acrylate (Ω)	7	91	9	0.961	[41]
CT absorption of 1-ethyl-4-methoxycarbonylpyridinium iodide (Z)	16	98	2	0.970	[43]
n-π^*-absorption of ketones (F)	7	84	16	0.956	[45]
$\bar{\nu}_{O\ D}$ of CH_3OD (Koppel-Pal'm parameter B)	15	22	78	0.954	[8]
^{23}Na-NMR chemical shift of $NaClO_4$ ($c = 0.05$ mol/l)	8	7	93	0.984	[89]

[a] Number of solvents considered. [b] Multiple regression correlation coefficient.

Comparison of the $\bar{\alpha}$ and $\bar{\beta}$ values in Table 3 shows that the empirical solvent parameters Y, $\lg k_{ion}$, Ω, Z, and F indicate above all the electrophilic solvation ability of the solvent, while the Koppel-Pal'm parameter B with a $\bar{\beta}$ value of 78% characterizes predominantly the nucleophilic solvation ability of the solvent. The two second-order substitution reactions with the azide ion as the nucleophile are also determined

Finally, we should also present a multiparametric equation for the assessment of ionic solvation that describes the substrate-solvent interaction as an interaction between the highest occupied orbitals (HOMOs) of ions and solvent and the corresponding lowest unoccupied orbitals (LUMOs) of solvent and ions. If one approximates the energies of these orbitals with the aid of the ionization potential IP and the electron affinity EA, then according to *Dougherty*[81], given certain simplifications, it is possible to formulate Eq. (25) for the ion-solvent interaction energy:

[*] Because of the consistency with Eq. (15), the letters A and A_0 were used in Eq. (22) instead of Q and Q_0 as in the original paper [80].

$$\delta E_{solv} = C_1 \times (IP_{solv} + EA_{solv}) + C_2 \times (IP_{solv}) + C_3 \times (EA_{solv})^2 + C_4 \quad (25)$$

The term $(IP_{solv} + EA_{solv})$ can be interpreted as an expression of the ionization ability of the solvent. The term (IP_{solv}) reflects the nucleophilicity of the solvent and the $(EA_{solv})^2$ represents its electrophilicity. Owing to the lack of sufficient data on electron affinities, it has so far only been possible to test Eq. (25) in very few solvent-dependent processes[81]. Thus, the Winstein-Grunwald parameter Y (solvolysis of *tert*-butyl chloride)[35, 36], for example, is controlled predominantly by the $(IP_{solv} + EA_{solv})$ term.

There is only space here merely to mention other multiparametric equations for the description of solvent effects on heterogeneous catalytic reactions (hydrogenation of C=C double bond systems, reduction of aromatic nitro compounds)[90] and on cationic copolymerization reactions (of *p*-substituted styrenes and alkyl vinyl ethers)[91].

Finally, it should be pointed out that the use of multiparametric equations instead of single-parameter equations has in many cases produced a dramatic improvement in the correlations between solvent-dependent processes (reactions, absorptions) and inherent solvent properties, since they take better account of the multiplicity of the substrate-solvent interactions than a singular parameter of solvent polarity. Nevertheless, the question in what way, and on the basis of what model concepts, the polarity or solvation ability of a solvent can best be broken down into a number of complementary interaction parameters as independent of each other as possible is still far from being answered. In this respect multiparametric equations have still not proved themselves.

6. Conclusion

Although LFE relationships of the type described above do not follow from the laws of thermodynamics, their appearance indicates the existence of real relationships between the parameters correlated, for whose nature there is in most cases a plausible explanation. On the basis of the extent to which the effect of a solvent on a standard process used to determine an empirical solvent parameter is understood, it is also possible to give a reasonable interpretation of the effect of a solvent on a series of reactions or absorptions correlating with this parameter. The method of LFE correlations is still the simplest and most practical method of predicting the effects of solvents (and substituents) on the rate and position of equilibrium of chemical reactions and also on spectral absorptions of organic molecules. The criticism that the procedure is far too empirical can be countered by saying that not only are the basic postulates of the LFE relationships (additivity and separability of the effects obtained) of theoretically acceptable form, but the selection of suitable standard processes to determine empirical parameters of solvent polarity also makes use of a number of theoretical considerations.

The author's own papers mentioned as examples were sponsored by the Fonds der Chemischen Industrie, for which the author would like to express his gratitude.

Received: March 13, 1978 [A 257 IE]
German version: Angew. Chem. *91*, 119 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] *C. Reichardt:* Lösungsmitteleffekte in der organischen Chemie. 2nd Ed. Verlag Chemie, Weinheim 1973.
[2] *C. Reichardt:* Solvent Effects in Organic Chemistry. Verlag Chemie, Weinheim 1979.
[3] *J. A. Riddick, W. B. Bunger:* Organic Solvents. 3rd Ed. Vol. II by *A. Weissberger:* Techniques of Chemistry, Wiley-Interscience, New York 1970.
[4] *C. Reichardt*, Angew. Chem. *77*, 30 (1965); Angew. Chem. Int. Ed. Engl. *4*, 29 (1965).
[5] *V. A. Pal'm:* Osnovy kolichestvennoi teorii organicheskikh reaktsii. Izdatel'stvo Khimiya, Leningrad 1967; Grundlagen der quantitativen Theorie organischer Reaktionen. Akademie-Verlag, Berlin 1971.
[6] *E. M. Kosower:* An Introduction to Physical Organic Chemistry. Wiley, New York 1968, pp. 293ff.
[7] *K. Schwetlick:* Kinetische Methoden zur Untersuchung von Reaktionsmechanismen. Deutscher Verlag der Wissenschaften, Berlin 1971, pp. 139ff.
[8] *I. A. Koppel, V. A. Pal'm* in *N. B. Chapman, J. Shorter:* Advances in Linear Free-Energy Relationships. Plenum, London 1972, Chap. 5, pp. 203ff.
[9] *M. R. J. Dack* in *M. R. J. Dack:* Solutions and Solubilities. Vol. VIII, Part 2 by *A. Weissberger:* Techniques of Chemistry. Wiley-Interscience, New York 1976, pp. 95ff.
[10] *V. Gutmann*, Electrochim. Acta *21*, 661 (1976).
[11] *L. P. Hammett:* Physical Organic Chemistry. McGraw-Hill, New York 1970; Physikalische Organische Chemie. Verlag Chemie, Weinheim 1973, pp. 346ff.
[12] *P. R. Wells:* Linear Free-Energy Relationships. Academic Press, London 1968.
[13] *N. B. Chapman, J. Shorter:* Advances in Linear Free-Energy Relationships. Plenum, London 1972.
[14] *J. Shorter:* Correlation Analysis in Organic Chemistry. An Introduction to Linear Free-Energy Relationships. Clarendon Press, Oxford 1973.
[15] *R. W. Hoffmann:* Aufklärung von Reaktionsmechanismen. Thieme, Stuttgart 1976.
[16] *L. P. Hammett*, J. Am. Chem. Soc. *59*, 96 (1937); Trans. Faraday Soc. *34*, 156 (1938).
[17] *C. Reichardt, R. Müller*, Justus Liebigs Ann. Chem. *1976*, 1953.
[18] *J. N. Brønsted, K. Pedersen*, Z. Phys. Chem. *108*, 185 (1924).
[19] *J. E. Leffler, E. Grunwald:* Rates and Equilibria of Organic Reactions. Wiley, New York 1963.
[20] *A. R. Katritzky, R. D. Topsom* in *N. B. Chapman, J. Shorter:* Advances in Linear Free-Energy Relationships. Plenum, London 1972, Chap. 3, pp. 119ff.
[21] a) *M. T. Tribble, J. G. Traynham* in *N. B. Chapman, J. Shorter:* Advances in Linear Free-Energy Relationships. Plenum, London 1972, Chap. 4, pp. 143ff; b) *E. M. Kosower, D. Hoffmann, K. Wallenfels*, J. Am. Chem. Soc. *84*, 2755 (1962).
[22] *C. Reichardt, W. Grahn*, Chem. Ber. *103*, 1072 (1970).
[23] *C. Reichardt, R. Müller*, Justus Liebigs Ann. Chem. *1976*, 1937.
[24] *C. Reichardt, K. Halbritter*, Chem. Ber. *104*, 822 (1971).
[25] *H. W. Gibson, F. C. Bailey*, Tetrahedron *30*, 2043 (1974); Can. J. Chem. *53*, 2162 (1975).
[26] *W. Liptay, B. Dumbacher, H. Weisenberger*, Z. Naturforsch. *A 23*, 1601 (1968).
[27] *K. Dimroth, C. Reichardt, T. Siepmann, F. Bohlmann*, Justus Liebigs Ann. Chem. *661*, 1 (1963); *K. Dimroth, C. Reichardt, ibid. 727*, 93 (1969); *C. Reichardt, ibid. 752*, 64 (1971).
[28] *K. Dimroth, C. Reichardt*, Z. Anal. Chem. *215*, 344 (1966); *Z. B. Maksimović, C. Reichardt, A. Spirić, ibid. 270*, 100 (1974): $E_T(30)$ values for binary solvent mixtures.
[29] *C. Reichardt, K. Dimroth*, Fortschr. Chem. Forsch. *11*, 1 (1968).
[30] *S. Dähne, F. Shob, K.-D. Nolte, R. Radeglia*, Ukr. Khim. Zh. (Russ. Ed.) *41*, 1170 (1975); Chem. Abstr. *84*, 43086j (1976).
[31] *K. H. Meyer*, Ber. Dtsch. Chem. Ges. *47*, 826 (1914); *53*, 1410 (1920); *54*, 579 (1921).
[32] *E. L. Eliel*, Supplement to Pure Appl. Chem. *1971*, 219ff.; *E. L. Eliel, O. Hofer*, J. Am. Chem. Soc. *95*, 8041 (1973).
[33] *J. Llor, M. Cortijo*, J. Chem. Soc. Perkin Trans. II *1977*, 1111.
[34] *V. Gutmann, E. Wychera*, Inorg. Nucl. Chem. Lett. *2*, 257 (1966); *V. Gutmann, A. Scherhaufer*, Monatsh. Chem. *99*, 335 (1968).
[35] *E. Grunwald, S. Winstein*, J. Am. Chem. Soc. *70*, 846 (1948); *A. H. Fainberg, S. Winstein, ibid. 78*, 2770 (1956).
[36] Cf. also *T. W. Bentley, P. v. R. Schleyer*, Adv. Phys. Org. Chem. *14*, 2 (1977).
[37] *S. G. Smith, A. H. Fainberg, S. Winstein*, J. Am. Chem. Soc. *83*, 618 (1961).
[38] *M. Gielen, J. Nasielski*, J. Organomet. Chem. *1*, 173 (1963); *7*, 273 (1967).
[39] *Y. Drougard, D. Decroocq*, Bull. Soc. Chim. Fr. *1969*, 2972.
[40] *C. Lassau, J. C. Jungers*, Bull. Soc. Chim. Fr. *1968*, 2678.

[41] *J. A. Berson, Z. Hamlet, W. A. Mueller*, J. Am. Chem. Soc. *84*, 297 (1962).
[42] Cf. also *B. Blankenburg, H. Fiedler, M. Hampel, H. G. Hauthal, G. Just, K. Kahlert, J. Korn, K.-H. Müller, W. Pritzkow, Y. Reinhold, M. Röllig, E. Sauer, D. Schnurpfeil, G. Zimmermann*, J. Prakt. Chem. *316*, 804 (1974).
[43] *E. M. Kosower*, J. Am. Chem. Soc. *80*, 3253 (1958); *E. M. Kosower, M. Mohammad, ibid. 90*, 3271 (1968); *93*, 2713 (1971); J. Phys. Chem. *74*, 1153 (1970).
[44] *L. G. S. Brooker, A. C. Craig, D. W. Heseltine, P. W. Jenkins, L. L. Lincoln*, J. Am. Chem. Soc. *87*, 2443 (1965).
[45] *J.-E. Dubois, A. Bienvenüe*, J. Chim. Phys. *65*, 1259 (1968).
[46] *D. Walter*, J. Prakt. Chem. *316*, 604 (1974).
[47] *W. Walter, O. H. Bauer*, Justus Liebigs Ann. Chem. *1977*, 421.
[48] *M. J. Kamlet, J. L. Abboud, R. W. Taft*, J. Am. Chem. Soc. *99*, 6027 (1977); *99*, 8325 (1977).
[49] *S. Brownstein*, Can. J. Chem. *38*, 1590 (1960).
[50] *A. Allerhand, P. v. R. Schleyer*, J. Am. Chem. Soc. *85*, 371 (1963); *86*, 5709 (1964).
[51] *A. G. Burden, G. Collier, J. Shorter*, J. Chem. Soc. Perkin Trans. II *1976*, 1627.
[52] *J. A. Koppel, A. I. Paju*, Reakts. Sposobn. Org. Soedin. *11*, 121 (1974); Chem. Abstr. *82*, 42805q (1975).
[53] *B. R. Knauer, J. J. Napier*, J. Am. Chem. Soc. *98*, 4395 (1976).
[54] Cf. also *O. W. Kolling*, Anal. Chem. *49*, 591 (1977).
[55] *R. W. Taft, G. B. Klingensmith, E. Price, I. R. Fox*, Preprints of papers presented at the Symposium on LFE Correlations. Durham/N. C., October 1964, pp. 265ff.
[56] A list of *P* values is given by *C. D. Ritchie* in *J. F. Coetzee, C. D. Ritchie:* Solute-Solvent Interactions. Marcel Dekker, New York 1969, Vol. 1, Tables 4–13, p. 281.
[57] *U. Mayer, V. Gutmann, W. Gerger*, Monatsh. Chem. *106*, 1235 (1975); *108*, 489 (1977).
[58] *C. Reichardt, E. Harbusch*, unpublished results.
[59] *W. Liptay*, Angew. Chem. *81*, 195 (1969); Angew. Chem. Int. Ed. Engl. *8*, 177 (1969).
[60] *A. Schweig*, Angew. Chem. *84*, 1074 (1972); Angew. Chem. Int. Ed. Engl. *11*, 1033 (1972).
[61] *M. F. Nicol*, Appl. Spectrosc. Rev. *8*, 183 (1974); Chem. Abstr. *82*, 9412m (1975).
[62] *K. D. Nolte, S. Dähne*, Adv. Mol. Relaxation Interaction Processes *10*, 2991 (1977); Chem. Abstr. *87*, 151529b (1977).
[63] *T. G. Beaumont, K. M. C. Davis*, J. Chem. Soc. *B1968*, 1010: dichloromethane/acetonitrile mixtures.
[64] *W. Koehler, P. Froelich, R. Radeglia*, Z. Phys. Chem. (Leipzig) *242*, 220 (1969): acetone/1,4-dioxane, and tetrahydrofuran/water mixtures.
[65] *K. Tamura, Y. Ogo, T. Imoto*, Bull. Chem. Soc. Jpn. *46*, 2988 (1973); nitrobenzene/benzene mixtures.
[66] *E. M. Kosower, H. Dodiuk, K. Tanizawa, M. Ottolenghi, N. Orbach*, J. Am. Chem. Soc. *97*, 2167 (1975): 1,4-dioxane/water mixtures.
[67] *K. Dimroth, C. Reichardt, A. Schweig*, Justus Liebigs Ann. Chem. *669*, 95 (1969).
[68] *K. Tamura, Y. Ogo, T. Imoto*, Chem. Lett. (Tokyo) *1973*, 625; *K. Tamura, T. Imoto*, Bull. Chem. Soc. Jpn. *48*, 369 (1975).
[69] *H. C. Andersen:* Sämtliche Märchen. Winkler-Verlag, München 1974; Complete Fairy-Tales and Stories. Gollancz, London 1974.
[70] *M. J. Kamlet, J. L. Abboud, R. W. Taft*, J. Am. Chem. Soc. *99*, 8325 (1977).
[71] *V. Gutmann:* Coordination Chemistry in Non-Aqueous Solvents. Springer, Wien 1968; Coord. Chem. Rev. *18*, 225 (1976).
[72] *M. J. Kamlet, R. W. Taft*, J. Am. Chem. Soc. *98*, 377, 2886 (1976).
[73] *H. Kwart, P. A. Silver*, J. Org. Chem. *40*, 3019 (1975); *H. Kwart, T. H. Lilley, ibid. 43*, 2374 (1978).
[74] *S. Ueji, M. Kitadani*, Bull. Chem. Soc. Jpn. *50*, 2819 (1977).
[75] *L. M. Jackman, B. C. Lange*, Tetrahedron *33*, 2737 (1977).
[76] *N. Tokura, T. Nagai, S. Takenaka, T. Oshima*, J. Chem. Soc. Perkin Trans. II *1974*, 337; *N. Tokura, S. Takenaka*, Kagaku No Ryoiki *31*, 622 (1977); Chem. Abstr. *89*, 41582x (1978).
[77] *M. Bohle, W. Kollecker, D. Martin*, Z. Chem. *17*, 161 (1977).
[78] *F. W. Fowler, A. R. Katritzky, R. J. D. Rutherford*, J. Chem. Soc. *B 1971*, 460.
[79] *I. A. Koppel, V. A. Pal'm*, Reakts. Sposobn. Org. Soedin. *8*, 291 (1971); Org. React. (USSR) *8*, 296 (1971); Chem. Abstr. *76*, 28418k (1972).
[80] *T. M. Krygowski, W. R. Fawcett*, J. Am. Chem. Soc. *97*, 2143 (1975); Austr. J. Chem. *28*, 2115 (1975); Can. J. Chem. *54*, 3283 (1976).
[81] *R. C. Dougherty*, Tetrahedron Lett. *1975*, 385.
[81a] *U. Mayer*, Monatsh. Chem. *109*, 421, 775 (1978).
[82] *T. M. Krygowski, W. R. Fawcett*, Can. J. Chem. *53*, 3622 (1975); J. Chem. Soc. Perkin Trans. II *1977*, 2033.
[83] *F. P. Ballistreri, E. Maccarone, G. Musumarra, G. A. Tomaselli*, J. Org. Chem. *42*, 1415 (1977).
[84] *I. A. Koppel, A. Paju*, Reakts. Sposobn. Org. Soedin. *11*, 139 (1974); Chem. Abstr. *82*, 42806r (1975).
[85] *A. Arcoria, V. Librando, E. Maccarone, G. Musumarra, G. A. Tomaselli*, Tetrahedron *33*, 105 (1977).
[85a] *E. Maccarone, A. Mamo*, Gazz. Chim. Ital. *108*, 101 (1978).
[86] *N. B. Chapman, M. R. J. Dack, D. J. Newman, J. Shorter, R. Wilkinson*, J. Chem. Soc. Perkin Trans. II *1974*, 962; *A. G. Burden, N. B. Chapman, H. F. Duggua, J. Shorter, ibid. 1978*, 296.
[87] *J. J. Delpuech*, Tetrahedron Lett. *1965*, 2111.
[88] *A. J. Parker*, Chem. Rev. *69*, 1 (1969).
[89] *R. H. Erlich, A. I. Popov*, J. Am. Chem. Soc. *93*, 5620 (1971).
[90] *L. Červený, J. Bartoň, V. Nevrkla, V. Růžička*, Collect. Czechoslov. Chem. Commun. *42*, 3325 (1977).
[91] *G. Heublein, P. Hallpap, J. Draffehn*, Z. Chem. *14*, 309 (1974); *G. Heublein, R. Wondraczek*, Makromol. Chem. *178*, 1853 (1977).

New Applications of Computers in Chemistry

By Ivar Ugi, Johannes Bauer, Josef Brandt, Josef Friedrich, Johann Gasteiger, Clemens Jochum, and Wolfgang Schubert[*]

The mathematical model of constitutional chemistry described here is based on a concept of isomerism which has been extended from molecules to ensembles of molecules. A chemical reaction is the conversion of an ensemble of molecules into an isomeric ensemble. An ensemble of molecules is representable by an atomic vector and an associated bond and electron (BE)-matrix, and a reaction by a reaction (R)-matrix. These BE- and R-matrices serve as a basis for computer programs for the deductive solution of chemical problems. We present here algorithms and computer programs based on the theory of BE- and R-matrices. They enable the classification and documentation of structures, substructures and reactions, the prognosis of reaction products, the design of syntheses, the construction of networks of mechanistic and synthetic pathways and the prediction of chemical reactions.

1. Approaches to the Deductive Solution of Chemical Problems

In chemistry the use of computers has been customary for a long time. Nevertheless, only a modest part of the inherent capabilities of modern computers is utilized for the solving of chemical problems. Numerical problems are solved, such as the ones encountered in quantum chemistry, and in the collection and evaluation of experimental data, or large sets of data are subjected to storage and retrieval operations. The challenge to solve chemical problems by algorithms which simulate human intelligence in the sense of decision processes and deductive thought was felt at a rather early stage. It led to studies in a direction which is now associated with the term "artificial intelligence".

This development began more than ten years ago with computer programs for the elucidation of molecular structures from measured physicochemical data[1] (*e.g.* mass spectra), and also with retrieval oriented computer assisted synthesis design[2]. In the latter type synthesis design programs, stored information on chemical reactions is used to generate the precursors of a given synthetic target molecule. Here the structural features of the target molecule are perceived and analyzed in order to determine which of the reactions in a library of stored known reactions may lead to the target. For such reactions the corresponding precursors of the target are generated.

A theory of constitutional chemistry is needed for the development of synthesis design programs which are also able to propose -- without detailed knowledge of chemical reactions —synthetic pathways containing unprecedented steps. This theory should be the basis for finding the molecular systems from which a given system may be formed by chemical reactions, or into which it may be converted.

Such a theory would not only serve as a suitable foundation for synthesis design programs, but it would also enable the solution of a great variety of other chemical problems.

Deductive computer programs which are based on mathematical representations and models of logical structures will play an essential role in future chemistry. With this approach, one is not restricted to the retrieval and manipulation of stored empirical data. Instead, the *whole set of conceivable solutions* of a chemical problem can be taken into account by *deduction* based on a suitable theory. There is no need to refrain from making use of relevant empirical data; it is possible and meaningful to condense these into the form of general selection rules which are applied in the analysis and evaluation of the intermediate and final results.

In this article a mathematical model of constitutional chemistry is described, and its use as a theoretical basis of deductive computer programs is demonstrated by some examples. This *mathematical model of constitutional chemistry*[3] is based on the consequent use of the equivalency concept in the representation and classification of molecular systems.

The basis for the additional treatment of stereochemical aspects has been discussed before[4].

2. A Mathematical Model of Constitutional Chemistry

As an introduction to representing the logical structure of constitutional chemistry by a mathematical model[3], we observe that: An ensemble of molecules (*EM*)[5, 6] consists of molecules which may be chemically different, or indistinguishable. Just like a molecule, an *EM* has an empirical formula. It is the union of the empirical formulas of the molecules belonging to the ensemble.

2.1. The Extended Concept of Isomerism

The above statement leads directly to an extension of the concept of isomerism to ensembles of molecules:

Ensembles of molecules (*EM*) are isomeric, if they have the same empirical formula. The empirical formula describes the collection **A** of atoms which the *EM* contains. All *EM*'s which can be formed from **A** have the same ensemble empirical formula $\langle \mathbf{A} \rangle$.

Accordingly, an *EM*(**A**) consists of one or more than one molecule that can be obtained from **A** by using each atom belonging to **A** exactly once.

An *FIEM*(**A**), the *family of the isomeric ensembles of molecules* which contains the atoms of **A**, is the collection of all

[*] Prof. Dr. I. Ugi, Dipl.-Inform. J. Bauer, Dr. J. Brandt, Dipl.-Inform. J. Friedrich, Dr. J. Gasteiger, Dr. C. Jochum, Dr. W. Schubert
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0202-0111 $ 02.50/0*

EM(**A**). An *FIEM* is simply determined by the empirical formula $\langle \mathbf{A} \rangle$ of the collection **A** of atoms.

A chemical reaction, or a sequence of chemical reactions, is the conversion of an *EM* into an isomeric *EM*. An *FIEM* contains all *EM*'s which are chemically interconvertible, as far as stoichiometry is concerned. Thus the *FIEM*(**A**) contains the whole chemistry of the collection **A** of atoms. Since any collection of atoms may be chosen here, a theory of the *FIEM* is a theory of all of chemistry.

The left-hand sides and the right-hand sides of the "chemical equations" (1) to (4) are pairs of isomeric *EM*'s whose empirical formulas are given in brackets. The addition of eqs. (1) to (3) results in eq. (4) for the overall reaction.

$$HCN + Cl_2 = ClCN + HCl \qquad \langle CHCl_2N \rangle \qquad (1)$$

$$NH_3 + ClCN = H_2NCN + HCl \qquad \langle CH_3ClN_2 \rangle \qquad (2)$$

$$H_2NCN + H_2O = H_2NCONH_2 \qquad \langle CH_4N_2O \rangle \qquad (3)$$

$$HCN + Cl_2 + NH_3 + H_2O = H_2NCONH_2 + HCl + HCl \qquad \langle CH_6Cl_2N_2O \rangle \qquad (4)$$

The *EM*'s which participate in the reactions (1) to (4) can be imbedded into the *FIEM* $\langle CH_6Cl_2N_2O \rangle$ when the ensembles of the reacting molecules are supplemented by those molecules that do not participate directly in the reactions [eq. (5)].

$$HCN + Cl_2 + NH_3 + H_2O \rightarrow ClCN + HCl + NH_3 + H_2O \rightarrow H_2NCN + HCl + HCl + H_2O \rightarrow H_2NCONH_2 + HCl + HCl \qquad (5)$$

2.2. BE-Matrices

Seen chemically, atoms consist of a core (atomic nucleus and the electrons of the inner orbitals) and the valence electrons (electrons of the outer orbitals). In molecules the cores are held together by the valence electrons. The chemical constitution of a molecular system is described in terms of its *covalently* bonded pairs of cores. The distribution of the "free" valence electrons which do not belong to covalent bonds can also be considered as part of the constitution. Customarily, the chemical constitution is described by constitutional formulas. In these the atomic cores are represented by element symbols, and covalent bonds by lines connecting the element symbols. The placement of the free valence electrons is generally indicated by dots next to the element symbols.

In our model, the chemical constitution of an *EM* is represented by its atomic vector, which corresponds to the atoms in **A**, and by the associated bond and electron (BE)-matrix, whose rows and columns belong to the individual atomic cores. The off-diagonal entries are the formal covalent bond orders, and the diagonal entries are the numbers of the free valence electrons[3-13].

In the past, some other matrix representations of the chemical constitution have been introduced: The adjacency matrix **J**, which originates in graph theory, indicates only, which atoms are bonded. *Spialter*[14] defined the connectivity matrix **C**, whose off-diagonal entries are the formal covalent bond orders; the diagonal entries contain the atomic vector. *E. Meyer*[15] used topological matrices for documentation purposes. *Yoneda*[16] uses a matrix representation for the treatment of heterogenous catalysis. The reactive centers of the reactants and the catalysts are accounted for on the diagonal.

The adjacency matrix **J**(HCN) (6) and the connectivity matrix **C**(HCN) (7) of hydrogen cyanide may serve as an illustration.

H—C≡N:

$$\mathbf{J}(HCN) = \begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{pmatrix} \qquad (6)$$

$$\mathbf{C}(HCN) = \begin{pmatrix} H & 1 & 0 \\ 1 & C & 3 \\ 0 & 3 & N \end{pmatrix} \qquad (7)$$

The BE-matrix **B** of an *EM*(**A**) with a set of n arbitrarily indexed atoms $\mathbf{A} = \{A_1, \ldots, A_n\}$ is an $n \times n$ matrix whose i-th row and column belong to the i-th atomic core A_i. The off-diagonal entry b_{ij} of the i-th row and j-th column is the formal bond order of the covalent bond from A_i to A_j. Since this corresponds to a bond with the same formal order from A_j to A_i, we have $b_{ij} = b_{ji}$. Thus the BE-matrices must be symmetric. The i-th diagonal entry b_{ii} indicates the number of free valence electrons of the atom A_i. For *EM*'s with closed valence shells and spin paired valence electrons all diagonal entries are even.

The BE-matrices **B**(HCN) and **B**(HNC) correspond to the formulas of hydrogen cyanide and hydrogen isocyanide.

$H^1—C^2 \equiv \ddot{N}^3$ $\qquad$ $H^1—\overset{\oplus}{N}^3 \equiv \overset{\ominus}{\ddot{C}}^2$

$H^1C^2N^3$ $\qquad$ $H^1C^2N^3$

$$\mathbf{B}(HCN) = \begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 3 \\ 0 & 3 & 2 \end{pmatrix} \begin{matrix} H^1 \\ C^2 \\ N^3 \end{matrix} \qquad (8) \qquad \mathbf{B}(HNC) = \begin{pmatrix} 0 & 0 & 1 \\ 0 & 2 & 3 \\ 1 & 3 & 0 \end{pmatrix} \begin{matrix} H^1 \\ C^2 \\ N^3 \end{matrix} \qquad (9)$$

In **B**(HCN) the entries $b_{12} = b_{21} = 1$ stand for the H—C bond, the entries $b_{23} = b_{32} = 3$ for the C≡N triple bond, and $b_{33} = 2$ for the pair of free electrons on the nitrogen atom.

As can be seen from the example, a BE-matrix is a representation of a resonance structure in the sense of the valence bond theory.

The number of valence electrons s_i which belong to the atom A_i is the sum over the entries of the i-th row or column of a BE-matrix:

$$s_i = \sum_{j=1}^{n} b_{ij} = \sum_{j=1}^{n} b_{ji} \qquad (10)$$

The formal electrical charge of the atom A_i is the core charge minus s_i. For the second row or column of **B**(HNC) we have $s_2 = 0 + 2 + 3 = 5$. It follows that the C-atom of HNC with a core charge of $+4$ has a formal electrical charge of -1. The cross sum

$$\hat{s}_i = 2s_i - b_{ii}$$

over a diagonal entry b_{ii} comprises the entries in the i-th row and column, *i.e.* all entries b_{ij} and b_{ji} whose indices include an i. This is twice the row/column sum s_i, minus the diagonal entry b_{ii}. The cross sum $\hat{s}_i$ is the number of

electrons in the valence orbitals of the atom A_i. For the C-atom of HNC we find

$$\begin{aligned} s_2 &= b_{21}+b_{22}+b_{23}+b_{12}+b_{23} \\ &= 0+2+3+0+3 = 2s_2-b_{22} \\ &= 2\times 5-2=8 \end{aligned} \tag{11}$$

i.e. this atom fulfils the octet rule.

The row of a BE-matrix describes the distribution of valence electrons at the respective atomic core. For a given core, only a limited number of such distributions (valence schemes) is permissible. These may be collected in a list of acceptable valence schemes[13].

The sum

$$S = \sum_i s_i = \sum_{ij} b_{ij} \tag{12}$$

over all entries of a BE-matrix is the number of valence electrons which the *EM* contains. This sum S has the same value for all *EM*'s belonging to the same *FIEM*.

The BE-matrices of all relevant resonance structures, or BE-matrices with fractional formal bond orders, may be used for the description of the constitution of chemical compounds which are not representable in terms of localized bonds, such as systems capable of resonance, or systems with multicenter bonds.

The n atoms of an *EM* can be numbered in up to $n!$ different ways, thus leading to up to n! distinguishable but equivalent BE-matrices. By appropriate rules *one* of these numberings can be declared canonical[17]. This numbering is important when dealing with stereochemical aspects.

2.3. R-Transformations

A chemical reaction is the conversion of an *EM* into an isomeric *EM* by the redistribution of valence electrons. Here the following invariances hold which are based on the conservation laws of matter and charge:

1. The atomic cores of an *EM* are preserved.
2. The total number of the valence electrons of an *EM* is preserved.

From 2 it follows that the conversion of the starting materials *EM*(**B**) into the final products *EM*(**E**) through a chemical reaction

$$EM(\mathbf{B}) \rightarrow EM(\mathbf{E}) \tag{13}$$

is representable by those transformations $\mathbf{B}\rightarrow\mathbf{E}$ of BE-matrices in which the sum over all entries (S) [see eq. (12)] is maintained.

2.3.1. *R*-Matrices

We define the *R-matrix* (reaction matrix) **R** through the transformation:

$$\mathbf{B}+\mathbf{R}=\mathbf{E} \tag{14}$$

The addition of an R-matrix to a BE-matrix may be interpreted as the action of an operator $\mathbf{R}_{op}$ on **B**:

$$\mathbf{R}_{op}(\mathbf{B})=\mathbf{B}+\mathbf{R}=\mathbf{E} \tag{15}$$

Since **B** and **E** have the same sum S of entries:

$$S = \sum_{i,j} b_{ij} = \sum_{i,j} e_{ij} = \sum_{i,j} b_{ij} + \sum_{i,j} r_{ij} \tag{16}$$

the sum of the entries $r_{ij}=e_{ij}-b_{ij}$ of the matrix $\mathbf{R}=\mathbf{E}-\mathbf{B}$ must be zero:

$$\sum_{i,j} r_{ij} = 0 \tag{17}$$

The matrix must be symmetric, because $\mathbf{E}=\mathbf{B}+\mathbf{R}$ is a BE-matrix, and must thus by definition be symmetric, *i.e.* from $b_{ij}=b_{ji}$ and $e_{ij}=e_{ji}$ follows $r_{ij}=r_{ji}$.

The off-diagonal negative entries $r_{ij}=r_{ji}=-1$ reflect the breaking of a covalent bond A_i—A_j; a negative diagonal entry r_{ii} indicates the number of free valence electrons that the atom A_i loses by a chemical reaction. Correspondingly, positive off-diagonal entries show how many bonds between A_i and A_j are made, and a positive diagonal entry shows how many free valence electrons the atom A_i gains during the reaction.

When **R** represents the reaction $EM(\mathbf{B})\rightarrow EM(\mathbf{E})$ according to $\mathbf{B}+\mathbf{R}=\mathbf{E}$, then its inverse $\bar{\mathbf{R}}$ describes the *retroreaction* $EM(\mathbf{E})\rightarrow EM(\mathbf{B})$ according to:

$$\mathbf{E}+\bar{\mathbf{R}}=\mathbf{E}-\mathbf{R}=\mathbf{B} \tag{18}$$

The entries of $\bar{\mathbf{R}}$ are thus given by:

$$\bar{r}_{ij} = -r_{ij} \tag{19}$$

For example, the reaction

$$HCN \rightarrow HNC$$

is represented by:

$$\begin{array}{ccccc} \mathbf{B}(HCN) & + & \mathbf{R} & \rightarrow & \mathbf{B}(HNC) \\ \begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 3 \\ 0 & 3 & 2 \end{pmatrix} & + & \begin{pmatrix} 0 & -1 & +1 \\ -1 & +2 & 0 \\ +1 & 0 & -2 \end{pmatrix} & = & \begin{pmatrix} 0 & 0 & 1 \\ 0 & 2 & 3 \\ 1 & 3 & 0 \end{pmatrix} \end{array} \tag{20}$$

The inverse matrix $\bar{\mathbf{R}}=-\mathbf{R}=\mathbf{B}(HCN)-\mathbf{B}(HNC)$ corresponds to the reaction HNC→HCN.

The R-matrices of reactions belonging to the chemistry of valence shells with paired electrons have in the diagonal zeros, or even numbers only. The R-matrices belonging to the octet chemistry of molecules without formally charged atoms have only zero entries in the diagonal. Such R-matrices exist only from $n\geq 4$ onwards. From this it follows, that one cannot obtain from any collection of three atoms more than *one* molecule or *EM* which belongs to the octet chemistry, and that no product of a reaction of this *EM* can also belong to octet chemistry[3].

2.3.2. The Basis Elements of *R*-Matrices

An R-matrix of the type

$$\mathbf{U}^{ij} = \begin{array}{c} \begin{matrix} & i & & j & \end{matrix} \\ \begin{pmatrix} \cdots & +1 & \cdots & 0 & \cdots \\ & \vdots & & \vdots & \\ \cdots & 0 & \cdots & -1 & \cdots \end{pmatrix} \begin{matrix} i \\ \\ j \end{matrix} \end{array} \tag{21}$$

with all entries = 0, except $u_{ii}^{ij} = +1$ and $u_{jj}^{ij} = -1$, describes an elementary *redox reaction*

$$A_i + {}^{\bullet}A_j \rightarrow {}^{\bullet}A_i + A_j \tag{22}$$

by which an electron is transferred from A_j to A_i. The elementary *homoapsis* according to

$${}^{\bullet}A_i + {}^{\bullet}A_j \rightarrow A_i\text{—}A_j \tag{23}$$

is represented by the R-matrix

$$\mathbf{V}^{ij} = \begin{array}{c} \begin{matrix} & i & & j & \end{matrix} \\ \begin{pmatrix} \cdots & -1 & \cdots & +1 & \cdots \\ & \vdots & & \vdots & \\ \cdots & +1 & \cdots & -1 & \cdots \end{pmatrix} \begin{matrix} i \\ \\ j \end{matrix} \end{array} \tag{24}$$

in which $v_{ij}^{ij} = v_{ji}^{ij} = +1$ and $v_{ii}^{ij} = v_{jj}^{ij} = -1$ are the only non-zero entries.

The R-matrix $-\mathbf{V}^{ij}$ describes the retroreaction, *i.e.* the elementary *homolysis*

$$A_i\text{—}A_j \rightarrow {}^{\bullet}A_i + {}^{\bullet}A_j \tag{25}$$

An R-matrix with the entries r_{ij} and the i-th row sum

$$r_i = \sum_j r_{ij} \tag{26}$$

is uniquely represented (up to sequence) as a sum of the R-matrices $\mathbf{U}^{in}$ and $\mathbf{V}^{ij}$.

$$\mathbf{R} = \sum_{i<j} r_{ij}\mathbf{V}^{ij} + \sum_{i<n} r_i \mathbf{U}^{in} \tag{27}$$

The set of the $\mathbf{U}^{in}$ and the $\mathbf{V}^{ij}$ forms a *basis* for the R-matrices. Since the R-matrices may be interpreted as vectors belonging to $\mathbb{R}^{n^2}$, the $\mathbf{U}^{in}$ and $\mathbf{V}^{ij}$ are also called the *basis vectors*.

The vector basis of the R-matrices of reactions within the chemistry of valence shells with paired electrons only (with $r_{ii} = 0, \pm 2, \ldots$) consists of R-matrices of the type $(\mathbf{U}^{ij} + \mathbf{V}^{ij})$ and $2\mathbf{U}^{in}$. The basis vector $(\mathbf{U}^{ij} + \mathbf{V}^{ij})$ represents reactions of the types (28) and (29):

$$A_i + :A_j \rightarrow A_i^{\ominus}\text{—}A_j^{\oplus} \tag{28}$$

$$A_i^{\oplus} + :A_j^{\ominus} \rightarrow A_i \text{—} A_j \tag{29}$$

The R-matrix from eq. (20) may serve to illustrate the decomposition of R-matrices into their basis vectors.

$$\mathbf{R}(\mathrm{HCN} \rightarrow \mathrm{HNC}) = -(\mathbf{U}^{12} + \mathbf{V}^{12}) + (\mathbf{U}^{13} + \mathbf{V}^{13}) \tag{30}$$

$$\mathbf{R}(\mathrm{HCN/HNC}) =$$

$$\begin{pmatrix} 0 & -1 & +1 \\ -1 & +2 & 0 \\ +1 & 0 & -2 \end{pmatrix} = -\begin{pmatrix} 0 & +1 & 0 \\ +1 & -2 & 0 \\ 0 & 0 & 0 \end{pmatrix} + \begin{pmatrix} 0 & 0 & +1 \\ 0 & 0 & 0 \\ +1 & 0 & -2 \end{pmatrix} \tag{31}$$

2.3.3. Fitting Conditions for R-Matrices

The transformation of a BE-matrix **B** by the addition of an R-matrix **R** according to $\mathbf{B} + \mathbf{R} = \mathbf{E}$ corresponds to a chemical reaction only, if we have for all entries:

$$e_{ij} = b_{ij} + r_{ij} \geq 0 \tag{32}$$

since, by definition, a BE-matrix cannot contain any negative entries. Thus the negative entries of an R-matrix must be chosen to satisfy

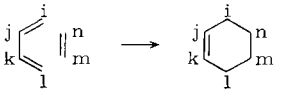
$$|r_{ij}| \leq b_{ij} \quad \text{for} \quad r_{ij} < 0 \tag{33}$$

Further, the entries e_{ij} of the resulting matrix **E** must have values which agree with the acceptable valence chemical schemes of the respective chemical elements.

With a given BE-matrix **B**, one can thus use its positive entries b_{ij} to determine the negative entries r_{ij} of the *mathematically fitting* R-matrices. The positive entries are then chosen to yield R-matrices with $\sum_{i,j} r_{ij} = 0$. Among these, one selects those R-matrices which are acceptable with respect to the valence chemical boundary conditions for **E**. The transformation properties of the BE-matrices, and the known valence chemical properties of the chemical elements can thus be used to predict all the conceivable reactions and their products for a given *EM*. The action of all fitting R-matrices on a single BE-matrix leads to the BE-matrices of the whole family of isomeric ensembles of molecules (*FIEM*).

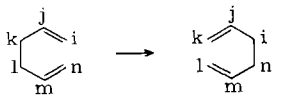
On investigating the conceivable reactions of HCN through the transformation properties of the BE-matrix **B**(HCN), one finds, *e. g.*, a fitting R-matrix with $r_{12} = r_{21} = -1$ and $r_{33} = -2$. Taking into account the structure of the R-matrices, as defined above, and the valence chemical properties of the elements H, C, and N, one finds that $r_{13} = r_{31} = +1$ and $r_{22} = +2$ are suitable as the complementary positive entries. The result is the R-matrix of eq. (20).

In general, there may be several BE-matrices having the required mathematical and valence chemical properties to fit a given R-matrix. Therefore an R-matrix represents a whole category of chemical reactions which have in common the "electron redistribution pattern" as given by the R-matrix and some features of the participating bond systems.



(34)

The reaction scheme (34) describes a Diels-Alder diene synthesis, while scheme (35) describes a Cope rearrangement.



(35)

The addition of an R-matrix of the form

$$\mathbf{R} = \begin{array}{c} \begin{matrix} i & j & k & l & m & n \end{matrix} \\ \begin{bmatrix} . & -1 & . & . & . & +1 \\ -1 & . & +1 & . & . & . \\ . & +1 & . & -1 & . & . \\ . & . & -1 & . & +1 & . \\ . & . & . & +1 & . & -1 \\ +1 & . & . & . & -1 & . \end{bmatrix} \end{array} \begin{matrix} i \\ j \\ k \\ l \\ m \\ n \end{matrix} \qquad (36)$$

to a BE-matrix corresponds to a Diels-Alder synthesis, or a Cope rearrangement, depending on the chemical constitution which this BE-matrix represents [cf. reactions (34) and (35)].

Any two R-matrices **R** and **R'** belong to the same R-category and represent similar reactions if there exists an R-matrix **R''** which can be transformed into **R** by row/column permutations, and which is convertible into **R'** by removal, or addition of rows and columns of zeros. Any two chemical reactions belong to the same R-category if they are represented by BE-matrix transformations of the same R-category.

In those reactions that are important for organic syntheses, generally a redistribution of electrons takes place in which up to six atoms participate and through which up to three covalent bonds are broken or made. The formal charge may increase by one unit at one of the atoms while decreasing by one unit at another atom, through participation of free valence electrons. Such reactions correspond to R-matrices with up to three pairs of negative and positive off-diagonal entries $r_{ij}=r_{ji}=-1$ and $r_{kl}=r_{lk}=+1$, respectively. The non-zero diagonal entries $r_{ii}=\pm 2$ are chosen to make all row/column sums of the R-matrix zero, except one pair of rows/columns with $r_i=\sum_j r_{ij}=\pm 1$.

2.4. Chemical Metric

An $n\times n$ BE-matrix **B** can also be represented as a vector **b** with n^2 components

$$\mathbf{b}=(b_{11},\ldots,b_{1n};\ b_{21},\ldots;\ \ldots b_{n1},\ldots,b_{nn}) \qquad (37)$$

This results in an imbedding of the BE-matrices **B** of an *FIEM* into $\mathbb{R}^{n^2}$, *i.e.* an n^2-dimensional metric space over the field of real numbers. The entries b_{ij} of **B** can also be interpreted as the cartesian coordinates of a point P(**B**) in $\mathbb{R}^{n^2}$, or as the components of a vector in $\mathbb{R}^{n^2}$. We call P(**B**) the BE-*point* of the BE-matrix **B**.

Since the BE-matrices are symmetric, any BE-matrix **B** can further be associated with a BE-point b in $\mathbb{R}^{n(n+1)/2}$, a space with fewer dimensions, by writing the upper triangle of **B** as a vector. In order to account for the constancy of the overall number of valence electrons, the lower triangle must be added to the upper one:

$$\mathbf{b}=(b_{11},2b_{12},\ldots,2b_{1n},b_{22},\ldots,2b_{n-1n},b_{nn}) \qquad (37a)$$

Accordingly, all resonance structures of the diatomic hydrogen fluoride are already representable in three dimensional space $\mathbb{R}^3$ (Fig. 1).

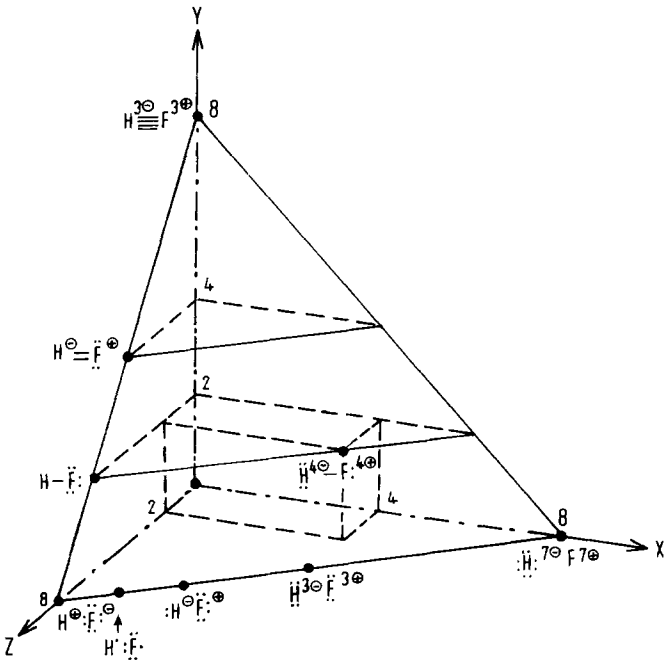


Fig. 1. The resonance structures of hydrogen fluoride lie on a plane which intersects the coordinate axes at 8 (= the number of valence electrons).

Similarly an R-matrix **R** corresponds to a vector **r** in $\mathbb{R}^{n^2}$. A chemical reaction as given by $\mathbf{B}+\mathbf{R}=\mathbf{E}$, is represented by the vector **r** from P(**B**) to P(**E**). The sum

$$D(\mathbf{B},\mathbf{E})=\sum_{i,j}|b_{ij}-e_{ij}|=\sum_{i,j}|r_{ij}| \qquad (38)$$

over the absolute values of the entries of **R** is twice the number of valence electrons which are redistributed during the reaction, since these are taken into account by the negative, as well as the positive entries of **R**.

We call D(**B**, **E**) the *chemical distance*[3] between **B** and **E**, and also between *EM*(**B**) and *EM*(**E**). By D(**B**, **E**) a metric is defined in the space $\mathbb{R}^{n^2}$ which is equivalent to the euclidean metric. The chemical distance is thus a genuine distance function for the BE-matrices of an *FIEM*. The origin of the coordinate system in $\mathbb{R}^{n^2}$ corresponds to the $n\times n$ zero matrix, **0**. The sum over the entries $S=\sum_{i,j} b_{ij}$ is the number of valence electrons, and has the same value for all BE-matrices of an *FIEM*. Therefore an *FIEM* can be mapped into a lattice of points with integral positive coordinates, on a surface with a "radius" S = D(**B**, **0**). Note that the chemical distance D(**B**, **E**) refers directly to the representation space $\mathbb{R}^{n^2}$.

3. Algorithms and Computer Programs Based on BE- and R-Matrices

A BE-matrix contains the complete constitutional information about a molecular system, including the placement of the free valence electrons. An R-matrix represents the "electron redistribution pattern" underlying a chemical reaction.

Documentation of structures and reactions: The BE-matrices are most suitable for the documentation of molecular structures and substructures (see Section 3.1.1).

A hierarchic order and documentation of chemical reactions is for the first time feasible, through the R-matrices which describe the reactions directly, in contrast to the customary methods by which the reactions are described in terms of the reactants only (see Section 3.1.2).

The transformation of BE-matrices by the addition of R-matrices leads to novel deductive methods for the solution of chemical problems with computers. One needs a universal model of the logical structure of chemistry, as described here, for the deductive approach by which the solutions of the individual problems are derived from general principles. Our model affords the following general ways to treat the dynamic aspect of chemistry:

One BE-matrix is given: It is possible to start from a given ensemble of molecules (*EM*) with the BE-matrix **B**, *EM*(**B**), and to generate the R-matrices which fit **B** mathematically within the valence chemical boundary conditions. This is one basis for programming the design of syntheses and the prediction of products which may be obtained from given starting materials (see Section 3.2).

Two BE-matrices are given: With two given BE-matrices, **B** and **E**, belonging to the same family of isomeric ensembles of molecules (*FIEM*), the expansion of the R-matrix $\mathbf{R}=\mathbf{E}-\mathbf{B}$ into its components $\mathbf{R}_1, \mathbf{R}_2, \ldots, \mathbf{R}_r$ according to $\mathbf{R}=\mathbf{R}_1+\mathbf{R}_2+\cdots\mathbf{R}_r$ yields information on the chemical pathways which lead from *EM*(**B**) to *EM*(**E**). Computer programs on this basis generate networks of reaction pathways which may consist of conceivable reaction mechanisms, or syntheses (see Section 3.3).

An R-matrix is given: The determination of all pairs (**B**,**E**) of BE-matrices which mathematically fit a given R-matrix, under the valence chemical boundary conditions, enables us to predict chemical reactions in a systematic manner (see Section 3.4).

3.1. Classification and Documentation

3.1.1. Structures and Substructures

In chemical documentation systems molecular structure is only one of many keys of access to further information, such as the contents of publications, and patents, as well as data on the properties of compounds. It is typical for chemical documentation systems that the key information is structured in a characteristic manner.

On the one hand, the structure of a chemical compound is subject to a variety of rules, in particular to valence chemical rules. On the other hand, it always contains substructures (functional groups, ring systems *etc.*), which may also serve as keys of access in their own right. This holds for applications such as

- searching files for molecules with a given substructure (pure retrieval)
- correlation of substructures with molecular properties (substructure/activity correlation)
- analogy search based on incomplete structural information (search for "similar" structures)
- recognition of substructures which target molecules of syntheses have in common with starting compounds
- documentation and analysis of spectroscopic data.

A documentation system capable of doing this must have the capacity for complete storage and retrieval of structural information. It must, however, also perform special manipulations, such as fragmentation, valence chemical plausibility checks, and afford access to substructures.

The representation of constitutional properties on the basis of a mathematical model is a prerequisite for the performance of such operations (see Section 2).

The treatment of chemical reactions is thus possible within the framework of a unified theory. It is described in more detail in the following sections. Firstly, the manipulation of chemical data on the basis of BE-matrices, which are defined as part of the mathematical model, is discussed.

Matrix representations of chemical constitution, *e.g.* the adjacency and connectivity matrices[14, 15], have been used in various documentation systems. Such matrices afford the basic services of a documentation system, *i.e.* storage and retrieval of data, but generally speaking they are not directly usable for valence chemical checks and the manipulation of data in the sense of chemical conversions.

The entries in any row of a BE-matrix must conform to at least one of the valence chemically acceptable electron distribution schemes of the respective atomic core. The permissible valence schemes for any given atomic core can be listed, and they determine the range of chemistry which is admitted for a particular purpose for the chemical element under consideration. The valence schemes afford effective plausibility checks on input data, or on recoding of foreign data. They are particularly useful when older data banks that represent a considerable investment are supplemented or tested for consistency. In such collections of data some of the structural information has been suppressed by the form of coding used. The information that is lacking must sometimes be reconstructed. Often the information on free electrons and formal electrical charges is missing. A comparison with the allowable valence schemes yields one or more proposals for the required supplementary data. These are further processed according to additional information, or, in exceptional cases, subjected to a manual selection procedure. In any case, this balance of the valence electrons ensures that only acceptable and complete constitutional information enters the collection of data. For documentation systems such perfect representation by BE-matrices has the unique advantage that the types of problems which may be of interest in the future do not have to be known when the system is implemented.

Hitherto, documentation systems usually have been so designed as to cope with the solution of particular problems. This approach frequently leads to some constitutional information being neglected. This is especially true for the widely used fragment codes.

On the basis of such a complete representation of chemical constitution, an interactive system for the filing and retrieval of chemical structures and substructures has been implemented.

The methods for plausibility checks, of fragmentation, and of substructure access have been realized in a FORTRAN program study. A more advanced system is being implemented

in PL/1. It offers higher performance in substructure retrieval and in substructure/activity correlation.

In order to cope with the conflicting requirements of semantic assistance (for example in synthesis design: recognition of functional groups and common substructures), minimal memory space, and minimal access time, the retrieval of substructures has been segmented into a time consuming fragmentation phase, and a fast retrieval phase.

By fragmentation (phase one) we mean the decomposition of molecular structures into partial structures (fragments) which are generated by breaking one bond, or lowering a bond order. Each particle which is thus obtained is associated with a reference to its immediate precursor (*father* reference), and *vice versa*: The molecule is tagged with references to the partial structures directly generated from it (*son* reference). This process of direct fragmentation is recursively applied to the partial structures, until single atoms are encountered as fragments. Thus one obtains a network in which the molecules and their fragments are the nodes, and the references are the oriented lines.

When the next molecule is fragmented, usually only rather large new substructures are found, while the smaller substructures are recognized as already being documented. They do not need further dissection.

Thus, the production of fragments leads to saturation of the substructure file (Fig. 2).

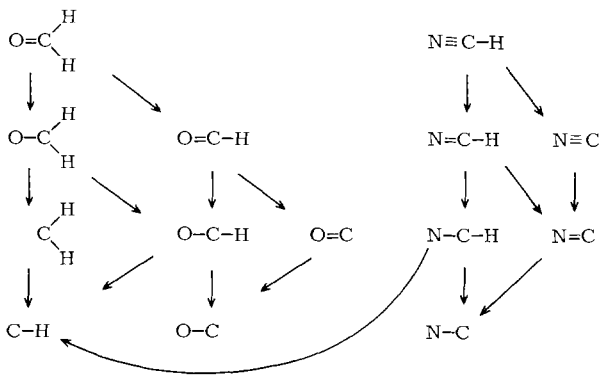


Fig. 2. Fragmentation of formaldehyde and hydrogen cyanide with son references.

A typical request for retrieval of a substructure is treated in the retrieval phase (phase two) as follows: The fragment to be retrieved (*e.g.* C—H) is brought into canonical form. Its memory address is computed from its canonical representation. This enables one to enter the network of references and follow the father references up to the molecule level. Because of the design of the reference network from phase one, the molecules arrived at contain the query fragment as a partial structure.

In the retrieval phase of an analysis of substructure/activity relations one is interested in the substructures common to those molecules which have a certain activity (*e.g.* antioxidant, fungicidal, bacteriostatic). Here, the program tracks the son references which originate from molecules with the considered activity, until, *via* many generations of sons, substructures are found which occur, with statistical significance, more often in the active molecules than in the other molecules[18].

3.1.2. Reactions

The systematics and nomenclature of chemical reactions are far less elaborate than those of chemical structures. It is symptomatic that the customary description of chemical reactions is still largely based on trivial names.

Hitherto, chemical reactions have been represented by their educts and products, wholly in the sense of a statically oriented approach based on structures. Traditional documentation systems for chemical reactions have been designed on this basis.

In terms of the mathematical model of chemistry, this means that two points in the vector space of an *FIEM* are used to describe a reaction. A description by the vector between these points was lacking.

In the description of a chemical reaction we begin with the underlying scheme of electron redistribution. This is represented by an R-matrix. Knowing that a chemical reaction can be represented by matrices of a certain kind (the R-matrices), and that this representation is in itself structured, affords the required generalization. The steps of the generalization are (for chemical reactions): irreducible R-matrices (nucleus of the reaction; see below) ⊃ nucleus of the reaction with associated atomic vector ⊃ BE-matrix of the nucleus ⊃ atomic vectors and BE-matrices of the spheres adjacent to the nucleus.

A given electron redistribution pattern may describe many different reactions which belong to the same R-category (see Section 2.3.2). A collection of chemical reactions grouped in this manner has been published recently (*cf.* Fig. 3)[19].

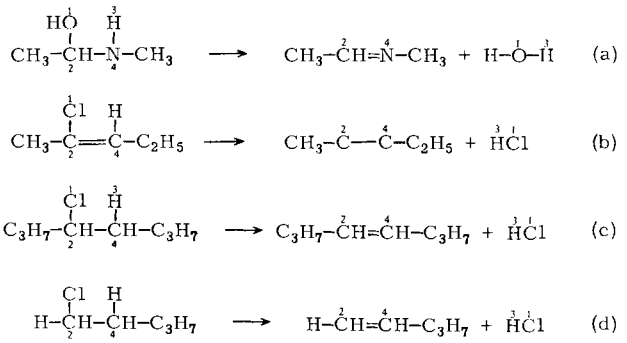


Fig. 3. Four reactions which belong to the same R-category. (a) differs from (b), (c), and (d) by different entries in the atomic vector at the nucleus of the reaction: O, C, H, N in (a), and Cl, C, H, C in (b), (c), (d) (same "RA-type"); (b) differs from (c) and (d) by differences in the BE-matrix at the nucleus of the reaction: $b_{24} = 2$ in (b), $b_{24} = 1$ in (c) and (d) (same "RB-type"); (c) and (d) differ only with respect to the vicinity of the nucleus. The R-matrix of this R-category is

$$\mathbf{R} = \begin{pmatrix} 0 & -1 & 1 & 0 \\ -1 & 0 & 0 & 1 \\ 1 & 0 & 0 & -1 \\ 0 & 1 & -1 & 0 \end{pmatrix}$$

It follows from the mathematical model that only a certain number of irreducible R-matrices can exist within given limits. Each one of these irreducible R-matrices defines an R-category, and any chemical reaction belongs to one of these R-categories. Some limited number of valence schemes may be associated with an R-category. These determine atomic vectors that fit an R-matrix. Here, only those atoms are taken into account which belong to the nucleus of the reaction, *i.e.* the atoms which do not correspond to any one of the all-zero rows/columns of the R-matrix. The distinct atomic vectors partition

an R-category into reaction types which we call the RA-types. These are, in turn, partitioned according to differences in bonding between the atoms of the reacting nucleus, *i.e.* by the differences in the entries in that block of the BE-matrix which belongs to (the atomic vector of) the reacting nucleus. Further specific classifications may be obtained by considering some additional neighboring spheres of the reacting nucleus. With this formalism, reactions may be coded in a general form. This opens new possibilities in the retrieval of reactions having unknown features.

3.2. Prediction of Reaction Products, and the Design of Syntheses

Designing syntheses usually involves analysis of the target molecule of the synthesis for those structural moieties which can be formed through known reactions, and one uses the retroreactions of these for the construction of the synthetic precursors. The realization of such an approach in a computer program would require a data bank of individual chemical reactions. Progressive improvement of such synthesis design programs would necessitate continuous maintenance, updating and extension of the reaction library—and yet a program of this kind could only reproduce known reactions.

Our mathematical model affords an entirely different approach in the design of syntheses[8, 20–22]. The application of R-matrices to BE-matrices of given molecules and *EM*'s leads to the BE-matrices of the reaction products into which they are convertible. The R-matrices may, however, not only be used to describe the conversion of some reactants into products, but they may also be interpreted as retroreactions which lead from the products to the educts. Beginning with the target molecule of a synthesis, one can thus infer the precursors which lead to that target molecule.

3.2.1. Operations with R-Matrices

The program EROS (Elaboration of Reactions for Organic Syntheses)[20] generates, by the action of R-matrices, from the BE-matrix of an ensemble of molecules (*EM*) the BE-matrices of further *EM*'s Depending on the direction in which the reactions are considered, forward or reverse, —this is a matter of formulation—EROS can be used to predict the products which are formed from given compounds, or it may serve in the design of syntheses.

If an *EM* consists of one molecule only, the program generates the products of rearrangements and fragmentations. Further molecules must be added if other types of reactions are to be included; the choice of the supplementary reactants depends on the problem at hand.

An investigation of the products which may be obtained from a given molecule requires the addition of its potential reaction partners: In a study of the products which may be formed from a chemical (*e.g.* an agricultural chemical) in the environment, these are H_2O, O_2, O_3, CO_2 *etc.* When searching for the potential uses of an industrial by-product some readily available chemical can be added as the supplement.

In the design of syntheses, the molecules by which the target molecule is to be augmented cannot be easily determined. A detailed study of the synthetically relevant reactions has shown that here mostly small molecules form the coproducts. One encounters again and again some low-energy species, like H_2O, HCl, NaCl, NH_3, CO_2, N_2. In a retrosynthetic approach, molecules of this kind are combined with the target into an *EM*. Thus those synthetic reactions are accounted for in which these molecules are the coproducts.

Since the mathematical model affords the elaboration of all conceivable reactions, the problem now is their meaningful evaluation from the standpoint of the given problem. A substantial part of the evaluation can be accomplished by the program itself. Physicochemical and heuristic criteria are used for this.

Multiple bonds and bonds involving heteroatoms, as well as their neighboring bonds are broken with preference. Parameters for 1,2- and 1,3-interactions are obtained from thermochemical data, and are used to estimate the enthalpy of the reactions[23].

Several models for estimating the activation parameters of reactions are being tested. The effect of steric influences of a reaction can be determined by looking at the bond lists of the participating atoms. Certain unfavorable combinations of atoms may be recognized through electronegativity considerations[24].

Since syntheses generally involve many steps, the problem of synthesis design cannot be solved by merely generating—from a target *EM* through R-matrices—the precursors of the first level, and subsequently evaluating these. Instead, the precursors of the first level are reintroduced into the program and used to generate precursors of a further level. Repetition of this procedure leads to a "synthesis tree" whose root is the target, and whose nodes are reactions, or molecules, respectively (see Fig. 4).

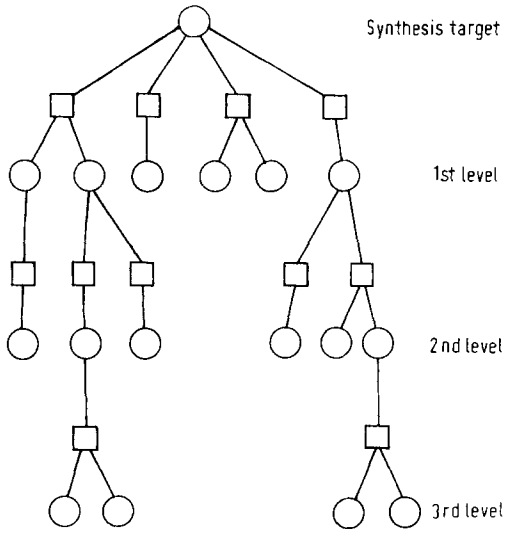


Fig. 4. "Synthesis tree"; ○ molecules; □ reactions.

A reaction may involve more than one precursor. The development of a synthetic pathway is complete when all required precursors can be identified as available starting materials.

In the evaluation of syntheses, it does not suffice to look at the individual steps, *i.e.* the individual synthetic reactions. Each branch of the synthesis tree must be considered as a whole, because success in a synthesis depends on the quality of all steps and the availability of all required compounds.

The program EROS has been used to study the formation of products from given *EM*'s, as well as the design of

syntheses, using examples from the fields of organic synthesis, industrial chemistry, and biochemistry. With such examples the flexibility and prediction capability of EROS could be demonstrated.

The synthetic pathway A encompasses the last two steps of the biosynthesis. Pathway B corresponds to the first two steps of Traube's synthesis of uric acid; its further development involving dicyanamide and glycine ester is novel. It has not

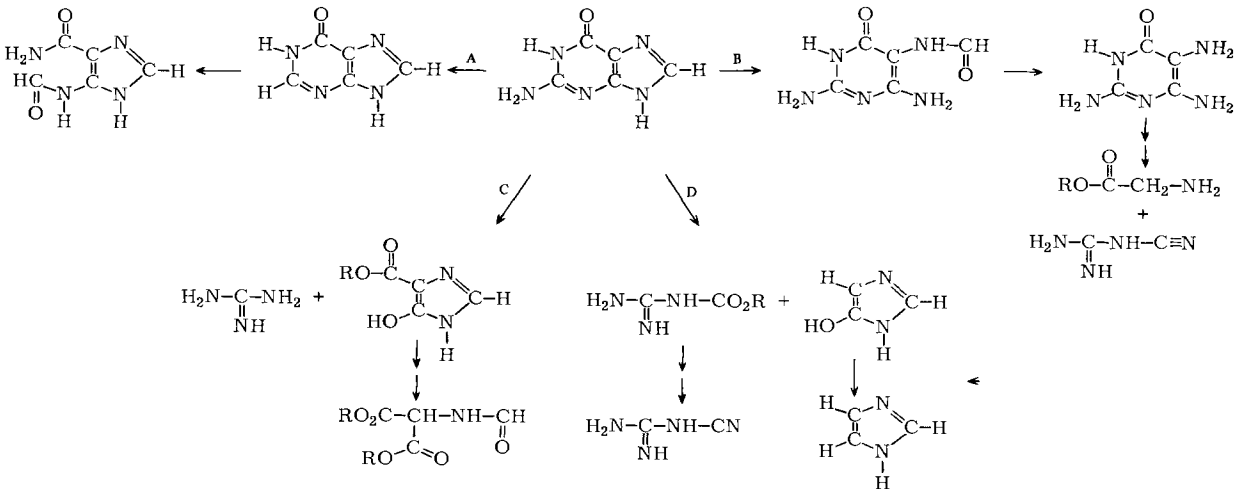


Fig. 5. Selected synthetic pathways which were generated by the program EROS for guanine.

A study of the syntheses of guanine may serve as an illustration. Figure 5 contains a selection of the proposed syntheses.

been checked in the literature whether there is precedence for pathways C and D. In order to influence the direction of

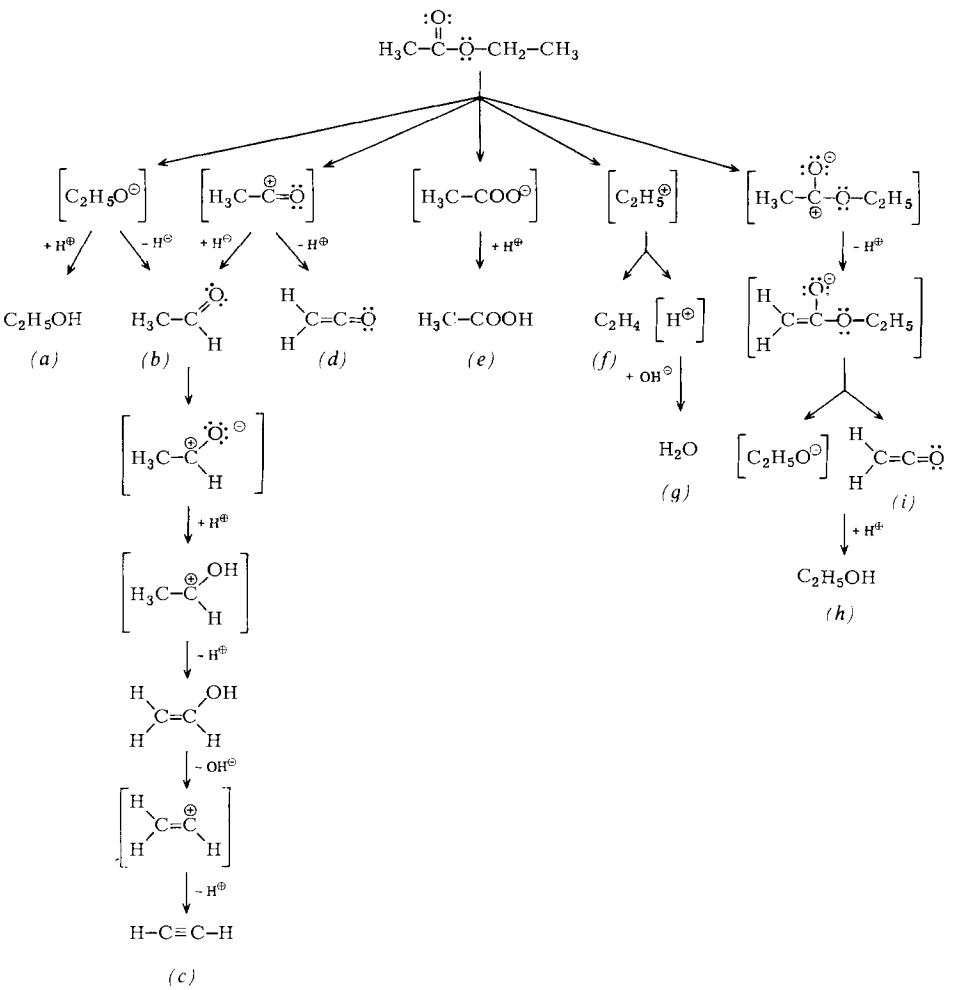


Fig. 6. Synthetic pathways from ethyl acetate which were generated with the basis elements of R-matrices by program system ASSOR. (a)+(e): esterification of acetic acid with ethanol; (b): dimerization of acetaldehyde (*Tischtschenko*); (c): addition of water to acetylene to form acetaldehyde; (a)+(d) or (h)+(i): addition of ethanol to ketene (*Wacker*); (f)+(g): addition of water to ethylene to form ethanol.

the syntheses favorably, it may be necessary to activate some of the reactive sites, and to protect others during certain synthetic steps.

3.2.2. Operations with Basis Elements of R-Matrices

Presently we are developing a program ASSOR[21] which does not use R-matrices as linear combinations of basis elements (see Section 2.3.1), but operates with the basis elements themselves in the simulation of chemical reactions. These basis elements form the simplest *complete* set of R-matrices by which *all* conceivable reactions can be represented. Since a reaction is simulated by the basis elements in terms of its elementary mechanistic steps, it is possible to decide through plausibility checks after any one of these steps whether or not the pathway should be pursued any further. This yields a network of reactions which consists of mechanistic steps. Such a network is free of mechanistically unrealizable branches. Besides this selection, which is associated with the generation of the pathways, further evaluation is still necessary in order to avoid too many proposals.

The result of a trial run with ethyl acetate as the target molecule and water as the coproduct is shown in Figure 6.

3.3. Networks of Reaction Mechanisms and Synthetic Pathways

Reaction mechanisms and synthetic pathways are equally well represented by the mathematical model of constitutional chemistry described above. In the investigation of a reaction mechanism the equation

$$\mathbf{B}+\mathbf{R}=\mathbf{E} \tag{14}$$

describes the overall reaction of the educts to the products. In the treatment of syntheses, eq. (14) refers to the union of all starting materials (**B**), and all products formed (**E**). Thus, in one case **R** indicates the bonds to be broken and made by a single reaction, whereas in the other case it represents all the bonds to be broken and made by the reactions of a whole pathway. Therefore, reaction mechanisms and synthetic pathways can mathematically be treated in rather a similar way. Only when the overall reaction matrix **R** is expanded into the matrices of individual steps, are a reaction mechanism or a synthesis treated differently (see below).

3.3.1. Shortest Reaction Pathways

We know by experience that chemical reactions tend to proceed with the redistribution of a minimal number of valence electrons. We therefore postulate: When a reaction is given in terms of its educts and products, the associated redistribution of electrons corresponds to an overall R-matrix which is close to the minimal chemical distance (D)[25].

If the atoms in the educts and products, *EM* (**B**) and *EM* (**E**) of a chemical reaction are indexed in an arbitrary manner, the mutual assigment of the atoms by their respective indices may falsely indicate a more complex reorganization of bonds and electrons (b) than is actually taking place (a) (Fig. 7).

The aim is to isolate the actual redistribution of bonds and electrons from such formal processes: in *EM* (**E**) the indexing of the atoms of the same chemical element must be permuted in such a manner that the reaction is formally achieved with

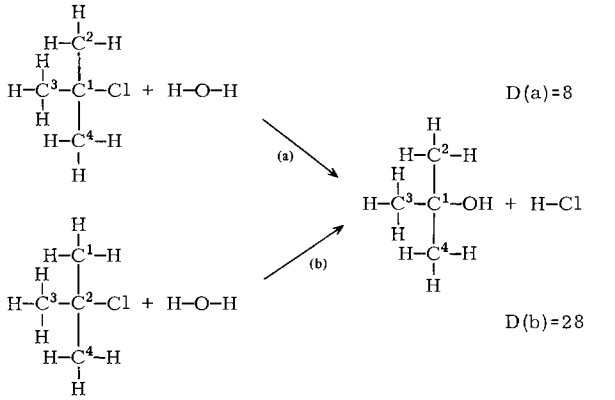


Fig. 7. To illustrate the postulate of minimal redistribution of electrons.

redistribution of a minimal number of electrons. This is equivalent to minimizing the chemical distance (see Section 2.4).

Mathematically, this means a permutation matrix **P** must be found for which the function

$$F(\mathbf{P})=D(\mathbf{B},\mathbf{PEP}^{T}) \tag{39}$$

has a minimal value.

Ansatz: Even with the use of modern computers and problems of moderate size performing all permutations is too time consuming. In the case of educts and products with 10 C-atoms more than three million permutations would have to be carried out.

We are therefore presently studying the applicability of some methods of integer optimization, namely quadratic assignment algorithms[26, 27], to this problem (see Fig. 8). In order to avoid excessive computation time, these methods need to start with a permutation **P**′ for which F(**P**′) is already close to the minimum. We have developed heuristic methods for finding such an approximate solution **P**′. These are based on a comparison of the vicinities $U(A_i,A_j)$ of the atoms A_i in *EM*(**B**) with A_j in *EM*(**E**). Here the attempt

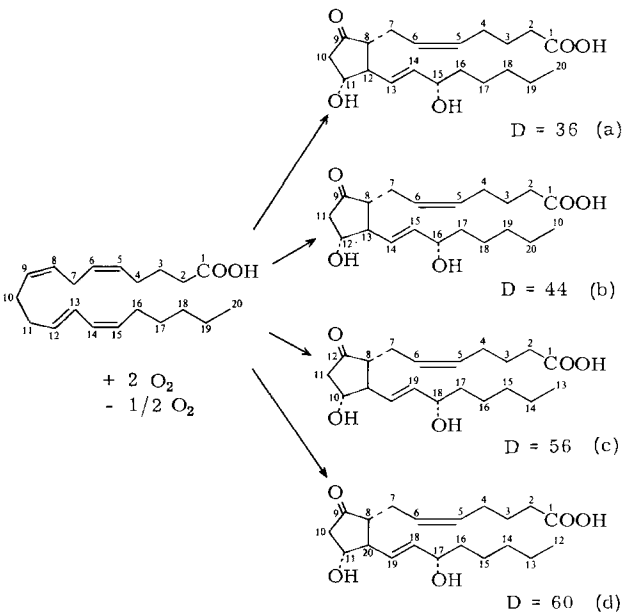


Fig. 8. The formation of prostaglandin E_2 from 5,8,12,14-eicosatetraenic acid and oxygen involving reactions which differ in chemical distance; (a) shows the correlation of the atoms at minimal chemical distance; (b) to (d) are examples for the many correlations near minimal chemical distance.

is made to map the atoms of *EM* (**B**) onto the atoms of *EM* (**E**), such that the vicinities "match" as well as possible.

Once the minimal chemical distance has been determined, we obtain a minimal reaction matrix $\mathbf{R}_{Min}$ by the formula

$$\mathbf{R}_{Min} = \mathbf{PEP}^T - \mathbf{B} \tag{40}$$

A suitable expansion of $\mathbf{R}_{Min}$ into components $\mathbf{R}^i$ with

$$\mathbf{R}_{Min} = \sum_i \mathbf{R}^i \tag{41}$$

leads to a description of the shortest reaction pathways.

3.3.2. Construction of Networks

Let *EM*(**B**) and *EM*(**E**) be some given initial and final *EM*. By minimization of the chemical distance D(**B**, **E**) (see above) we obtain a minimal reaction matrix $\mathbf{R}_{Min}$ which satisfies the equation

$$\mathbf{B} + \mathbf{R}_{Min} = \mathbf{E} \tag{42}$$

In order to find the reaction mechanisms or synthetic pathways by which *EM*(**B**) is convertible into *EM*(**E**), the overall reaction matrix is expanded into sums S^k of components:

$$S^k: \mathbf{R}_{Min} = \sum_i {}^k\mathbf{R}^i \quad (k = 1, \ldots, m) \tag{43}$$

This corresponds to an expansion of an overall reaction into partial reactions. In the elucidation of reaction mechanisms rather small partial reactions may be chosen (*e.g.* a basis vector, or a sum of a few basis vectors), because as many as possible intermediates should be considered, the unstable ones, too. When synthetic pathways are determined the ${}^k\mathbf{R}^i$ are chosen to yield intermediates only. For both types of problems those R-matrix components are also admissible whose entries cancel in the overall matrix, *i.e.* along some reaction pathway certain bonds are broken and remade, and appear as unchanged by the overall reaction.

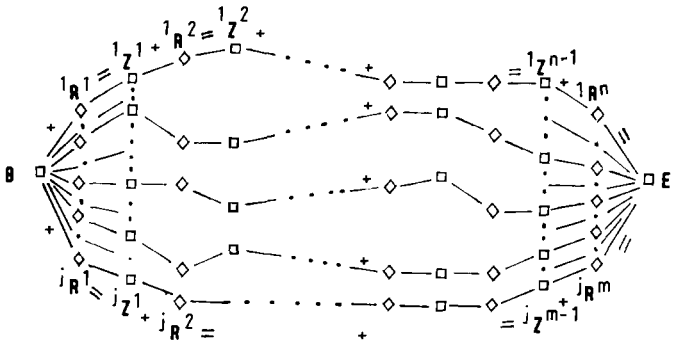


Fig. 9. Construction of a network of synthetic pathways between the educts and products **B** and **E**.

A network of intermediates ${}^k\mathbf{Z}^i$ is constructed from such components of R-matrices (Fig. 9). The components of the reaction matrices must, however, be chosen to yield intermediates that lie close to a shortest pathway within a network of reaction or synthetic pathways. This is so, because, on the one hand, the actual reactions proceed presumably close to a minimal pathway, and on the other hand, synthetic pathways must be rejected as wasteful if they are too remote from a minimal pathway.

3.4. Prediction of Chemical Reactions

In the preceding section we discussed the construction of R-matrices which are acceptable when pairs of BE-matrices are given. Now the opposite approach is described, namely the generation of all reactions which "fit chemically" a given electron redistribution scheme. This means the search for pairs of BE-matrices which "fit" a given R-matrix, The creative aspect of this approach lies in the fact that it leads to a complete set which also contains the reactions without precedence.

To generate *all combinatorially* possible reactions is neither chemically meaningful, nor feasible with present computer technology. Instead, one must restrict the solution space to some domain through suitable boundary conditions. Within

Given reaction scheme

:A + B– C → A—B + :C

Equivalent R-matrix:

$$\mathbf{R} = \begin{pmatrix} -2 & 1 & 0 \\ 1 & 0 & -1 \\ 0 & -1 & 2 \end{pmatrix} \begin{matrix} \text{A} \\ \text{B} \\ \text{C} \end{matrix}$$

Extract from a list of valence schemes:

No.	Symbol	Valence scheme f, s, d, t	Elements
v1	:Ẍ:	8, 0, 0, 0,	Cl; Br; I;
v2	–Ẍ:	6, 1, 0, 0,	O; Cl;, Br; I;
v3	–Ẍ—	4, 2, 0, 0,	O;
v4	—X—	0, 4, 0, 0,	C;
v5	—X	0, 1, 0, 0,	H;

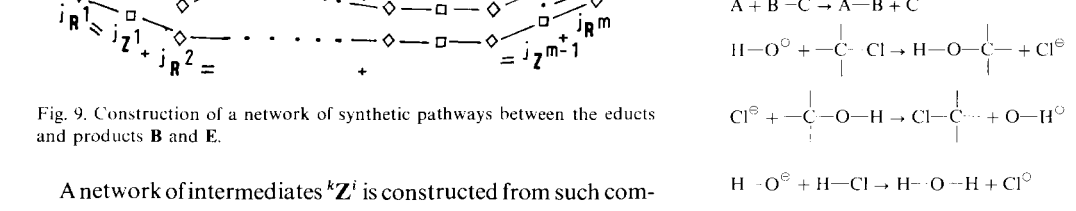
f = number of free electrons; s, d, t = number of single, double, triple bonds, respectively

Possible valence scheme pairs and element assignment:

A	v1→v2	Cl; Br; I;	O; Cl; Br; I;
	v2→v3	O;	
B	v2→v2	O; Cl; Br; I;	O; Cl; Br; I; C; H;
	v3→v3	O;	
	v4→v4	C;	
	v5→v5	H;	
C	v2→v1	Cl; Br; I;	O; Cl; Br; I;
	v3→v2	O;	

Worked out examples:

A + B –C → A—B + C



etc.

Fig. 10. Simplified example for the representation of reactions belonging to the same R-category. The atomic vectors which are compatible with a list of valence schemes (here appreciably abbreviated) describe the whole set of the conceivable reactions, regardless whether or not they are realizable.

this domain exhaustive treatment of the problem is feasible, and desirable. For the R-matrices this can be achieved through suitable restrictions. The BE-matrices can then be generated according to the valence schemes. Such valence schemes are mappings of the individual rows in the BE-matrices. Suitable BE-matrices are constructed from these row by row. The addition of a corresponding row of an R-matrix yields a new valence scheme. Each chemical element is assigned to one or several valence schemes. Each row of the initial, and of the final BE-matrix results in a *pair* of valence schemes. If such a pair is contained in the list of valence schemes of some chemical element, this element may occupy the site in the atomic vector which corresponds to the row in question. As a result one obtains for each site of the atomic vector a list of all allowable element assignments (see Fig. 10). These combinations of element assignments are further restricted by additional valence chemical, physicochemical and heuristic rules.

4. Perspectives

In chemistry, progress is achieved through the results of experiments which have been initiated by heuristically valuable hypotheses. The need for a universal theory with predictive power has not yet been satisfied. As a theoretical foundation of chemistry, quantum theory, too, has not attained the impact which had been expected because of the comprehensive nature of its approach. Up to now, inductive inference and reasoning by analogy have dominated in the interpretation and planning of chemical experiments. When proceeding in this way progress depends very much on chance. In order to open up new possibilities in a systematic manner, it is necessary to supplement the known approaches by deductive procedures. For this the prerequisite is a theory which permits one to take into account all of the conceivable solutions for a wide variety of problems[28].

The theory of *a family of isomeric ensembles of molecules*, as presented in this article, satisfies these requirements. In the mathematical formulation of this theory BE-matrices are used to represent the chemical constitution. The electron redistribution schemes of the chemical reactions are expressed by R-matrices. A chemical reaction is then described by the addition of an R-matrix to a given BE-matrix, according to the master equation

$$\mathbf{B}+\mathbf{R}=\mathbf{E} \qquad (14)$$

of the model.

In this equation **B** stands for the ensemble of molecules at the beginning of the reaction, and **E** for the ensemble on termination of the reaction.

It is essential for the applications of the master equation that it can be solved when one of the matrices is known. This is possible, using our theory. In order to select from the set of all conceivable solutions of the master equation those which are likely to be relevant to the issue, without discarding valuable information, one needs selection rules. These rules must be based on chemical experience. Thus empirical data are used to *restrict, and not to generate*, the solutions of the problems[28].

For the deductive chemical computer programs chemical literature is not only a source of general selection rules; in the form of suitably organized files on chemical compounds and reactions, chemical literature can also be used to determine whether a computer generated solution of a problem is already known. For future developments this approach is particularly promising, because it comprises access to the literature, and it enjoys the advantages of the mathematical model which enables one to take into account all of the conceivable possibilities. As a computer operation, matrix addition is much more effective than the manipulation of data based on published reactions.

The programs which have hitherto been implemented, and the results obtained with them, have demonstrated that computer programs for the deductive solution of chemical problems in combination with suitably organized documentation, will relieve the research chemist in his routine information and planning work, and will call to his attention possibilities which he might otherwise have overlooked. This will never replace the chemist; with the computer and its new applications, however, he has a tool which will help him to perform his tasks more effectively.

We acknowledge gratefully the financial support of our work by Stiftung Volkswagenwerk e.V. (development and testing of mathematical models, in particular in stereochemistry), the Deutsche Forschungsgemeinschaft (synthesis design), the European Communities (Contract Nos. 115-74-10-ENV-D and 310-77-5-ENV-D, documentation and ecology) and the Bundesministerium für Forschung und Technologie, project administrator: Gesellschaft für Information und Dokumentation (classification of reactions). We wish to thank Profs. J. Dugundji, Los Angeles, and R. E. Burkard, Köln, for helpful discussions and stimulating suggestions. The Institut für Plasmaphysik (Garching), and the Leibniz-Rechenzentrum kindly provided us with computer time.

Received: December 27, 1977 [A 256 IE]
Supplemented: November 9, 1978
German version: Angew. Chem. *91*, 99 (1979)

[1] *J. Lederberg, G. L. Sutherland, B. G. Buchanan, E. A. Feigenbaum, A. V. Robertson, A. M. Duffield, C. Djerassi*, J. Am. Chem. Soc. *91*, 2973 (1969).

[2] a) *I. Ugi, G. Kaufhold* (unpublished 1966—67), described in [5] and *I. Ugi*, Rec. Chem. Progr. *30*, 289 (1969); b) *E. J. Corey, W. T. Wipke*, Science *166*, 178 (1969); c) *E. J. Corey, W. T. Wipke, R. D. Cramer, W. J. Howe*, J. Am. Chem. Soc. *94*, 421, 431 (1972); d) *H. Gelernter, N. S. Sridharan, A. J. Hart, S. C. Yen, F. W. Fowler, H. J. Shue*, Top. Curr. Chem. *41*, 113 (1973); e) *H. Gelernter et al.*, Science *197*, 1041 (1977).

[3] a) *J. Dugundji, I. Ugi*, Top. Curr. Chem. *39*, 19 (1973); b) *I. Ugi, J. Bauer, J. Brandt, J. Friedrich, J. Gasteiger, C. Jochum, W. Schubert, J. Dugundji*, Informal Commun. Math. Chem., in press.

[4] *J. Blair, J. Gasteiger, C. Gillespie, P. D. Gillespie, I. Ugi*, Tetrahedron *30*, 1845 (1974).

[5] *I. Ugi*, Intra-Sci. Chem. Rep. *5*, 229 (1971).

[6] *I. Ugi, P. D. Gillespie*, Angew. Chem. *83*, 982, 990 (1971); Angew. Chem. Int. Ed. Engl. *10*, 914, 915 (1971).

[7] *I. Ugi, P. Gillespie, C. Gillespie*, Ann. N. Y. Acad. Sci. *34*, 416 (1972).

[8] *J. Blair, J. Gasteiger, C. Gillespie, P. Gillespie, I. Ugi* in *W. T. Wipke, S. Heller, R. Feldmann, E. Hyde*: Computer Representation and Manipulation of Chemical Information. Wiley, New York 1974, p. 129.

[9] *I. Ugi*, IBM-Nachr. *24*, 180 (1974).

[10] *I. Ugi, J. Gasteiger, J. Brandt, J. Brunnert, W. Schubert*, IBM-Nachr. *24*, 185 (1974).

[11] *J. Brandt, J. Friedrich, J. Gasteiger, C. Jochum, W. Schubert, I. Ugi* in *E. V. Ludeña, N. H. Sabelli, A. C. Wahl*: Computers in Chemical Education and Research. Plenum, New York 1977.

[12] *J. Brandt, J. Friedrich, J. Gasteiger, C. Jochum, W. Schubert, I. Ugi*: Computer-Assisted Organic Synthesis. ACS Symposium Ser. 61.

[13] J. Brandt, J. Friedrich, J. Gasteiger, C. Jochum, W. Schubert, P. Lemmen, I. Ugi, Pure Appl. Chem. 50, 1303 (1978).
[14] L. Spialter, J. Chem. Doc. 4, 261, 269 (1964).
[15] E. Meyer, Angew. Chem. 82, 605 (1970); Angew. Chem. Int. Ed. Engl. 9, 583 (1970).
[16] a) Y. Yoneda: Saikin no Kagakukogaku (Progress of Chemical Engineering), Maruzen, Tokio 1970, p. 145ff.; b) Y. Yoneda: Kemoguramu 1—Keisanki Kogyo Kagaku (Chemogram 1—Computer Industrial Chemistry). Band 1. Maruzen, Tokio 1972, p. 309ff.
[17] a) W. Schubert, I. Ugi, J. Am. Chem. Soc. 100, 37 (1978); b) C. Jochum, J. Gasteiger, J. Chem. Inf. Comput. Sci. 17, 113 (1977).
[18] J. Friedrich, I. Ugi, Informal Commun. Math. Chem., in press.
[19] J. C. J. Bart, E. Garagnani, Z. Naturforsch. B31, 1646 (1976); B32, 455, 465, 678 (1977).
[20] a) J. Gasteiger, C. Jochum, Top. Curr. Chem. 74, 93 (1978); b) J. Gasteiger, C. Jochum, M. Marsili, J. Thoma, Informal Commun. Math. Chem., in press.
[21] a) W. Schubert, I. Ugi, Chimia, in press; b) W. Schubert, Informal Commun. Math. Chem., in press.
[22] A. Weise, Z. Chem. 15, 33 (1975).
[23] J. Gasteiger, Comput. Chem. 2, 85 (1978).
[24] J. Gasteiger, M. Marsili, Tetrahedron Lett. 1978, 3184.
[25] C. Jochum, J. Gasteiger, I. Ugi, unpublished.
[26] a) K. H. Stratmann, Diplomarbeit, Universität Köln 1976; b) R. E. Burkard, K. H. Stratmann, Naval Res. Logistics Quart., in press.
[27] R. E. Burkard: Methoden der Ganzzahligen Optimierung. Springer, Wien 1972.
[28] I. Ugi, Giessener Universitätsbl. 11, 68 (1978).

Activation Analysis—Its Present State of Development and Its Importance as an Analytical Tool

By Viliam Krivan[*]

Activation analysis is one of the most important methods available for the determination of traces of elements and of isotopes. One special advantage of activation analysis is its ability to cope with the simultaneous determination of many elements with very high detection sensitivity—for many elements lying below the ppb level. In some cases as little as 10^{-14}—10^{-15} g of an element can be detected. A number of sources of systematic errors common to other analytical procedures, mainly those caused by the blank, are eliminated in activation methods. The disadvantages may be seen as the inconvenience of handling radioactive materials, the dependence on large irradiation facilities, and sometimes the unavoidably long irradiation and cooling periods. On account of its unique capabilities activation analysis finds applications in all fields of endeavor where minute amounts of elements are of significance, from materials research through medicine to archaeology. Further improvements in performance and increases in scope are seen to lie in the development of new radiation sources, activation techniques, measurement systems, and separation procedures.

1. Introduction

A knowledge of the occurrence and content of trace elements in various materials is often absolutely necessary for the success of the actual investigations in fields such as medicine, environmental studies, and life, earth, and materials sciences[1–5]. In many branches of industry trace analysis of elements has already become a routine procedure.

Activation analysis has always played an important role in the determination of trace elements. Following its tempestuous development in the post-war years, the attraction and significance of activation analysis lay primarily in the uniquely high sensitivity which it offered for the detection of many elements. The subsequent introduction of high-resolution Ge(Li) detectors in the sixties opened the way for instrumental multi-element analysis.

In the sixties and seventies, some powerful methods based on atomic spectroscopy and other techniques were developed in addition to activation analysis, and sometimes with comparable sensitivities. It is only since analysts have had access to several high-performance techniques, that they have been able to assess the reliability and accuracy of the individual methods. Comparisons of analytical results obtained by various techniques and in particular of interlaboratory results obtained from collaborative investigations—so-called round-robins—have revealed the real limitations of all these methods[6–8]: the lower the levels of the elements being determined, the greater the deviations of the results obtained by individual laboratories from the mean experimental value, or from the "true" value. At the ppb level and below, deviations of several orders of magnitude are by no means uncommon.

The main problem in element trace analysis is undoubtedly that of the accuracy of the results, *i. e.* the problem of systematic

[*] Prof. Dr. V. Krivan
Sektion Analytik und Höchstreinigung der Universität Ulm
Oberer Eselsberg N-26
D-7900 Ulm (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979
0570-0833/79/0202-0123 $ 02.50/0

errors and their elimination. Other criteria such as detection limits, precision, and cost in terms of equipment and manpower are of course very important, but the decisive factor is the extent to which the sources of systematic error can be identified and then eliminated. False conclusions based on spurious analytical results can have far-reaching consequences. The squandering of substantial financial and manpower resources would not even be the greatest evil: "Unfortunately, too many situations exist in which the price of some analytical errors, no matter how infrequent, is measured in lives, and therefore is unacceptable"—this was how *Hirschfeld* described the situation[9].

It is precisely in connection with these problems that activation analysis has begun to reassert itself, for one of its special advantages lies in the complete absence of a number of sources of error characteristic for other methods. Moreover, there are some trace analytical problems which can only be solved by activation methods, such as the determination of oxygen in the lower ppb range. In spite of these special advantages of activation analysis, its significance should not be overestimated and it should rather be considered as just one of the indispensible tools of modern analytical chemistry.

2. Principle of Activation Analysis

Activation analysis constitutes a method for the determination of elements and isotopes (standard texts, see [10–15]). It is based on the conversion of the stable nuclides of the element to be determined into radioactive nuclides of the same element or of a neighboring element with a difference in atomic number of ± 1 or 2. These reactions are induced by irradiating the sample with neutrons, charged particles, or high-energy photons. The indicator radionuclide produced in such a nuclear reaction decays with a known half-life, which process is accompanied by the emission of characteristic radiation. Indicator radionuclides can be identified by these two properties and, considering the appropriate reaction type, they can be attributed to the presence of particular stable nuclides in the original sample. Quantitative determination is based on the linear relationship between the activity of the indicator radionuclide produced and the amount of the element present in the sample. After irradiation, the activity of the sample is measured either directly (instrumental activation analysis) or after prior radiochemical separation processes (radiochemical activation analysis). The principal steps in an activation analysis are summarized in Figure 1.

The relationship between the activity of the indicator radionuclide produced, the amount of the element being determined, and the activation and decay parameters involved is given by:

$$A = \Phi\sigma(m/A_r)h N_A(1 - e^{-0.693 t_B / t_{1/2}}) \quad (1)$$

where A is the activity of the indicator radionuclide (disintegrations per second), Φ is the projectile flux (per cm^2 and s), σ is the activation cross-section (in cm^2), m is the weight of the element present (in g), A_r is the atomic weight of the element, h is the relative abundance of the reacting nuclide, N_A is Avogadro's number, t_B is the irradiation time, and $t_{1/2}$ is the half-life of the indicator radionuclide.

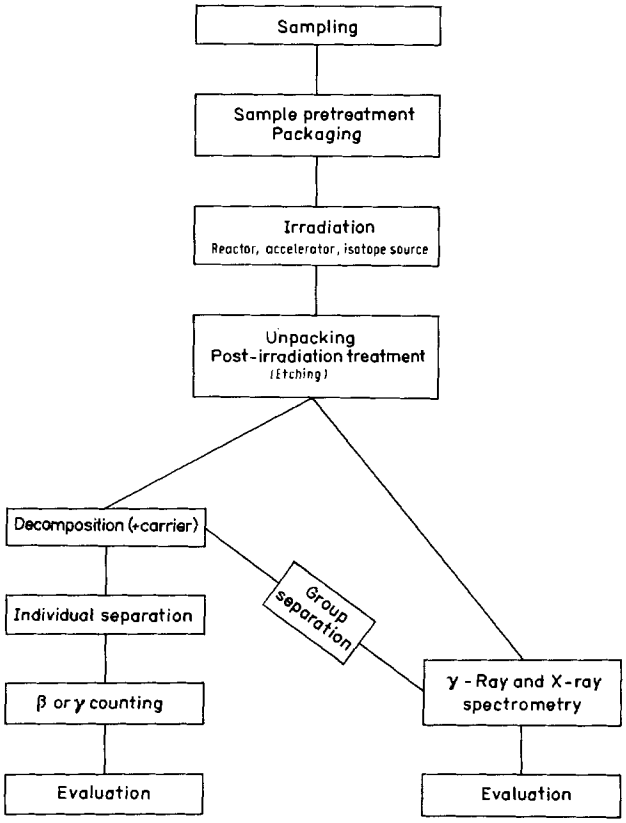


Fig. 1. The sequence of steps in an activation analysis.

The factor which in most cases decides the analytical sensitivity of a given nuclear reaction is the product $\Phi\sigma$. The saturation factor (the term in parentheses) accounts for the decay of the resulting radioactive nuclide during the irradiation period. Figure 2 illustrates the variation of activity with time from the beginning of irradiation to the end of the measurement.

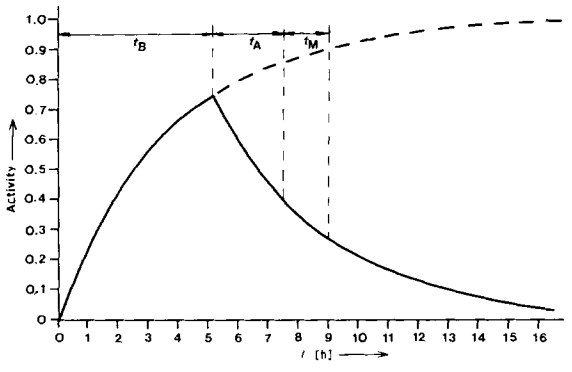


Fig. 2. The radioactivity of ^{56}Mn ($t_{1/2} = 2.58$ h) during and after the irradiation of manganese. The activity is in arbitrary units. t_B = irradiation time, t_A = cooling time, and t_M = measurement time.

The form of the activation equation given by (1) is only valid for cases where the particle flux Φ and the activation cross-section σ can be expressed in discrete values, as for example in activation analysis with thermal neutrons in a reactor or with 14-MeV neutrons. If the energy distribution and the angular distribution of the particles have to be taken into consideration, as in the case of fast neutrons produced by a cyclotron or bremsstrahlung photons, then the product of these two quantities must be integrated over the whole

energy spectrum of the particles and over the relevant solid angle.

Apart from the activation process itself, specific detection of the indicator radionuclide is of fundamental importance for activation analysis. Table 1 summarizes the possible modes of decay, and the types of radiation emitted which may be used for detection of the indicator radionuclides. α-decay is not considered here; it is only of interest for nuclides with $Z > 83$.

Table 1. Possible decay processes of indicator radionuclides and the types of emitted radiation.

Decay process	γ-photon emitted	Possible types of radiation emitted: Particles	Photons
${}^{A}_{Z}X \xrightarrow{\beta^-} {}^{A}_{Z+1}X + \beta^- + \bar{\nu}$	no	β-rays with continuous energy spectrum	bremsstrahlung with continuous spectrum
	yes	β-rays with continuous energy spectrum	mono-energetic γ-rays
		mono-energetic conversion electrons from γ-rays	characteristic X-rays from conversion electrons
			bremsstrahlung with continuous energy from conversion electrons
${}^{A}_{Z}X \xrightarrow{\beta^+} {}^{A}_{Z-1}X + \beta^+ + \nu$	no	positron emission with continuous energy spectrum	511 keV annihilation radiation (gamma) bremsstrahlung with continuous energy from positrons (β^+)
	yes	positron emission with continuous energy spectrum	mono-energy γ-rays
		mono-energetic conversion electrons from γ-rays	511 keV annihilation radiation
			characteristic X-rays from conversion electrons bremsstrahlung with continuous energy from conversion electrons and positrons
Electron capture ${}^{A}_{Z}X + e^- \rightarrow {}^{A}_{Z-1}X + \nu$	no	none	characteristic X-rays from electron capture
	yes	mono-energetic conversion electrons from γ-rays	mono-energetic γ-rays
			characteristic X-rays from electron-capture and conversion electrons
			bremsstrahlung with continuous energy from conversion electrons
Isomeric transition ${}^{Am}_{Z}X \rightarrow {}^{A}_{Z}X + \gamma$ (delayed emission of excitation energy)	only yes	mono-energetic conversion electrons from γ-rays	mono-energetic γ-rays
			characteristic X-rays from conversion electrons
			bremsstrahlung with continuous energy from conversion electrons

β-particles can be detected very easily; however, their continuous energy spectrum generally precludes identification of a radionuclide unless an appropriate chemical separation precedes counting. On the other hand, γ-photons are emitted with discrete energies characteristic for each radionuclide. This is the basis of gamma spectrometry — nowadays the most important counting technique for instrumental activation analysis. The characteristic X-rays associated with each electron capture or internal conversion process can also be used as a means of detection measurement in many cases.

Quantitative determinations can be performed either by the relative (comparative) method or by the absolute standardization method.

In the absolute method[16–18], the amount of element present is calculated from the activities measured with a gamma-ray spectrometer calibrated in absolute terms by using equation (1). Considerable systematic errors can, however, creep in when this approach is used, largely due to the uncertainty in the values for the nuclear constants taken for the calculations[19]. The absolute method should therefore be used with great caution.

For the same reasons, the more time-consuming relative method is mostly used in practice: the sample is irradiated simultaneously with a separate standard for each of the elements to be determined, then both sample and standards are counted. The amount of the element present in the sample is calculated by simple proportions using the ratio of the counting rates of sample and standard and the amount of the element present in the standard. The standards may be purely synthetic, prepared to contain the desired elements, or may be similar materials to the samples, but of known composition. Use of the relative method requires no knowledge of the projectile flux or the detector efficiency.

The time-saving single-standard procedure is being increasingly used in neutron activation analysis[20–23]. In this approach only one element is irradiated as the standard, *e.g.* cobalt, gold, ruthenium, or zirconium, and the amounts of other elements present in the sample are calculated using the previously experimentally determined *k*-factors relating the sensitivities of the chosen standard to that of the element in question.

Finally, it may be possible to use one of the elements present in the sample itself as the standard, provided that suitable radionuclides are produced from this element on activation[24–26].

3. Characteristic Features of Activation Analysis

An impressive array of powerful methods based on a variety of physical principles is available nowadays for the determination of the elements: the analytical procedures using them

can be classified as direct instrumental procedures, or as combined procedures in which dissolution, separation, and sometimes other operations precede the actual measurement step.

The direct procedures for trace analysis, such as optical emission spectroscopy with spark or arc sources, X-ray spectroscopy, and spark-source mass spectrometry permit determination of elements at levels down to the order of 10 to 0.1 ppm, depending on the method, the element, and the matrix composition.

Below these levels, however, the analyst has to rely mainly on the combined procedures of trace analysis. The problem in these methods is to take the μg-, ng-, and pg-amounts of the elements to be determined through all steps of the procedure from sampling to detection without introducing systematic errors. These systematic errors include blanks and losses.

On going to lower trace concentrations, the blank not only determines the limits of detection but also becomes the predominating factor affecting the accuracy in each wet chemical combined method. Recent experience has shown[27, 28] that it is only possible to obtain correct results in extreme trace analysis if extensive precautions are taken to reduce the blank values, such as working in dust-free clean rooms and/or clean benches and using specially purified reagents as has been done, for example, in the analytical laboratories of the U. S. National Bureau of Standards in Gaithersburg[27], and in the Laboratory for High-Purity Materials at the Max Planck Institute in Schwäbisch Gmünd[29]. This is a general principle to be applied in all combined procedures whatever the principle upon which the determination step is based.

Activation analysis occupies a special position in connection with the problem of the blank, even when radiochemical separations are involved. Depending on the nature of the sample, the blank can be almost entirely or largely eliminated. At present, this would seem to be the principal advantage of activation analysis.

The problem of the blank does not occur at all when the samples are compact solids. For example, the contamination on the surface of a metal sample arising from handling before and during irradiation can be removed by etching after irradiation (Figure 1). However, the possibility of enrichment of the trace elements during the etching procedure should not be overlooked[30]. Contamination is no longer possible after the irradiation step; indeed it is common practice to add inactive carriers (1—10 mg) to facilitate execution of radiochemical operations.

In the case of samples which cannot be etched, such as many environmental and biological samples, it is not possible to eliminate all sources of contamination contributing to the blank, but at least the most important—that of contamination from reagents used for dissolution and separation—can be avoided. Possible contamination or losses incurred during sampling, pretreatment and storage, however, must be taken into account in activation analysis as with other approaches. There is also the possibility of contamination from the capsule in which the sample is irradiated[31].

Of all trace analytical methods for the determination of elements, then, activation analysis would seem best to meet the stringent requirements and to offer the best chance of obtaining correct results for elements at extremely low concentration levels, *i. e.* in the ppb range and below.

Another characteristic feature of activation analysis is its high sensitivity: for many elements it is the most sensitive method of determination available. If one considers all the various means of activation, separation of the radionuclides, and counting, and also the possibility of employing short-lived indicator radionuclides, then one can say that practically every naturally occurring element can be determined in ng-amounts or at the ppb level (see Section 4). At the same time the technique offers a high degree of selectivity, since each radionuclide is identified on the basis of two characteristic properties: the energies of the gamma rays or of the X-rays emitted, and the half-life. No other analytical technique offers such a combination of decisive advantages for determinations at the extreme trace level.

Activation analysis employed as a typical multi-element analytical technique can often be carried out nondestructively, which can be of importance when only minute amounts of sample are available. The extent to which the nondestructive approach can be adopted depends on the elemental composition of the sample. However, one has to consider that the analysis is nondestructive only with respect to the elemental composition of the sample material but not with respect to its structure and physical properties which can change as a result of radiation effects during the bombardment. Our experience in activation analysis with thermal and fission neutrons in a reactor, with fast neutrons produced by a cyclotron and with charged particles, has shown that element contents < 0.1 ppm can only occasionally be determined reliably by the nondestructive approach in conjunction with high-resolution gamma spectrometry. Other multi-element instrumental methods would seem to offer similar limits of detection (*e. g.* spark-source mass spectrometry) or worse, even by two or three orders of magnitude (*e. g.* direct optical emission spectroscopy or X-ray fluorescence analysis). In some special cases, the decisive factor may be that activation techniques can be employed for analysis *in situ* and *in vivo*, as well as for localization microanalysis and surface analysis.

Like any other technique activation analysis also has its problems and its limitations. As the information provided by activation analysis is gained *via* nuclear processes and properties, valid analytical conclusions can be drawn only about the amounts of elements or isotopes present, and not about the state of chemical combination. A possible exception involves analytical use of the Szilard-Chalmers reactions which, however, are difficult to handle[32].

A disadvantage is that activation analysis for very low levels requires large and expensive irradiation sources, either to be used in nuclear research centers, or to be purchased at considerable expense. The latter is increasingly the case, although irradiation facilities are generally well organized for use by outside parties at nuclear research centers, particularly at reactor centers.

The necessity of handling radioactive materials certainly complicates experimental work, and sometimes long irradiation and cooling times (up to a few weeks) are required to obtain the desired sensitivities or to be able to process the sample in the post-irradiation steps, all of which can lead to delays in evaluation of the analytical results.

The financial cost of activation analysis largely depends on the source of radiation required and on the time involved (instrumental or radiochemical procedures). The desired preci-

sion and the numbers of elements to be determined and of samples also affect the final cost. If the irradiation is carried out in a nuclear reactor followed by instrumental multi-element analysis (*e.g.* for a rock sample), the cost may be as low as 15 DM per element per sample[33]. When a large accelerator is used for the irradiation, the time factor is most critical as the cost can run to 500 DM per hour. In some cases, then, the high performance of activation analysis must be paid for dearly.

4. The Activation Process

The sources which provide the projectiles usable for activation analysis, and their most important properties, are summarized in Table 2. Three properties of these projectiles are of fundamental significance for activation analysis: the type of particle, the energy, and the intensity. The projectiles of interest are of three types: neutrons, charged particles, and photons. The analytical reaction taking place, and therefore also the indicator radionuclide produced, are determined by the type of projectile used, which is illustrated in Table 3 for copper. For most elements one has a choice of a number of sensitive reactions which can be used, depending on the availability of the radiation sources.

sensitivity is proportional to this factor, as can be seen from equation (1).

Table 3. Some analytically interesting nuclear reactions induced by various particles in copper.

Projectile	Reaction	Cross-section [barn]	Product half-life $t_{1/2}$
Thermal and epithermal neutrons	$^{63}Cu(n,\gamma)^{64}Cu$	4.5	12.7 h
14-MeV neutrons	$^{63}Cu(n,2n)^{62}Cu$	0.52	9.76 min
	$^{65}Cu(n,p)^{65}Ni$	0.024	2.52 h
Protons	$^{63}Cu(p,n)^{63}Zn$	0.56 [a]	38.4 min
Deuterons	$^{63}Cu(d,p)^{64}Cu$	0.30 [a]	12.7 h
^{3}He-particles	$^{65}Cu(^3He,2n)^{66}Ga$	0.28 [a]	9.3 h
α-Particles	$^{65}Cu(\alpha,2n)^{67}Ga$	0.52 [a]	78.3 h
Photons	$^{63}Cu(\gamma,n)^{62}Cu$	0.07 [a]	9.76 min

[a] Maximum of the excitation function.

The type of radiation used also determines the maximum volume of sample which can be handled, the uniformity of the activation of the sample, the necessary cooling during irradiation, and the irradiation time. The accessibility of the source, the cost of irradiation, and other factors should also be taken into consideration.

Table 2. Survey of different activation techniques.

Projectiles and source	Mode of projectile production	Projectile energy	Typical analytical reaction	Projectile flux [$cm^{-2}\ s^{-1}$]	Range of analytical application
Neutrons					
Nuclear reactor	fission	fission spectrum	(n,γ)	high, 10^{12}—10^{15}	trace to extreme trace components with $Z>10$
Neutron generator	$^3T(d,n)^4He$	14 MeV	(n,p), (n,α) (n,2n)	medium, 10^8—10^{10}	main to trace components
Cyclotron	d + Be → n	variable spectrum	(n,p), (n,α) (n,2n)	high, 10^{10}—10^{12}	trace to extreme trace components
$^{252}Cf/^{235}U$	spontaneous and neutron fission	fission spectrum	(n,γ)	medium, 10^8—10^{10}	minor to trace components, elements with $Z>10$
^{252}Cf	spontaneous fission	fission spectrum	(n,γ)	low, 10^6—10^8	main and minor components, elements with $Z>10$
(α,n)-sources	(α,n)-reaction	medium energies, 4—6 MeV	(n,γ), (n,p) (n,α), (n,2n)	low, 10^5—10^6	main and minor components
Charged particles					
$\tau = p,d,^3He,\alpha$ Cyclotron, linear accelerator	acceleration	variable	(τ,n), (τ,2n) (τ,p), (τ,γ)	high, 10^{13}—10^{14} [a]	trace to extreme trace components
Photons					
Electron accelerator	bremsstrahlung production	variable spectrum	(γ,n), (γ,p)	high, 10^{13}	trace to extreme trace components

[a] Number of particles per second; beam intensity = 1 μA = 6.2×10^{12} singly charged particles per second.

Some of the sources listed in Table 2 yield particles with variable energy. This is often a very important aspect, since, in each particular case, optimum projectile energy can be chosen with regard to the sensitivity of the analytical reaction, to the occurrence of interfering reactions, and/or to the instrumental performance of the analysis. The projectile flux (or the beam intensity) is of course also important, since the

4.1. Activation with Neutrons

Since neutrons carry no electrical charge they can easily penetrate the sample material. This facilitates (i) uniform irradiation throughout the sample and (ii) standardization since both sample and standard can be irradiated simultaneously. The high penetrating power of neutrons brings with it further

important advantages: the samples can be irradiated in closed containers (made, *e.g.*, from high-purity quartz or polyethylene) which prevent the escape of volatile substances and reduce the risk of contamination to a minimum. The sample material is not heated to high temperatures during the irradiation, which may be advantageous for biological materials, for example.

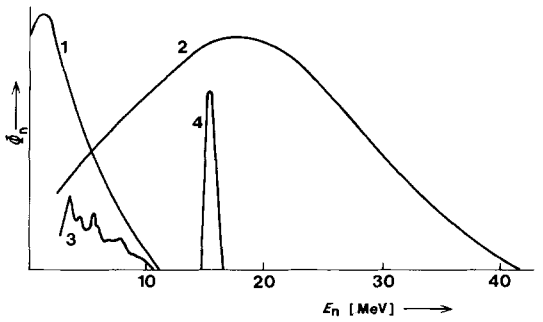


Fig. 3. Energy spectra of neutrons from different sources 1, nuclear reactor and ^{252}Cf isotope source; 2, cyclotron: beryllium target bombarded with 40-MeV deuterons; 3, ^{241}Am/Be isotope source; 14-MeV neutron generator. Φ_n = neutron flux (arbitrary scale).

Neutron sources for activation analysis are nuclear reactors, particle accelerators, and radioactive nuclides. The neutrons from these sources differ markedly in both energy spectrum and flux (see Figure 3 and Table 2) and therefore permit a differential approach to activation analysis.

4.1.1. Activation with Reactor Neutrons

Nuclear reactors are the most intense sources of projectiles. According to design, they can provide steady fluxes of up to 10^{15} neutrons cm^{-2} s^{-1} or pulsed neutron fluxes of up to 10^{18} neutrons cm^{-2} s^{-1}. For most reactors, the steady fluxes lie in the range 10^{12}—10^{14} neutrons cm^{-2} s^{-1}.

There has been notable recent progress in the development of nuclear reactors for use in activation analysis. Small reactors of the new generation are good value for money, easy to handle, reliable in operation, and yet relatively powerful. For example, fluxes of 3.5×10^{12} neutrons cm^{-2} s^{-1} can be achieved in the mini-TRIGA reactor, and 10^{12} neutrons cm^{-2} s^{-1} in the recently developed Slowpoke-2 reactor[33a]. Pneumatic sample-handling facilitates the speedy transfer of samples into and out of the irradiation position. These small reactors are in many instances well suited to the requirements for good sensitivity in trace analysis, as has been shown by the analyses of biological, environmental, and other samples[34, 35].

With few exceptions, activation analysis using nuclear reactors is based on the production of radionuclides *via* (n,γ) reactions with thermal neutrons (energies E_n ranging from zero to 0.2 eV) and with epithermal neutrons (E_n between 0.2 eV and 0.5 MeV), while the (n,p) and (n,α) threshold reactions caused by fast neutrons ($E_n > 0.5$ MeV) must be considered as possible primary interfering reactions. The thermal activation cross-section σ_{th} and the activation resonance integral I vary considerably from one target nuclide to the next[36]. Values of σ_{th} lie between 2.4×10^{-5} barns for the reaction ^{15}N(n,γ)^{16}N and 5300 barns for ^{151}Eu(n,γ)^{152g}Eu.

In principle, it is possible to carry out activations in a reactor using neutrons of varying energies[12, 37], since the spectrum of fission neutrons at the irradiation positions of the reactor normally includes thermal, epithermal, and fast neutrons. In such irradiations the highest flux of thermal neutrons can be achieved, and hence also the highest sensitivity for the determination in question, since the contribution of thermal neutrons is responsible for the (n,γ) reactions; however, the epithermal neutrons can also contribute to production of the indicator radionuclide by way of (n,γ) resonance activation. For this reason irradiation with fission neutrons is most commonly employed in activation analysis.

When the analysis is carried out instrumentally, the limits of detection can often be considerably improved by eliminating the thermal neutrons and activating only with resonance neutrons. Sometimes instrumental activation analysis is possible only by this approach, for example when irradiation with resonance neutrons suppresses the production of interfering activity from the nuclides of the matrix elements and leads to a relatively increased production of indicator radionuclides from the element to be determined. Activation by the thermal neutrons, the flux of which is generally much higher than that of the others, can be eliminated by surrounding the sample with a filter of cadmium or of boron[38] as these elements absorb the thermal neutrons almost completely while transmitting the resonance neutrons practically without attenuation. Activation using resonance neutrons has been used in recent years for the analysis of geological[39–42], biological[43–46], and environmental[47] samples, with limits of detection considerably lower than had previously been attainable, *e.g.* lower by a factor of about 20 for the determination of U, Th, Mo, W, As, and Sb in granitic rocks.

Activation analysis in a reactor is characterized by a very high sensitivity of detection for most elements. The figures quoted in Table 4 give some impression of the detectabilities which can be achieved using reactor neutrons, 14-MeV neutrons, and photons.

The methodology of activation analysis with reactor neutrons is well established, and as far as the activation step is concerned, is unlikely to be improved on much. It is possible to make good estimates of the limits of detection and nuclear interferences for determinations of all the elements. Significant improvements are only likely to be made in the separation and measurement techniques involved in the post-irradiation steps.

4.1.2. Accelerators as Sources of Fast Neutrons

For the determination of a number of elements, activation with fast neutrons *via* threshold reactions of the (n,p), (n,α), (n,2n), and (n,n'γ) types is a well suited technique since such reactions lead to the production of suitable indicator radionuclides in relatively high yields.

The most important source of fast neutrons is the neutron generator[13], in which 14-MeV neutrons are produced in the reaction ^{3}T(d,n)^{4}He. To induce this reaction, an intense beam of deuterium ions is produced, with energies in the range 50 to 600 keV, and focused onto a tritium target from which the neutrons are emitted with a fairly uniform 4π angular distribution. The commercially available generators provide neutron fluxes of the order of 10^9 neutrons cm^{-2} s^{-1}.

These fluxes, together with acceptable activation cross-sections, which are now quite well characterized[36] and exhibit

Table 4. Limits of detection for activation analysis with reactor neutrons, 14-MeV neutrons, and photons.

Order of magnitude of limit of detection in g [a]	Elements detected Reactor neutrons [b]	14-MeV neutrons [c]	Photons [d]
10^{-15}	Eu		
10^{-14}	In, Dy		
10^{-13}	Mn, Sm, Ho, Lu, Re, Ir, Au		
10^{-12}	Na, Ar, V, Co, Cu, Ga, As, Br, Kr, Rh, Pd, Ag, I, Cs, La, Pr, Yb, W		
10^{-11}	Al, Cl, K, Sc, Ge, Se, Y, Sb, Xe, Ba, Gd, Tb, Er, Tm, Pt, Os, Hf, Hg, Th, U		
10^{-10}	Si, P, Cr, Ni, Zn, Sr, Nb, Ru, Cd, Sn, Te, Ce, Nd, Ta		Ho
10^{-9}	F, Ne, Mg, Ti, Rb, Mo, Tl, Bi		Cl, Ar, Cu, Zn, Br, Ag, Pr, Na, Er, Ta
10^{-8}	S, Ca, Zr, Pb	F	C, N, O, F, P, S, K, Ti, Cr, Ge, Zr, Nb, Mo, Ru, In, Sn, Sb, I, Cs, Sm, Gd, Re, Au
10^{-7}	Fe	Na, P, Sc, Cu, Zn, Ga, Br, Ag, Cd, Sb, Te, Ba, Ce, Pr, Ho, Ta	Mg, Si, Fe, Ni, As, Rb, Y, Cd, Ce, Tm, Yb, Os, Ir, Hg, Tl, Pb
10^{-6}		B, N, O, Mg, Al, Ar, V, Cr, Mn, Fe, Co, Ni, Ge, Se, Sr, Zr, Pd, In, Sn, Xe, Nd, Sm, Eu, Gd, Er, W, Os, Ir, Pt, Hg, Th	Mn, Co, Sr, Rh, Pd, Dy, Lu, W
10^{-5}		Cl, S, K, As, Kr, Rb, Nb, Mo, Rh, I, Cs, La, Re, Au, Pb	Na
10^{-4}	N, O	Ca, Ti, Y, Ru, Tb, Dy, Tm, Yb, Lu, Bi, U	Tb
10^{-3}		Hf, Tl	

[a] Activity assumed to be necessary for detection of indicator radionuclide: 0.1 nCi for $t_{1/2} > 30$ min; 0.5 nCi for 1 min $< t_{1/2} < 30$ min; 1 nCi for 1 s $< t_{1/2} < 1$ min. [b] Thermal neutron flux $= 5 \times 10^{13}$ n cm^{-2} s^{-1}; epithermal neutron flux $= 10^{12}$ n cm^{-2} s^{-1}; irradiation time $t_B = 24$ h. [c] Neutron flux $= 10^{10}$ n cm^{-2} s^{-1}, irradiation time $t_B = 1$ h. [d] Electron beam current = 100 μA, irradiation time $t_B = 4$ h.

systematic trends[48,49], enable an impressive number of elements to be determined with good sensitivity (see Table 4). However, 14-MeV activation analysis is limited by the following three factors: by the relatively low neutron flux (compared with reactor fluxes), by the invariable, and for many elements unfavorable, neutron energy of 14 MeV, and by the limited operating life of the tritium target and the resulting operating cost.

Recently, a high-power neutron generator has been developed at the Nuclear Research Center at Karlsruhe which yields 5×10^{12} neutrons s^{-1}[50], from which a flux of 6×10^{10} neutrons cm^{-2}s^{-1} can be achieved for irradiating samples up to 25 cm^3 in volume. The working life of the tube was several hundred hours. Work is in progress[51] at the Sandia Laboratories on a high-power neutron generator which is designed to yield 5×10^{13} neutrons s^{-1} and fluxes of up to 5×10^{11} neutrons cm^{-2}s^{-1}. These new generators now make it possible to apply activation analysis with fast neutrons to the determination of elements even below the ppm level. In some cases it will be possible to make use of nuclear reactions not previously used for analytical purposes, such as, for example, in the determination of silicon *via* the reaction ^{29}Si(n,p)^{29}Al ($t_{1/2}$ for ^{29}Al = 6.6 min) which does not suffer from any interfering reactions, while in the reaction previously employed ^{28}Si(n,p)^{28}Al the indicator radionuclide can also be produced by two other reactions, namely ^{27}Al(n,γ)^{28}Al and ^{31}P(n,α)^{28}Al.

Very promising development possibilities are offered by the use of a cyclotron to produce fast neutrons of variable energy. Though in principle a large number of reactions could be used to produce neutrons[52-54], bombardment of a thick beryllium target with high-energy deuterons has proved to be best suited[55,56]. The neutrons are produced largely as

Table 5. Characteristic parameters for cyclotron-produced neutrons emitted in the forward direction [55, 56].

E_d [MeV]	Neutron yield [n s^{-1} μA^{-1}] [a]	Energy distribution maximum [MeV]	FWHM of the energy distribution [MeV]	FWHM of the angular distribution [b] [°]
18	1.2×10^{10}	6	8.3	31.6
23	1.8×10^{10}	7.5	10.5	27.4
28	2.6×10^{10}	10.5	12.4	24.6
33	3.3×10^{10}	13	13.6	22.7
38	3.9×10^{10}	15	15.4	21.3
45	5.1×10^{10}	18	17.3	19.5
53	7.3×10^{10}	22	19.0	19.0

[a] For neutrons with energy $E_n \geq 2$ MeV and angular range $0 < \varphi < 20°$ (see Figure 5).
[b] Relative to the original direction of the deuteron beam.

a result of stripping and break-up processes, and are emitted preferentially in the forward direction distributed as a cone. The sample is positioned so as to lie in this cone of neutrons as indicated in Figure 4. Figure 5 illustrates the energy spectra for neutrons in the forward direction over a range of angles $0 < \varphi < 20°$ resulting from bombardment with deuterons of different energies. Table 5 summarizes the fluxes which are attainable at the sample position, along with other characteristic parameters, for various energies of deuterons. As the deuteron beam current available usually lies in the range 10—50 μA, the fluxes of fast neutrons which can be achieved from this source are higher than those which can be produced by other sources.

All this makes it possible to achieve exceptionally high sensitivities and correspondingly low limits of detection by the use of cyclotron-produced fast neutrons. Approximations based on systematics of the excitation functions[57] have indicated that the limit of detection attainable when 14-MeV neutrons are used (with a flux of 10^{10} neutrons cm^{-2} s^{-1}) can be improved by a factor of between 20 and 100[55]. The experimentally determined sensitivities and limits of detection

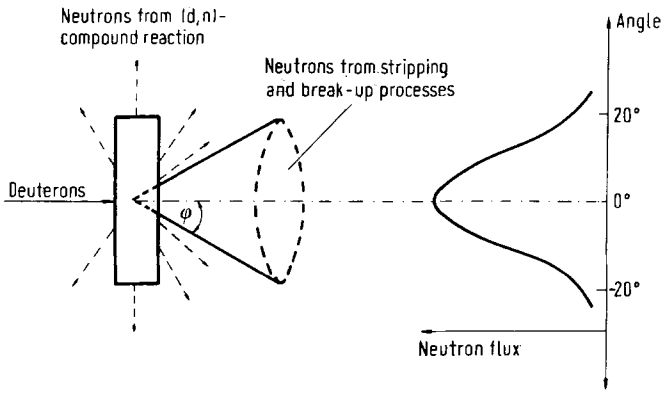


Fig. 4. Production of neutrons by bombardement of a thick beryllium target with fast deuterons.

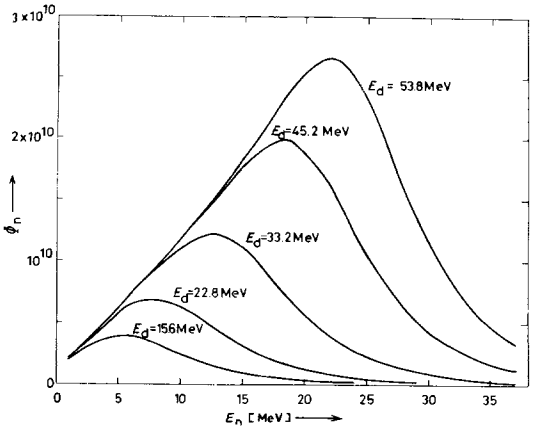


Fig. 5. Energy distributions of the neutrons produced by bombarding a beryllium target with deuterons of different energies E_d [55]. Φ_n = neutron emission in the forward direction [n μC^{-1} MeV^{-1} sr^{-1}].

terons. In each particular case the energy spectrum of the neutrons can be optimized with respect to the sensitivity of the determination and the minimization of interfering reactions, *i.e.* the maximum in the energy distribution of the neutrons can be made to coincide with the maximum in the excitation function for the analytical reaction.

Activation using cyclotron-produced neutrons has recently been made use of for the determination of fluorine in a variety of samples, including geological ones, *via* the $^{19}F(n,2n)^{18}F$ reaction with subsequent separation of the ^{18}F (limit of detection = 2.5 ng), for multi-element analyses (K, Ca, Ti, Fe, Rb, Sr, Hg, Pb) of several Bowen and NBS reference standards[59], and for the determination of oxygen in metals[60].

4.1.3. Radioisotope Sources of Neutrons

The radioactive neutron sources possess a number of noteworthy advantages. They are entirely reliable systems with no mechanical or electrical components, and they are simple, clean, and cheap. Two types of isotopic neutron sources are in use: the spontaneous fission emitters and the two-component sources. The most important of these are listed in Table 7.

Table 6. Limits of detection for activation analysis with cyclotron-produced neutrons and 14-MeV neutrons for the elements Mg, Al, Si, P, Zr and Mo.

Analytical reaction	Limit of detection in g [a] Cyclotron neutrons [b]			
	E_d = 15 MeV	E_d = 30 MeV	E_d = 45 MeV	14-MeV neutrons [c]
$Mg + n \rightarrow {}^{24}Na$	1.1×10^{-6}	1.1×10^{-7}	3.8×10^{-8}	1.1×10^{-5}
$^{27}Al(n,p)^{27}Mg$	1.1×10^{-7}	1.7×10^{-8}	5.8×10^{-9}	2.1×10^{-6}
$Si + n \rightarrow {}^{28}Al$	4.8×10^{-8}	6.9×10^{-9}	2.2×10^{-9}	7.5×10^{-7}
$^{31}P(n,\alpha)^{28}Al$	1.4×10^{-7}	1.4×10^{-8}	4.6×10^{-9}	1.6×10^{-6}
$Zr + n \rightarrow {}^{89m}Zr$	5.5×10^{-6}	8.5×10^{-8}	1.6×10^{-8}	8.5×10^{-6}
$Mo + n \rightarrow {}^{97}Nb$	1.1×10^{-4}	2.3×10^{-6}	2.9×10^{-7}	7.4×10^{-4}

[a] Activity assumed to be necessary for detection of indicator radionuclide: 0.1 nCi for $t_{1/2} > 30$ min and 0.5 nCi for $t_{1/2} < 30$ min at the end of the irradiation. [b] Deuteron beam current = 10 μA. [c] Neutron flux = 10^9 n cm^{-2} s^{-1}.

for Mg, Si, Al, P, Zr, and Mo activated by cyclotron-produced fast neutrons and by 14-MeV neutrons are compared in Table 6[58].

A further advantage in using cyclotron-produced neutrons for the activation is that the mean energy of the neutrons can be varied by varying the energy of the accelerated deu-

For a number of years the availability of ^{252}Cf has made it possible to produce quite a powerful source of fission neutrons in a very small volume (see Tables 2 and 7). The energy spectrum of the neutrons resembles that of fission neutrons

Table 7. Characteristics of the principal radionuclide neutron sources.

	Cf	Am/Be	Pu/Be	Ac/Be	Sb/Be
Radionuclide	^{252}Cf	^{241}Am	^{238}Pu	^{227}Ac	^{124}Sb
Half-life	2.62a	433a	87.7a	21.8a	60.3d
Reaction producing neutrons	spontaneous fission	$^{9}Be(\alpha,n)^{12}C$	$^{9}Be(\alpha,n)^{12}C$	$^{9}Be(\alpha,n)^{12}C$	$^{9}Be(\gamma,n)^{4}He$
Neutron yield [$ns^{-1}\ Ci^{-1}$]	4.3×10^{9}	2.2×10^{6}	2.3×10^{6}	1.5×10^{7}	1.3×10^{6}
Neutron yield [$ns^{-1}\ g^{-1}$]	2.3×10^{12}	7×10^{6}	4.1×10^{7}	1.1×10^{9}	—
Mean energy [MeV]	<2	4—6	4—6	4—6	0.024
Volume required [cm^3 per 10^8 n/s]	<0.05	100	19	1	2

from ^{235}U, so that the resulting reactions are usually of the (n,γ) type. These ^{252}Cf sources have already found employment in a number of laboratories[61–64].

A recent development utilizes ^{235}U as a neutron multiplier surrounding the ^{252}Cf source. Each neutron reaching the shield produces further neutrons, which are in turn moderated by passage through polyethylene or water. The use of such subcritical systems can lead to thermal fluxes being multiplied by factors between 25 and 100. As an example one might quote a source consisting of a milligram of ^{252}Cf surrounded by 1.4 kg of 93.4 % enriched ^{235}U, which, with a multiplication factor of 33, produces a thermal neutron flux of 4×10^{8} neutrons $cm^{-2}\ s^{-1}$[65]. A similar source with 2 mg of ^{252}Cf was installed in the laboratories of Eastman Kodak[66]. The most intense source of this kind has recently been developed at the Battelle Laboratories in Richland (USA) and commissioned specially for use in activation analysis[67]. This installation consists of six ^{252}Cf sources with a total weight of 105 mg which are positioned in a subcritical lattice of rods of 93.2 % enriched uranium, and produces a thermal neutron flux of 3.5×10^{10} neutrons $cm^{-2}\ s^{-1}$ (see Figure 6).

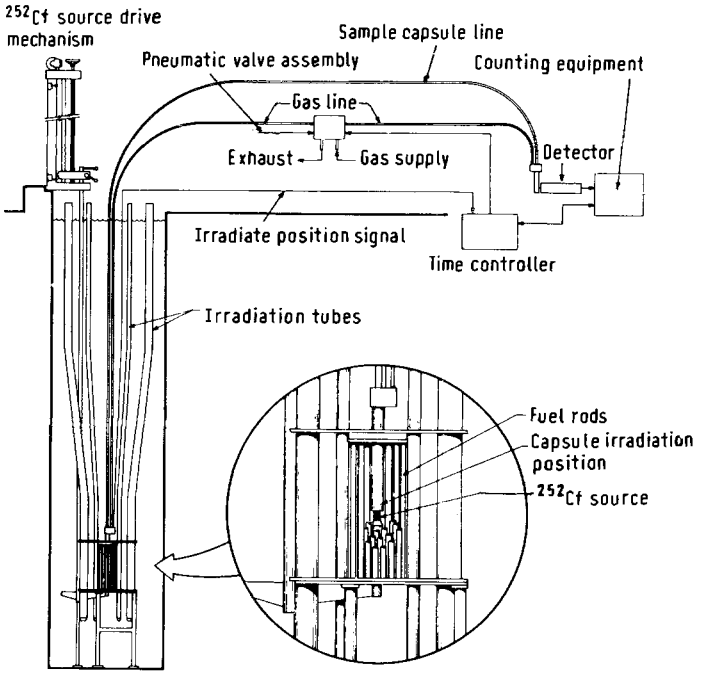


Fig. 6. A ^{252}Cf neutron source with ^{235}U neutron multiplier shield capable of producing a thermal neutron flux of $3.5\times10^{10}\ cm^{-2}\ s^{-1}$ [67].

Thanks to the constancy of the neutron flux and of its energy spectrum it is possible to work with short-lived indicator radionuclides with repeated cyclic irradiations so as to improve the limits of detection. Table 8 presents some limits of detection which have been achieved using the source at the Battelle Laboratories just mentioned.

Table 8. Limits of detection for activation analysis with neutrons produced in a subcritical assembly containing 105 mg of ^{252}Cf with 93.2 % enriched ^{235}U as neutron multiplier [67].

Limit of detection, in ppm [a]	Element
0.001	Eu, Dy
0.001— 0.01	Mn, In, ^{129}I, Ir, Au, Lu, Ho, Sm, Re
0.01 — 0.1	Na, Sc, Co, Ga, Br, Ag, Sb, I, Cs, La, Pr, Tm, Yb, Ta, W, Pt, As, Se
0.1 — 1.0	Ar, K, Cr, V, Cu, Cd, Ce, Nd, Gd, Tb, Er, Hg, Hf, Ge, Sr, Na
1.0 — 10	Cl, Zn, Mo, Ru, Rh, Pd, Te, Ba, Os
10 — 100	F, Mg, Al, Ti, Ni, Sn, Rb, Y
100 —1000	Ca, Fe, Zr
1000	Pb, O, S

[a] Based on the assumptions: amount of sample = 1 g, activity measured = 200 counts, efficiency of the Ge(Li)-detector = 15 %. The lowest limit of detection was selected from those given by four combinations of irradiation time t_B, cooling time t_A, counting time t_M, and number of cycles:
1) 6 s, 1 s, 6 s, for 50 cycles
2) 1 h, 5 min, 30 min, 1 cycle
3) 1 d, 1 h, 30 min, 1 cycle
4) 7 d, 1 h, 30 min, 1 cycle.

These new neutron sources certainly offer an alternative to the large irradiation facilities (nuclear reactors) for many applications, and are well suited for use in universities, research centers, industrial laboratories, and hospitals.

The two-component sources[68, 69] consist of an alpha- or gamma-emitting isotope and beryllium, in which the neutrons are produced in (α,n) or (γ,n) reactions. Neutron fluxes from such sources can only reach values of between 10^5 and 10^7 neutrons $cm^{-2}\ s^{-1}$, and they are therefore suitable only for the determination of major or at best minor components. On the other hand, because the stability of these sources is so good, both with respect to time and to spatial distribution of the neutron flux, the results obtained from their use in activation analysis can show high precision and accuracy[70, 71].

4.2. Activation with Charged Particles

In contrast to the behavior of neutrons and photons, charged particles are quickly slowed down and stopped when they hit the sample (see Figure 7). This has many consequences, not least for the question of standardization. It makes a difference whether the samples to be irradiated are thick or thin. The necessary mathematical treatments have been performed for both cases, which take into account the degradation of energy of the particles and the way in which this affects the activation processes: these are the procedure of the equiva-

lent thickness, for thin samples[73], and the procedure of the average cross-section, for thick samples[74]. In the case of thin samples, sample and standard are irradiated simultaneously. In the more usual case of irradiation of thick samples, the activation is achieved with a continuous energy spectrum between the original particle energy on the surface of the sample and the threshold energy for the given reaction at the depth corresponding to the effective penetration of the particles in the sample. Since, however, the cross-section is strongly dependent on the energy of the particles, the amount of indicator radionuclide produced exhibits a distribution depending on the depth in the sample. An example of this is shown in Figure 8. With thick samples, simultaneous irradiation of sample and standard is only possible with some kind of rotating arrangement, which, however, results in a lowering of the activity produced. Because of this the sample and the standard are usually irradiated separately, and the intensity of the particle beam is measured with a Faraday cup or a monitor foil.

The rapid deceleration of the fast particles can result in the sample being heated up, and therefore necessitates efficient cooling of the sample during the irradiation. Even then, beam currents over 10 μA can rarely be used.

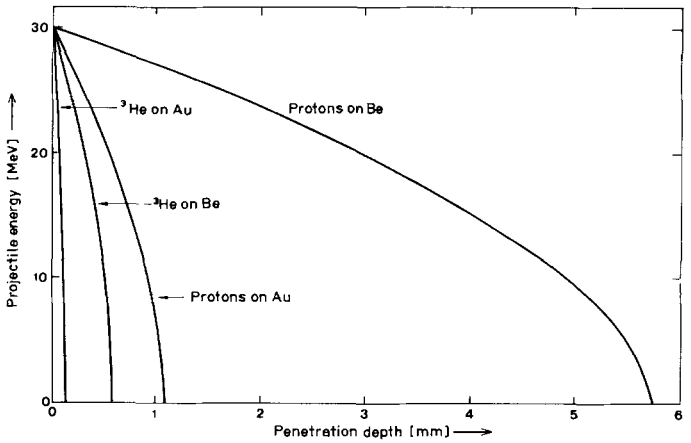


Fig. 7. Energy degradation of 30-MeV protons and ^{3}He-particles when they penetrate targets of beryllium or gold [72].

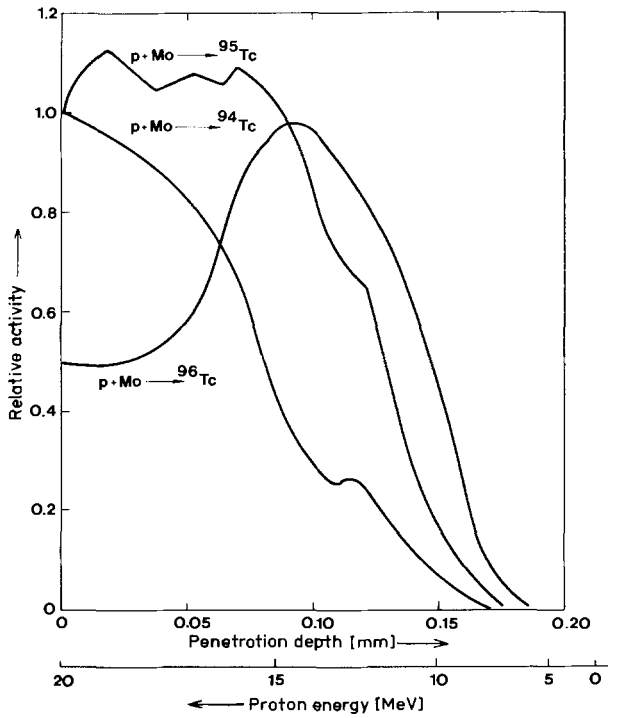


Fig. 8. Irradiation of a thick molybdenum target with 20-MeV protons: relative distributions of the radionuclides ^{94}Tc, ^{95}Tc, and ^{96}Tc as a function of the penetration depth of the proton beam.

Table 9. Survey of the most important data for projectiles and analytical reactions used in activation analysis with charged particles.

Particle/ binding energy [MeV]	Most important reaction types	σ_{max} [mbarn]	Position of maximum [MeV]
p	(p,n)	100—900	8—15
	(p,2n)	200—1300	17—27
	(p,pn)	100—600	23—43
	(γ,α)	20—200	7—23
d	(d,n)	30—400	2—13
2.2	(d,2n)	200—1100	11—17
	(d,p)	100—500	4—15
^{3}He	(^{3}He,n)	10—100	5—13
7.7	(^{3}He,2n)	20—300	15—25
	(^{3}He,p)	40—400	6—17
	(^{3}He,pn)	100—700	12—20
	(^{3}He,α)	20—400	6—22
α	(α,n)	50—1000	12—23
28.3	(α,2n)	100—1300	25—33
	(α,p)	100—600	16—30
	(α,pn)	50—1000	27—42

Table 9 summarizes a number of important parameters for the commonly used charged particles. One can see that for any given target nuclide and any given type of particle, a number of reactions is possible, so that for practically every element at least one, and usually several sensitive nuclear reactions can occur and give rise to the production of indicator radionuclides with suitable properties. Tritons (^{3}H nuclei)[75] and heavy particles[76] have also been used to induce analytical reactions. Thanks to the relatively high cross-sections for such activation processes (several hundred millibarns) and the high beam intensities which can be used (10^{12} to 10^{14} particles per second) trace elements can be determined at the ppb level and lower. It is a great advantage that the most suitable particle and the optimum energy can be selected for each application. Typical limits of detection for a number of elements are given in Table 10.

The most suitable source of charged particles for use in activation analysis is the cyclotron[84, 85]—particularly the recently developed compact cyclotrons with variable energy of the external beam. These machines are small, simple to operate, and considerably cheaper to buy than the big cyclotrons of the old generation. Figure 9 shows as an example the CV-28 compact cyclotron (Cyclotron Corporation, Berkeley) which can produce particle energies in the external beam in the following ranges: protons, 2—24 MeV, deuterons, 4—14 MeV, ^{3}He, 6—36 MeV, and alpha particles, 8—28 MeV. These compact cyclotrons are suitable for use, besides activation analysis, also in other fields of applied research and in nuclear medicine. In the Federal Republic of Germany alone, seven compact cyclotrons have been installed in recent years, four of them of the variable energy type, and similar

Table 10. Limits of detection for activation analysis with charged particles for the light and some heavy elements.

Element	Activation reaction	Particle energy [MeV]	Limit of detection in ppb [a]	Ref.
Li	$^{7}Li(p,n)^{7}Be$	15	19.4	77
Be	$^{9}Be(^{3}He,n)^{11}C$	20	4.9	78
B	$^{11}B(p,n)^{11}C$	15	0.2	78
C	$^{12}C(d,n)^{13}N$	15	0.7	78
N	$^{14}N(p,\alpha)^{11}C$	15	0.3	78
O	$^{16}O(^{3}He,p)^{18}F$	20	1.6	78
F	$^{19}F(p,pn)^{18}F$	15	2.4	78
P	$^{31}P(\alpha,n)^{34m}Cl$	25	0.4	79
Ti	$^{48}Ti(p,n)^{48}V$	12	25.7	80
Ni	$^{58}Ni(p,pn)^{57}Ni$	30	2.6	81
Cu	$^{63}Cu(p,n)^{63}Zn$	15	0.2	82
Zn	$^{66}Zn(p,n)^{66}Ga$	12	2.0	80
Ge	$^{70}Ge(p,n)^{70}As$	12	1.2	80
Zr	$^{90}Zr(p,n)^{90}Nb$	12	3.1	80
Nb	$^{93}Nb(p,n)^{93m}Mo$	12	20.0	80
Tl	$^{203}Tl(d,2n)^{203}Pb$	22	8.5	83
Pb	$^{206}Pb(p,n)^{206}Bi$	22	12.9	84

[a] Beam intensity = 5 μA, irradiation time = $2\,t_{1/2}$ or at most 5 h. The limit of detectability of the indicator radionuclide is based on 0.1 nCi for $t_{1/2} > 30$ min, and 0.5 nCi for $t_{1/2} < 30$ min.



Fig. 9. The variable-energy compact cyclotron model CV-28 (produced by Cyclotron Corporation (Berkeley)).

developments can be observed in other industrial countries. They are therefore quite likely to find increasing application in the field of activation analysis.

4.3. Activation with Photons

Photon activation analysis represents an interesting extension of the techniques discussed so far. It offers good sensitivities for a large number of elements (see Table 4) and combines some of the advantages of neutrons with those of charged particles for carrying out the activation. Samples are effectively transparent to high-energy photons, as they are to neutrons, thus simplifying standardization. The similarity with charged particles lies in the possibility of varying the energy spectrum of the bremsstrahlung photons.

The determination of most elements depends on (γ,n) type reactions[86, 87]. This has the disadvantage that practically all the radionuclides produced by such reactions are positron emitters, in which case the annihilation process giving rise to a line at 511 keV in the gamma spectrum can cause difficulties. For a number of elements the (γ,p) and (γ,γ') type reactions can also be of analytical interest.

Photon activation analysis requires a beam of gamma rays of variable energy up to about 30 MeV. The only way to produce a beam of these high-energy photons with an adequate intensity is to bombard a metal target of high atomic number with high-energy electrons, thus giving rise to the emission of bremsstrahlung radiation. The bremsstrahlung photons show a continuous spectrum, the maximum energy of which corresponds to the energy of the accelerated electrons (Figure 10). The shape of the energy spectrum depends on the target material and on the energy of the electrons. The spatial distribution of the photon beam shows a sharp maximum in the forward direction relative to the direction of the electron beam[88].

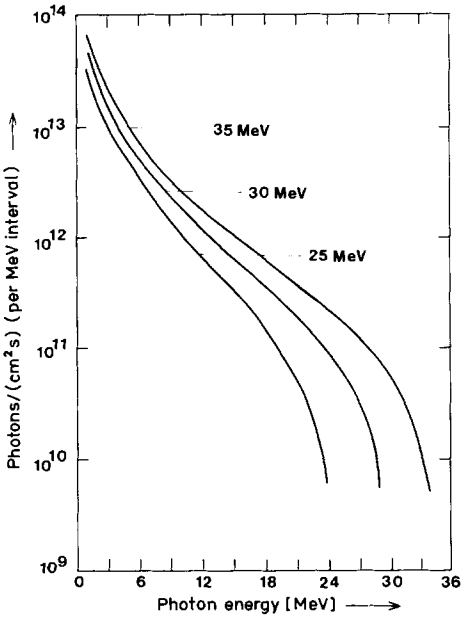


Fig. 10. Bremsstrahlung spectra produced by bombarding a tungsten target with 25-, 30-, and 35-MeV electrons [87]. Electron beam current assumed to be 100 μA.

The most important type of electron accelerator capable of producing a beam of electrons of sufficiently high energy and intensity (up to about 100 μA) is the Linac (linear accelerator)[89, 90]. It is also possible to accelerate electrons to the energies required in a betatron, but this type of machine provides neither an adequate intensity nor a sufficiently stable energy required for activation analysis.

The practical application of photon activation analysis is therefore restricted by the very small number of suitable linear accelerators which are available for such work: in the whole of the Federal Republic of Germany and West Berlin, for example, there is only one, at the Bundesanstalt für Materialprüfung in Berlin.

4.4. Interfering Nuclear Reactions

Several kinds of nuclear reactions can occur in the activation which can upset the expected proportionality between the activity of the indicator radionuclide and the amount of the element to be determined. If these interfering reactions are not taken into consideration they can be the cause of very serious systematic errors in analyses. We differentiate between

primary and secondary interfering reactions, and second-order interfering reactions.

Table 11. Examples of primary interfering reactions.

Projectile	Analytical reaction	Threshold energy [MeV]	Primary interfering reaction	Threshold energy [MeV]
Fission neutrons	$^{23}Na(n,\gamma)^{24}Na$	0	$^{24}Mg(n,p)^{24}Na$	4.9
			$^{27}Al(n,\alpha)^{24}Na$	3.2
Fast neutrons (14 MeV)	$^{28}Si(n,p)^{28}Al$	4.0	$^{31}P(n,\alpha)^{28}Al$	2.0
			$^{27}Al(n,\gamma)^{28}Al$	0
Protons	$^{51}V(p,n)^{51}Cr$	1.6	$^{55}Mn(p,\alpha n)^{51}Cr$	9.6
			$^{52}Cr(p,pn)^{51}Cr$	12.3
^{3}He-particles	$^{16}O(^3He,p)^{18}F$	0	$^{19}F(^3He,\alpha)^{18}F$	0
	+	3.8	$^{20}Ne(^3He,\alpha p)^{18}F$	3.1
	$^{16}O(^3He,n)^{18}Ne$		$^{23}Na(^3He,2\alpha)^{18}F$	0.4
	$\beta^+ \rightarrow {}^{18}F$		$^{24}Mg(^3He,2\alpha p)^{18}F$	13.5
			$^{27}Al(^3He,3\alpha)^{18}F$	11.5
Photons	$^{12}C(\gamma,n)^{11}C$	18.7	$^{14}N(\gamma,t)^{11}C$	22.7
			$^{16}O(\gamma,\alpha n)^{11}C$	26

Primary interfering reactions are those in which the indicator radionuclide is produced in nuclear reactions between the original bombarding particles and nuclei of other elements in the sample than the one being determined. Table 11 shows some examples of such interferences for the different activation techniques. These interfering reactions can often be eliminated by suitable choice of particle energy. The primary interfering reactions in activation analysis with reactor neutrons are easily predicted and can in the main also be evaluated by calculation using the appropriate nuclear data, and to a large extent this is also true for activation with 14-MeV neutrons[91]. For the other activation techniques the excitation functions are generally not known with sufficient accuracy for corrections to be carried out purely by calculation[92]. The contribution from these interfering reactions is therefore normally determined experimentally from activation curves. Figure 11 shows an example.

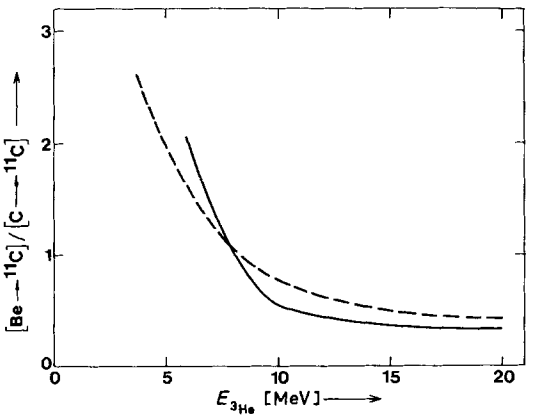


Fig. 11. The extent of interference by beryllium on the determination of carbon by activation analysis with ^{3}He as a function of the ^{3}He energy, $E_{^3He}$. Comparison of the calculated ---- [92] and experimentally found —— [93] ratio of the amount of ^{11}C formed from beryllium and from carbon. The amounts of beryllium and carbon present are assumed to be equal.

Secondary interfering reactions are those in which the indicator radionuclide is produced in nuclear reactions between secondary particles and nuclei of other elements in the sample than the one of interest. They arise almost exclusively in the case of activation with high-energy projectiles. The secondary particles can be produced in reactions between the primary projectiles and the sample material or its surroundings (see Table 12). Activation with charged particles[52-54, 80] or with photons[94] sometimes gives rise to considerable neutron fluxes (see Section 4.1.2). When organic matter is irradiated with fast neutrons, protons are produced by collisions between neutrons and hydrogen atoms. For instance, the interfering reaction $^{16}O(p,\alpha)^{13}N$ occurring in the determination of nitrogen by the reaction $^{14}N(n,2n)^{13}N$ can cause errors equivalent to several hundred ppm[95].

Table 12. Examples of secondary interfering reactions.

Projectiles	Analytical reaction	Production of secondary particles	Interfering reaction
Fast neutrons	$^{14}N(n,2n)^{13}N$	p-knock-out	$^{13}C(p,n)^{13}N$
			$^{16}O(p,\alpha)^{13}N$
Protons	$^{15}V(p,n)^{51}Cr$	(p,xn)	$^{50}Cr(n,\gamma)^{51}Cr$
			$^{52}Cr(n,2n)^{51}Cr$
Deuterons	$^{12}C(d,n)^{13}N$	Stripping, break-up, and (d,xn)	$^{14}N(n,2n)^{13}N$
Photons	$^{25}Mg(\gamma,p)^{24}Na$	(γ,xn)	$^{23}Na(n,\gamma)^{24}Na$
			$^{27}Al(n,\alpha)^{24}Na$

Second-order interfering reactions are those involving the products of the primary reactions. They fall into two categories:

1) The decay product of a radionuclide, arising from activation of a neighboring element also present in the sample, can be identical with the target nuclide of the element being determined or with its indicator radionuclide. For example, if phosphorus is to be determined in silicon *via* the reaction $^{31}P(n,\gamma)^{32}P$, then the interference arising from the processes

$$^{30}Si(n,\gamma)^{31}Si \xrightarrow[2.6\,h]{\beta^-} {}^{31}P(n,\gamma)^{32}P$$

must be taken into consideration when the phosphorus level lies below 0.1 ppm[96]. Similar interferences have been reported in about 65 cases of activation with thermal neutrons[97–100].

2) The quantity of indicator radionuclide produced can be reduced substantially if it has a high effective cross-section (say 10^3—10^4 barns) for the (n,γ) reaction. This phenomenon is known as double capture. As an example one might mention the determination of tantalum *via* ^{182}Ta as the indicator radionuclide, where, at long irradiation times, ^{183}Ta is produced *via* the processes

$$^{181}\text{Ta} \xrightarrow[21\ \text{barn}]{n,\gamma} {}^{182}\text{Ta} \xrightarrow[8200\ \text{barn}]{n,\gamma} {}^{183}\text{Ta}$$

by which an error of up to 10% can be introduced[101]. This type of interfering reaction need only be considered for very long irradiation times with high projectile fluxes, *i.e.* only in the case of activation with reactor neutrons.

The attenuation of the projectile flux within the sample itself has also to be taken into account as a possible source of systematic errors. This effect is particularly significant in activation with thermal or epithermal neutrons, since a number of elements have very high total effective capture cross-sections for these entities. As a rule, this effect must be considered when the sample contains more than one gram of a matrix element with a cross-section greater than about one barn. The attenuation of the flux can be estimated satisfactorily by calculation or by graphical correction procedures[102–105]. Similar correction procedures have also been worked out for activation with 14-MeV neutrons[106–107], or with photons[86,108]. When charged particles are used for activation, the problem to be considered is their decrease in energy as they pass through the sample[109].

5. Instrumental Activation Analysis

Whether the indicator radionuclides produced during the irradiation can be detected by purely instrumental means or must first be subjected to a radiochemical separation from the matrix elements (see Figure 1) will depend on the irradiation and cooling, on the composition of the matrix, on the decay characteristics of the activation products, and on the measuring equipment available.

5.1. Gamma-Ray and X-Ray Spectrometry

Gamma-ray spectrometry provides the basis for instrumental activation analysis[110–112]. As it involves the use of much the same equipment, X-ray spectrometry can be seen as an extension of this field. Figure 12 shows schematically the construction of a gamma-ray spectrometer. At the present time, high-resolution semiconductor detectors, such as Si(Li), Ge, and Ge(Li) detectors, are used almost exclusively. The most important performance criteria for a detector system are the energy resolution, the efficiency, the peak-to-Compton ratio, and the linearity between the pulse height and the energy of the gamma photons. Each of these three detectors exhibits its optimum performance in a different energy region of the gamma-ray spectrum, but all three offer excellent linearity.

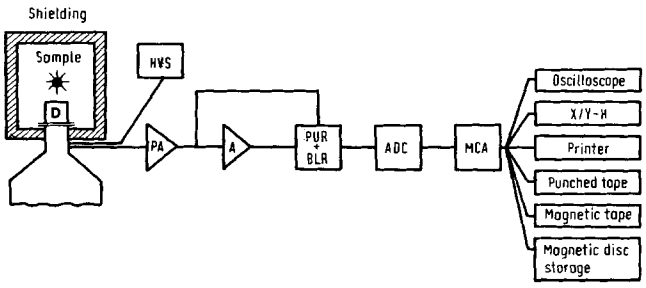


Fig. 12. Schematic construction of a gamma-ray spectrometer: D = detector; HVS = high-voltage supply; PA = pre-amplifier; A = linear amplifier (main amplifier); PUR = pile-up rejector; BLR = baseline restorer; ADC = analog-to-digital converter; MCA = multi-channel pulse-height analyzer.

The Si(Li) detectors possess exceptionally good efficiency for photon energies in the range 1—30 keV, and also offer the best energy resolution. For energies between 30 keV and about 150—200 keV small intrinsic germanium or planar Ge(Li) detectors are most suitable. An additional advantage of the intrinsic germanium detectors is that they can be stored at room temperature, while the lithium-drifted detectors must be kept permanently cooled with liquid nitrogen. These low energy photon detectors give relatively low background due to Compton scattering from gamma-rays of higher energy and permit attainment of enhanced peak-to-background ratios in the low energy region.

Gamma rays with energies higher than 150—200 keV are normally counted with a Ge(Li) detector. Large lithium-drifted germanium detectors have recently become available with an energy resolution down to 1.7 keV (FWHM) for 1.33 MeV photons, an efficiency over 30% of that of a 3×3″ NaI(Tl) crystal detector, and a peak-to-Compton ratio up to over 50:1, though they are not cheap. The efficiency depends not only on the size but also on the shape of the detector. For a given size, the maximum efficiency is obtained with a well-type detector[113,114]. However, it must be kept in mind that both the peak-to-Compton ratio and the energy resolution are lowered with this type of detector.

Users should be aware that semiconductor detectors can themselves be sources of systematic errors, due for example to the counting geometry being wrong[115], to the efficiency decreasing with time[116] or varying from one part of the detector to another[117].

The capabilities of a high-resolution gamma-ray spectrometer depend also on the electronic system[118,119], since the energy resolution, the peak symmetry, the linearity, and the time resolution are dependent both on the detector itself and on the amplification and analysis circuitry. Modern gamma-ray spectrometer systems use a FET pre-amplifier followed by a linear amplifier with "pole-zero control", "pile-up rejector", and "baseline restorer" circuits. At energies > *ca.* 100 keV and at counting rates up to around 10^4 per second, using the above-mentioned equipment, the energy resolution depends largely on the detector. In low-energy photon detection, the energy resolution has been considerably improved by using preamplifiers with "pulsed optical feedback". For example, with a lithium-drifted silicon detector or an intrinsic germanium one, a resolution of 145 eV can be achieved for photons of 5.9 keV. Inserting a "pile-up rejector" in the amplification circuit effects a significant improvement of the energy resolution at high counting rates[120], as this arrangement

permits distinction between the undistorted pulses which are accepted and the distorted ones which are rejected. An example is shown in Figure 13. It should be added, however, that the pile-up effect cannot be completely eliminated using the pile-up rejector.

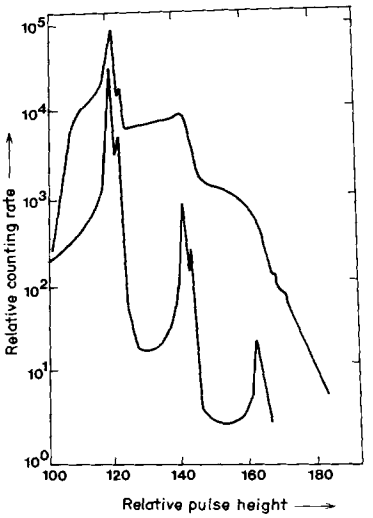


Fig. 13. Spectra of ^{55}Fe recorded without (above) and with (below) pile-up rejector, using a Ge(Li) detector system at a counting rate of 40000 cps [121].

A gamma-ray spectrometer system recently developed[122,123] is capable of producing high-quality spectra with input counting rates as high as 10^6 counts/s, with the energy resolution for the ^{60}Co peak at 1.33 MeV remaining constant up to 3.2×10^5 counts/s (see Figure 14). Electronic systems such as these are going to become of increasing importance for instrumental activation analysis, since in the detection of short-lived radionuclides high energy resolution and high counting rates are conflicting requirements.

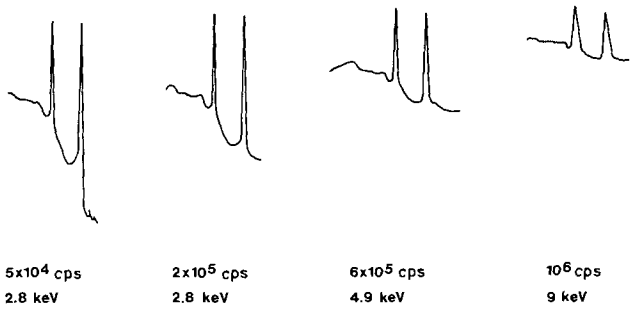


Fig. 14. Sections from gamma-ray spectra of ^{60}Co recorded with an improved high-performance gamma spectrometer system for different counting rates [123]. The energy resolution for the 1.33-MeV line is given for each case.

Computer-controlled multichannel analyzers are nowadays considered indispensible for the measurement, evaluation, and interpretation of gamma-ray spectra. The most important aspects of practically all spectrum evaluations are smoothing, peak-finding, determining the position and the net area of the peaks, peak fitting, resolving complex peaks, identifying the radionuclides present, and calculating the amount of the element present in the sample, along with limits of detection and error analysis. Numerous evaluation procedures and programs have been developed to computerize activation analysis (for a critical review, see [124]).

Because of the complexity and the great amount of data measured, efforts have been made to automate the evaluation and interpretation of gamma-ray and X-ray spectra, and even the entire measurement procedure, by incorporating an automatic sample-changer[125–127].

5.2. Special Counting Techniques

The presence of Compton continua in the spectra still presents a major problem in gamma-ray spectrometry as it can often drastically impair the limits of detection of an activation analysis procedure. The scope of instrumental activation analysis can be broadened considerably if special counting techniques are used which are highly specific or which suppress the Compton background.

Coincidence counting arrangements allow the selectivity to be improved and the limit of detection to be lowered. The two-channel system normally used consists of two detectors. Two (or more) gamma-rays to be observed in the two detector circuits are selected using two timing single-channel analyzers. Use of the coincidence technique makes it possible to employ instrumental activation analysis even at the ppb level and sometimes lower than that. The disadvantage of this technique is the considerable reduction of the counting rates and therefore the necessity of long counting times. A further inconvenience is that only one radionuclide can be measured at any one time as the equipment is effectively a single-channel spectrometer.

The performance of gamma-ray spectrometry can be significantly improved if the contribution of the Compton-scattered gamma-rays to the pulse-height spectrum is suppressed by the use of anticoincidence counting techniques[128–130]. In this technique the Compton scattering radiation in one detector is compensated for by a second detector. The electronic circuitry is so arranged that only those pulses are selected and stored which do not coincide with events in the second detector. The extent to which the Compton background can be suppressed depends very much on the size, design, and geometrical arrangement of the two detectors. Very good results can be obtained with an asymmetric arrangement like that depicted in Figure 15. As the example in Figure 16 shows, it is possible with modern anticoincidence spectrometers to reduce the Compton background by a factor of up to 20 in the low-energy part of the spectrum where it is normally most serious, and thus to improve significantly

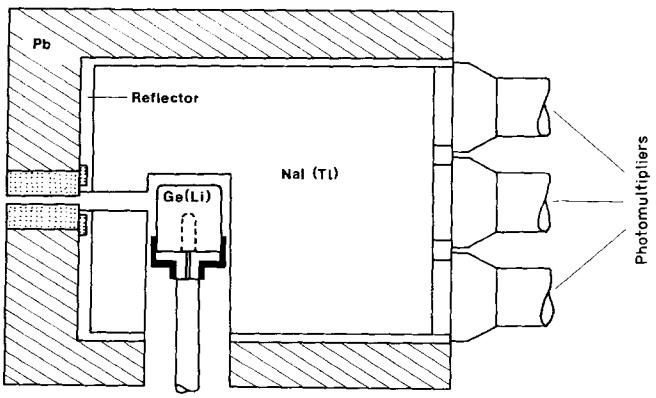


Fig. 15. Construction of a detector system for anticoincidence spectrometry.

the limit of detection of instrumental activation analysis[131]. This approach has been used with success in the analysis of biological and evironmental samples[129, 130], of meteorites and lunar samples[132], and of high-purity materials[133]. In contrast to the limitations of coincidence counting techniques, anticoincidence techniques do allow the simultaneous detection of many radionuclides in the whole energy region of interest, and, furthermore, the use of the anticoincidence principle does not cause any considerable losses in peak intensity.

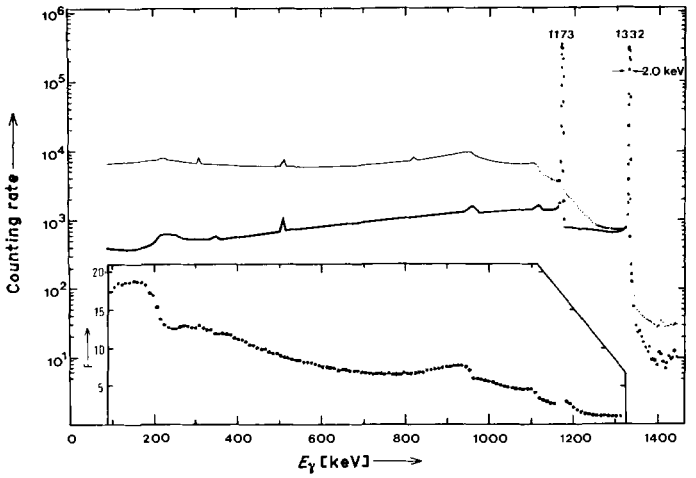


Fig. 16. Spectra of ^{60}Co, taken with a conventional gamma-ray spectrometer (upper spectrum) and taken with an anticoincidence spectrometer (lower spectrum) [131]. The Compton suppression factor F as a function of gamma energy is shown in the lower part of the figure. A 100-cm^3 Ge(Li) detector and a 9 × 9" NaI(Tl) detector were used. The numbers over the peaks are the energies of the gamma photons in keV.

A further problem in X-ray and gamma-ray spectrometry is presented by the interference due to β-particles. They give rise to bremsstrahlung which contributes significantly to the background in the low energy part of the spectrum, increase the dead-time, and impair the energy resolution of the spectrometer system. It is possible to place a magnet between the sample and the detector so that the electrons are deflected from their path and their interference is largely eliminated[133a,133b]. The background can be reduced by up to 99% by this means (see Fig. 17).

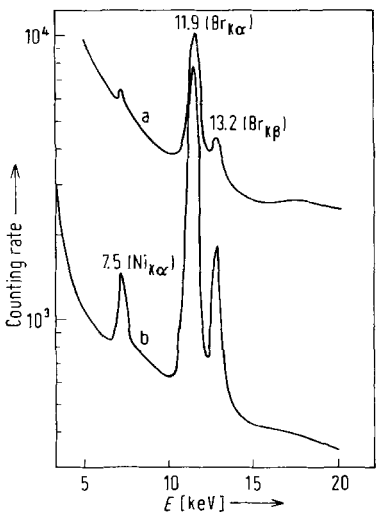


Fig. 17. X-ray spectra from a sample of hair irradiated with reactor neutrons [133b]. Sample size = 90 mg, irradiation time = 30 min, measuring time = 40 min. Curves were recorded a) without and b) with a magnetic field being used to deflect beta rays away from the detector.

6. Radiochemical Separations

The limitations of instrumental activation analysis by gamma-ray spectrometry are, as we have seen, determined largely by Compton and bremsstrahlung background, by the relatively low efficiency of the semiconductor detectors used, and by possible overlapping of gamma spectral lines from different radionuclides. For these reasons, radiochemical separations are often unavoidable.

All the common separation techniques used in trace analysis, and a few special ones as well, can be applied to activation analysis. According to the function of the separation step a distinction is to be made between a) separation of the radionuclides produced from the matrix, b) separation of groups of elements, and c) selective individual separations. The most important criteria for choice of a separation technique are high speed—dependent on the half-life of the radionuclide being determined—high yield, and high selectivity.

6.1. Removal of the Radionuclides Produced from the Matrix Elements

It is often sufficient to eliminate the activity of the matrix, or any other predominating activity, by a suitable single separation and to rely on the gamma-ray or X-ray spectrometer for subsequent resolution of the minor components. As an example we can consider the application of activation analysis to the determination of trace impurities in high-purity selenium: the ^{75}Se produced in extremely high yield from the matrix element can be removed up to 99.9999% by bromination and distillation of volatile $SeBr_4$, leaving 14 trace elements to be determined by gamma-ray spectrometry with a Ge(Li) detector[134].

When biological samples are activated by reactor neutrons, it is the ^{24}Na which is responsible for most of the activity – up to 99% in some cases. If the activity of the sodium can be specifically removed, then many elements can be determined simultaneously by gamma-ray spectrometry. Several procedures, utilizing a variety of separation principles, have been suggested for separating the sodium from the other elements, but the simple approach of *Girardi et al.*[135, 136], in which the sodium is adsorbed onto hydrated antimony pentoxide while 58 other ions are quantitatively eluted with 12 M hydrochloric acid (yields in the range 97–100%), is probably of the greatest practical importance. Almost all the essential and the toxic trace elements are included in this number. For some samples it may be necessary to remove ^{32}P, ^{82}Br, and ^{42}K before the trace elements are determined, but procedures similar to that outlined for sodium have been developed for such cases[137–139].

6.2. Group Separations

If it is not possible to tackle an analytical problem by the direct instrumental approach or by preliminary removal of the matrix activity, it may be helpful to try a group separation scheme: the radionuclides produced by activation are

separated into groups, each of which can then be examined by gamma-ray spectrometry.

When developing such separation schemes one attempts to collect in each group indicator radionuclides of similar activities but with well separated gamma energies and sufficiently different half-lives. Many useful schemes have been developed over the years, which depend on a number of basic separation principles, or combinations of these, such as liquid-liquid extraction, ion-exchange, column chromatography, and distillation. Some examples are given in Table 13. Group separation schemes have in common the advantage over individual separation procedures that they are quicker to carry out and relatively easy to automate.

Table 13. Examples of group separations used in activation analysis.

Elements and groups	Separation techniques	Typical sample material	Ref.
[Br,I,Os] [Ir,Mo,Pa,W] [Cd] [Zn] [Fe,Ca,In] [Co,Cu,Np] [Hf,Sc,Zr] [Ag] [Cr,Mn,Ni] [Ba,Ca,Mg,Sr] [Cs,K,Rb] [Na,P] [Au,Hg,Re,Tc] [Sb,Sn] [As,Se] [Lanthanoids]	Distillation, ion-exchange, extraction-chromatography	Biological	[152]
[Ag,Cl,Br] [Au,Ba,Pt,Ta] [Mn] [In] [Cu,As,Se,Sb,Pd] [Fe] [Cr,Hf,Sc] [Ni] [Co,Ga,Zn] [Ca,Sr] [K,Rb,Cs] [Lanthanoids]	Liquid-liquid extraction, precipitation	Geological	[153]
[As,Br] [Na,Ta] [Zn,Sb,Hg] [Fe,Co,Cu,Ga,Np,W,Mo] [Hf,Zr,Sc,Pa] [K,Rb,Cs,Sc,Ba,Sr,Cr,Ca] [Lanthanoids]	Distillation, adsorption, ion-exchange, liquid-liquid extraction	Geological and biological	[154]

6.3. Individual Separations

Maximum efficiency can be attained in activation analysis in terms of limit of detection, accuracy, and number of elements which can be determined when the respective indicator radionuclides are selectively separated from each other after the irradiation. The activity of each nuclide can then be measured with a simple but efficient detector system using for example a Geiger-Müller tube or a sodium iodide well-type crystal scintillation counter. This type of procedure is capable of exploiting to the full the very high potential sensitivity of activation analysis.

6.3.1. Individual Separations with Determinations of Yield

In these procedures, a known amount of carrier (1—10 mg) is added to the sample after its irradiation to assist the separation of the desired indicator radionuclide. Thus it is possible to separate a relatively high and always constant amount of the component in question—assuming that the amount of the element in the sample is negligibly small in comparison to the amount of carrier added. After chemical equilibration, the carrier is separated from the mixture of nuclides: this separation need not be quantitative, as long as the yield is determined by some conventional chemical method such as gravimetry, titrimetry, spectrophotometry, or atomic absorption spectrometry. It is even possible to add another radionuclide—a radioisotope not produced by irradiation under the conditions used for the sample—in order to check the yield. When this approach is adopted, activation analysis combined with individual separation and determination of the carrier recovery yield is capable of giving correct results even for very low concentrations of elements, at or below the ppb level.

The disadvantage of the individual separation procedure with yield determination is the high cost in terms of man-hours and use of ancillary equipment.

6.3.2. Substoichiometric Separations

The necessity of determining the yield can be avoided by making use of the principle of substoichiometry in separation[140]. In this approach the sample and the standard are irradiated simultaneously and are then treated in exactly the same way. After the irradiation and dissolution steps, the same amount of inactive carrier is added to both the sample and the standard solutions and then a fixed amount is recovered following the addition of an equal and substoichiometric amount of reagent to each solution. The relative activities of the two portions are then measured under the same conditions and the amount of the element present in the original sample is calculated on the basis of the measured activities, without the need for a yield determination.

Most of the published substoichiometric procedures involve liquid-liquid extraction of metal chelates using complexing reagents to effect the separations[141–143]; but some procedures use other separation techniques including precipitation, ion-exchange, and electrolytic deposition with equal success.

One important condition must be fulfilled when less than the stoichiometric amount of reagent is added: the reagent must still react quantitatively with the carrier element. The need to meet this condition often causes problems connected with the danger that the reagent can also react with other species present. Recently a new and universally applicable substoichiometric procedure has been developed[144] which represents a significant advance for radiochemical activation analysis, especially when one considers how simply elements even at the ppb level can be determined both precisely and accurately. In this development, similar amounts of all the matrix elements are added to both sample and standard after the irradiation step. The addition of the same amount of non-irradiated sample to the standard irradiated is the simplest and most elegant way of ensuring identical chemical conditions for the separation step on both sample and standard. The interferences which may arise do so to the same extent for

both, and the determination remains free from the unknown error. As an example one might cite the determination of traces of gold in the presence of gallium, which normally interferes strongly, in samples of silica. The exceptionally high precision for the gold value of 26.6 ± 0.3 ng could be obtained when the amount of gallium in sample and standard was varied over the range 0—2.5 mg.

6.3.3. Other Separations

In addition to the procedures just described, isotope-exchange procedures[145] and mass separators[146, 147] have been employed for certain specific separations of indicator radionuclides. The results obtained in the development of very rapid separation methods[147a, 147b] give grounds to hope that the capability of activation analysis by way of short-lived indicator radionuclides can yet be significantly improved.

6.4. Separation and Enrichment Prior to Irradiation

There are some applications in which activation analysis can only be used successfully when combined with a separation or enrichment step preceding irradiation.

Separation before irradiation is unavoidable when activation produces only a low activity of a short-lived indicator radionuclide but large activities of interfering radionuclides with a similar or even longer half-life, and when no simple, rapid dissolution and separation procedure is available.

Enrichment before irradiation is necessary if the contents of the elements to be determined are very low and therefore very large volumes of samples must be irradiated in order to achieve enough activity of the indicator radionuclides for measurement. The maximum volume of sample which can be taken for irradiation is, however, in most sources limited for technical reasons, and prolonged irradiation of liquid samples is not possible. Such problems may be encountered with a variety of samples of natural origin including water, air, and blood. Drying, ashing, chromatography, ion-exchange, extraction, coprecipitation, and other procedures have been employed for enrichment of trace elements[148].

The determination of trace elements in glacier ice samples by neutron activation analysis can serve as an example of enrichment prior to irradiation[149]. The drilled core ice pieces are melted and filtered through a membrane filter. The filtrate is treated with a small amount of ammonium nitrate as carrier for dissolved trace elements, and is then freeze-dried. The dried residue is then taken for analysis. Instrumental activation analysis is used for the determination of Al, V, Ca, Cl, Mn, Na, K, and Br, while radiochemical separations precede the determinations of Cu, Mo, Cd, Zn, As, Sb, Fe, Co, and Se along with the lanthanides. The amounts determined lie between 2×10^{-6} g for cobalt and 2×10^{-11} g for samarium.

Trace levels of Ba, Ca, Cd, Ce, Co, Cr, Cu, Fe, La, Mg, Mn, Se, V, Y, and Zn have been determined in samples of sea and fresh water by neutron activation analysis following pre-concentration of the ions on a mixture of Chelex-100[*] and glass powder[150]. Active charcoal[151] and other carrier substances have also been used as collectors for the enrichment of trace elements in water samples.

[*] The ion-exchanger Chelex-100 is a styrene-divinylbenzene copolymer containing aminodiacetic acid groups.

The wide use of this approach should not detract from the fact that the unique advantage of activation analysis in having virtually no blank or errors through losses is discarded the moment any separation or enrichment step is introduced prior to irradiation. For this reason, such procedures should be avoided whenever possible.

7. Special Activation Analysis Procedures

7.1. Activation Analysis Using Very Short-Lived Indicator Radionuclides

The technical requirements for the use of very short-lived indicator radionuclides with $t_{1/2} < 1$ s have been fulfilled in recent years. Ultra-high-speed transport systems incorporating automatic separation of the sample from the transporting capsule have been developed[155, 156] which permit measurement to be started only 30 ms after the end of irradiation; the transport time is reproducible to within $\pm 1.5\,\%$.

Another important factor upon which the detection of short-lived radionuclides depends has been the development of gamma-ray spectrometers capable of handling the extremely high counting rates involved[122, 123] (see Section 5.1). The use of such high-speed transport systems and counting equipment, together with pulsed reactors, 14-MeV neutron generators, and cyclotrons has made it possible to determine 34 elements *via* indicator radionuclides with half-lives $t_{1/2} < 1$ s, 18 of them, including Li, Be, and B, by neutron activation. These three elements, for example, cannot be determined by conventional neutron activation analysis. Table 14 presents some data for analytically interesting reactions of this type. The hard β-rays are detected by a Cherenkov counter, or by coincidence counting using two thin discs of plastic scintillator material[157]. Good limits of detection have been achieved in some cases, for example 0.5 μg for lead using reactor activation[156], and < 1 ppm for Li, B, and C using activation by charged particles[157].

Table 14. Nuclear reactions producing radionuclides with half-lives < 1 s, and properties of the reaction products.

Reaction	$t_{1/2}$ [ms]	E_{max} of the β [MeV]	E_γ [MeV]
Activation with neutrons			
$^{7}Li(n,\gamma)^{8}Li$	844	12.5	—
$^{6}Li(n,p)^{6}He$ $^{7}Li(n,pn)^{6}He$	802	3.5	—
$^{9}Be(n,p)^{9}Li$	176	13.5	—
$^{9}Be(n,\alpha)^{6}He$	802	3.5	—
$^{11}B(n,\gamma)^{12}B$	20.3	13.4	4.439 (1.3 %)
$^{11}B(n,\alpha)^{8}Li$	844	12.5	—
$^{12}C(n,p)^{12}B$	20.3	13.4	4.439 (1.3 %)
$^{13}C(n,p)^{13}B$	17.3	13.4	3.684 (7.0 %)
$^{206}Pb(n,\gamma)^{207m}Pb$	795	—	0.570 (98.0 %)
$^{207}Pb(n,n')^{207m}Pb$ $^{208}Pb(n,2n)^{207m}Pb$			1.063 (90.0 %)
Activation with charged particles			
$^{7}Li(d,p)^{8}Li$	844	12.5	—
$^{11}B(d,p)^{12}B$	20.3	13.4	4.439 (1.3 %)
$^{12}C(p,n)^{12}N$	11	16.4	4.439 (1.3 %)
$^{28}Si(p,n)^{28}P$	268	11.5	1.779 (100.0 %)
			4.497 (29.0 %)
$^{32}S(p,n)^{32}Cl$	291	11.7	2.230 (89.0 %)
			4.770 (25.0 %)
$^{32}S(^{3}He,n)^{34}Ar$	839	5.0	0.665

7.2. Analyses Involving Detection of Prompt Radiation

The detection of new particles or of gamma photons formed during a nuclear reaction has now become an important extension of conventional activation analysis. The so-called prompt radiation is usually emitted within 10^{-14} s following the particle capture event leading to the creation of a compound nucleus.

The measurement of prompt gamma rays following neutron capture has made it possible to determine numerous elements with low limits of detection[158]. The gamma rays have energies lying between 50 keV and about 10 MeV. The gamma-ray spectra are relatively complex, as a result of numerous intermediate energy levels, but are nevertheless characteristic for each target nuclide. The sensitivity of the technique depends only on the product $\Phi\sigma$ (see Section 2), and the nuclear properties of the product nuclide, which can also be stable, do not affect the performance. This technique is of special interest for those elements which cannot be determined by conventional activation analysis (or can, but with very poor sensitivity) because of the unfavorable properties of indicator radionuclides produced. As an example we can quote boron, which cannot be determined at all by conventional methods, but which can be determined with high sensitivity if the prompt gamma photons are counted. Table 15 presents essential data for a few elements which can be determined successfully by this technique. Prompt gamma measurement techniques are also of interest for *in situ* analyses (see Section 8.2). It is also possible to detect prompt charged particles produced in nuclear reactions arising from neutron irradiation, which opens up yet another range of applications.

Table 15. Limits of detection for analysis by detecting prompt gamma radiation from neutron-capture processes [158].

Element	Low energy region		High energy region	
	E_γ [MeV]	Limit of detection in g [a]	E_γ [MeV]	Limit of detection in g [a]
B	0.477	2×10^{-10}	—	—
Cl	1.163	4.6×10^{-8}	6.111	5×10^{-7}
Sc	0.228	2.4×10^{-8}	8.175	1.6×10^{-6}
Ti	1.378	1×10^{-7}	6.759	1×10^{-6}
Mg	0.212	2.8×10^{-7}	7.243	2.4×10^{-6}
Fe	0.353	8×10^{-7}	7.631	6×10^{-6}
Co	0.230	2.6×10^{-8}	6.877	1.5×10^{-6}
Ni	0.465	3×10^{-7}	8.999	2.0×10^{-6}
Cu	0.279	2.2×10^{-7}	7.914	4.3×10^{-6}
Rh	0.181	1.1×10^{-8}	5.917	7.0×10^{-6}
Ag	0.198	1.6×10^{-8}	—	—
Cd	0.559	7×10^{-10}	5.824	2×10^{-7}
In	0.276	5.3×10^{-9}	—	—
Gd	0.182	1×10^{-10}	6.749	8×10^{-8}
Ir	0.217	1.2×10^{-8}	5.958	5.4×10^{-6}
Au	0.216	6.5×10^{-8}	6.252	3.2×10^{-6}
Hg	0.371	2.9×10^{-9}	5.967	2.5×10^{-7}

[a] Estimate based on a thermal neutron flux $= 1.5 \times 10^{10}$ neutrons cm^{-2} s^{-1}; counting time = 20 min.
Limit of detection is taken as being that amount of an element which gives rise to a counting rate equal to twice the standard deviation of the background.

If charged particles are used to bombard the sample, analyses can be carried out by measuring the elastically scattered original particles[159-162], the new charged particles produced as a result of a nuclear reaction[163,164], neutrons, γ-rays[165,166], or the emitted X-rays[167,168]. Each of these types of prompt radiation can be identified by its energy, characteristic of the nuclide from which it originates, and this permits their analytical utilization. The latest developments in this field involve the use of different kinds of detectors so as to be able to observe several different processes occurring simultaneously by looking at the different kinds of radiation emitted. Figure 18 is a diagrammatic representation of such an arrangement.

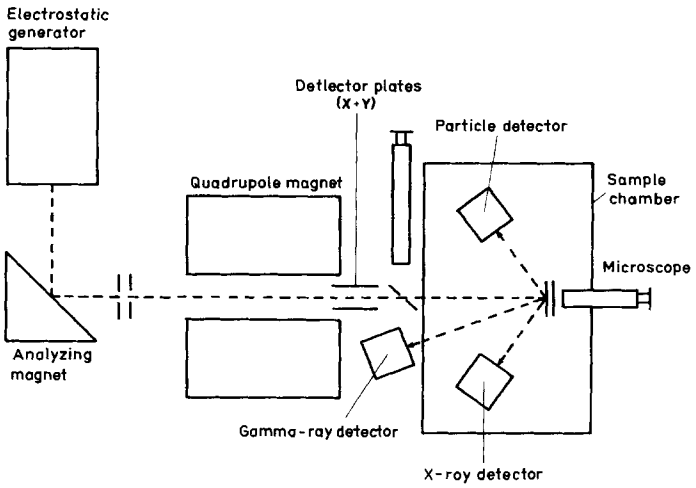


Fig. 18. Schematic construction of a nuclear microprobe [169].

8. Applications

Activation analysis occupies an important position, indeed very often a key position, in all those areas of science, industry, and medicine where the most minute amounts of elements have to be determined. Table 16 summarizes the most important fields of application and also the individual scope of the various activation techniques.

8.1. High-Purity Materials and Reagents

Activation analysis is probably the most effective analytical technique known for characterizing high-purity materials and reagents in terms of the trace element contents. For the determination of elements with $Z > 11$, activation with reactor neutrons has the greatest practical significance. There is hardly a single type of material of scientific or technological interest which has not been investigated by this technique[170]. Multi-element analyses of many high-purity materials have been carried out for trace impurities at the ppb and ppt[*] level: *e.g.* silica[171], optical glasses[172], aluminum[173], titanium[174], selenium[134], palladium, platinum, rhodium and gold[175], gallium phosphide[176], various reagents[176-178], and catalysts[179]. A procedure involving a long irradiation in a medium flux reactor followed by specific separation of the indicator radionuclides made it possible to determine 25 ppt of chromium, 7 ppb of iron, and 19 ppt of cobalt in high-purity niobium[179a]. The use of an anti-Compton spectrometer permitted the determination of 24 elements in high-purity lead at levels < 1 ppm by instrumental neutron activation analysis[133].

[*] ppt = parts per trillion = 10^{-12} g/g.

Table 16. Applications of activation analysis. MEA = multi-element analysis; ● technique very well suited; ○ technique only suitable under certain conditions; — technique has little to offer.

Application	Activation technique					
	Reactor neutrons	14-MeV neutrons	Cyclotron neutrons	Neutrons from isotope sources	Charged particles	Photons
MEA, $Z \gtrsim 11$ Geology and cosmology	●	○	○	●	●	●
MEA, $Z \gtrsim 11$ High-purity and technical materials	●	○	○	○	●	○
MEA, $Z \gtrsim 11$ High-purity reagents	●	—	○	○	○	○
Determination of light elements (Li, Be, B, C, N, O, P)	—	○	○	—	●	●
MEA, $Z \gtrsim 11$ Aerosols and water	●	○	●	○	○	●
MEA, $Z \gtrsim 11$ Biological material	●	○	○	○	○	●
On-line process control	—	○	—	●	—	—
In situ analysis	—	●	—	●	—	—
In vivo analysis	—	●	●	●	—	—
Surface and local microanalysis	—	—	—	—	●	—

For some trace analytical problems activation with charged particles is more appropriate than that with reactor neutrons. Thus, while cobalt can be determined with very high sensitivity by neutron activation analysis (the limit of detection for cobalt in niobium is about 4 ppt[179a]), proton activation analysis can be used to determine 14 elements nondestructively in a cobalt matrix[180]. Instrumental proton activation analysis has been employed in the analytical characterization of tantalum[180a], rhodium[180b], aluminum[180c], various semiconductors[180d], niobium[181], and other materials. In the case of niobium, as little as 0.2 ppb of chromium and 5 ppb of iron can be detected if radiochemical proton activation analysis is used[181a].

Activation with charged particles is the only technique which can be used for the determination of practically all the light elements (H, Li, Be, B, C, N, O, and F) at the ppb level (see Table 10). Some very thorough investigations into the systematic errors from surface oxygen and recoil oxygen[182–185] have made it possible to determine oxygen at the 1-ppm level with an accuracy of around $\pm 10\%$[186]. The elements C, N, O, and F can, however, also be determined satisfactorily by photon activation analysis[187,188]. The most suitable technique for the determination of oxygen at levels above 1—5 ppm would seem to be activation with 14-MeV neutrons[13,189,190], a technique which is now used routinely in industry for this application. A precision of 1% relative is attainable by this means[191].

8.2. Geochemical and Cosmochemical Applications

Neutron activation analysis is one of the most important analytical tools for these branches of science[192–195]. Of the 74 elements which have been detected in the standard rocks G-1 and W-1, 63 have been determined by activation analysis, seven of them only by this means[196]. At least 60 elements have so far been determined in stony and iron meteorites by the same approach.

Activation with reactor neutrons followed by radiochemical separation has enabled a number of elements to be determined even at the ppt level: *e.g.* 4 ppt iridium in basalt BCR-1, a U.S. Geological Survey silicate rock standard, or 9 ppt in andesite AGV-1[197]. Radiochemical separation procedures have been used for the determination of 39 elements in geological samples[153], 42 elements in lunar samples[198], and 38 in meteorites[199]. Very often instrumental analysis can make a useful contribution: depending on the type of sample, up to over 20 elements can be determined simultaneously, *e.g.* 23 in U.S. Geological Survey standards (a sub-alkaline basalt and rhyolite)[200], 24 in granitic rocks[201], 25 in plagioclases, pyroxenes, and magnesite[202], and 23 in iron meteorites[203].

If the activity of the irradiated sample is measured not only with a conventional Ge(Li) detector but also with a planar low-energy Si(Li) detector or an intrinsic germanium detector, then it is possible to obtain results with a better precision and accuracy, and to increase the number of elements which can be determined instrumentally, *e.g.* in basaltic rocks up to 34 elements[204]. Sometimes, activation with epithermal neutrons can be advantageous[39–42]. Activation with 14-MeV neutrons is a well suited technique for the determination of O, F, Si, Al, and P[190].

In situ measurement techniques are playing an increasingly important role in the earth sciences. Probes with a diameter



Fig. 19. A mobile field laboratory (Mobil Research and Development Corporation, Dallas) for activation analysis with 14-MeV neutrons using a bore-hole probe consisting of a pulsed 14-MeV neutron generator, a gamma-ray detector, and a neutron detector.

of only 4.3 cm have been developed for lowering down test bore-holes, which have a pulsed 14-MeV neutron source and both gamma-ray and neutron detectors[204]. Such probes offer particular advantages as far as the problem of radiation protection is concerned. Similar probes have been constructed using ^{252}Cf sources: one containing 170 μg of ^{252}Cf and a planar intrinsic germanium detector with an area of 200 mm^2, has an overall diameter of 7.3 cm and a length of 1.7 m[205]. Borehole probes such as these can be used as mobile analyzers (Figure 19) for investigating the porosity, mineral composition, and ore-metal content of rocks in geological prospecting[204–207], as well as for studying deep-sea sediments[208]. The successful surface analysis of other planets is of course one of the more striking examples of the kind of work these probes can accomplish[209].

Activation with charged particles has been used for the determination of lithium and boron[210, 211], while up to 30 elements may be determined in garden soil samples by photon activation analysis[212].

8.3. Environmental Analysis

Instrumental neutron activation methods are being used on an increasing scale for carrying out elemental analysis of environmental samples. The potential of activation analysis for analyzing atmospheric samples has been widely studied (*e.g.* [213–221]). If the samples are irradiated twice (for 5 min and then later for 7—21 h) in a neutron flux of 10^{12} neutrons cm^{-2} s^{-1} and left for three different cooling times before counting, then 33 elements can be determined by instrumental means, including most of the toxic ones such as arsenic, antimony, and mercury[213]. In another approach, three cycles of irradiation, cooling, and counting (2 min + 10 min, 10 min + 10—15 h, and 7 days + 1—3 weeks) employing a neutron flux of 9×10^{13} neutrons cm^{-2} s^{-1} enabled 42 elements to be determined in atmospheric aerosols, again by instrumental techniques. Silicon and oxygen were determined separately by irradiation with 14-MeV neutrons[221]. If it is necessary to improve the limit of detection and/or the accuracy of any of the determinations, then one or more radiochemical separations can be introduced. Instrumental neutron activation analysis has also been used to look for trace elements in hair, to see to what extent it can be used as a monitor for the pollution of the environment by inorganic toxins as far as it affects people[35, 221a].

Instrumental and radiochemical neutron activation procedures have often been used for multi-element analyses of drinking water[222–224], rain water[225, 226], river water[218, 222, 227], lake water[222], seawater[225, 228], and various other water samples[218, 229].

Other environmental samples which have been investigated have included fly ash and similar industrial emissions[230–232], automobile exhaust emissions[233], and cigarette smoke[234].

Activation with photons[235–238] and with charged particles[239–242] has also been used to advantage in some special environmental problems.

8.4. Biological and Medical Applications

It is now recognized that in addition to the principal body-building elements, a number of trace elements, including F, Si, V, Mn, Cr, Fe, Co, Ni, Cu, Zn, Se, Mo, Sn and I, are essential for growth and health in mammals both animal and human. Just as important, however, is the recognition that some elements are toxic for the same group of species, *e.g.* Li, Be, As, Br, Ag, Cd, Sb, Ba, Pb, and Bi, though to widely differing extents. Activation analysis with reactor neutrons, having proved to be a very effective method for the determination of most of these trace elements in biological samples, is nowadays widely used for this task[243–247]. Researchers have so far been able to determine 43 elements in such samples by direct instrumental activation analysis. Separation procedures can of course be incorporated if need be for particularly awkward cases[248] (see Section 6). The outstanding sensitivity of activation analysis comes into its own for the investigation of biopsy samples, which are normally only about 2—10 mg in total: this is an excellent example of multi-element micro-trace analysis.

With the help of this technique, samples from nearly every part of the human body have been analyzed: whole blood, blood plasma and serum[249, 250], urine[251], lung[252], liver[253], kidney[254], placenta[240], bone[255], and hair[256] for example. The collaboration between activation analysts and medical researchers has resulted in a much deeper understanding of the function of trace elements in the body, and of the correlation between the amounts present and the occurrence of different diseases. Because of this, activation analysis can now play a role in diagnostic medicine[257], particularly in diagnosing certain diseases which give rise to significant changes in the levels of some trace elements in the blood or in the tissue of specific organs. It is easy to see how important the accuracy of these analytical results is for establishing the "normal" values for these elements, and even more so when actual clinical samples are being handled. As is the case with most biological samples, the factors involved in taking the sample so as to ensure its homogeneity and that it is representative of the whole are added to the usual problems of sample handling for all trace analyses[258, 259, 259a].

Various kinds of samples from animals[260–263], plants[264, 265], and foodstuffs[266–269] have also been subjected to activation analysis. A more recent application of activation techniques has been to aid in the elucidation of the pathways of trace elements from the environment into the human body[270].

A special field of application of activation analysis has been the determination of trace elements *in vivo*, making use of neutrons from isotope sources[271–274], 14-MeV neutrons[275], and cyclotron-produced neutrons[276–278]. The elements N, Na, P, Cl, Ca, Cu, Cd, and I have been the ones usually determined, either in specific organs or in whole-body analyses. The *in vivo* technique creates problems for the researcher, however, both ethical (concerning the acceptable radiation dose) and experimental (concerning standardization procedures), but it nevertheless seems to be developing into a useful analytical tool. The problems of standardization associated with whole-body analyses are to some extent being overcome by the use of anthropomorphic "phantoms" of the same size, shape, and approximate elemental composition as the human body[278a].

In addition to activation with neutrons, activation with photons[279, 280] and with charged particles[281] also offer interesting possibilities in this field, and significantly extend

the number of elements which can be determined. As an example, the lead content of teeth can be determined by activation with ^{3}He projectiles[282].

8.5. Other Applications

Other fields in which problems have been solved by means of activation methods are archaeometry[283], archaeology, and history of art[284–287], forensic science[288], and isotopic analysis[289,290].

8.6. Local Microanalysis and Surface Analysis

While the total amount of an element present in a sample has usually been the main point of interest in the past, increasing attention is now being paid to the spatial distribution of the traces in a matrix. In many cases, physical and mechanical properties of materials are strongly dependent on local variations in the levels of trace constituents. Such problems can often be studied by combining activation analysis with autoradiography[30,291,292]. Figure 20 shows an example of such an application. A significant advance in the evaluation of the two-dimensional pictures has been the use of colored autoradiograms[293]. The continuous shades of gray in the conventional autoradiograms are transformed into different color shades by a special process. The quantitative relationship between concentration of the element present and the color shade is found by treating standards in the same way as the samples. The technique has been used to investigate the distribution of doping elements and of contaminants in silicon, and of tantalum and tungsten in high-purity niobium to be used as a superconductor: concentrations of impurities at the ppb level can be detected this way, *e.g.* of phosphorus and gold in silicon. The same combination of activation by irradiation with neutrons followed by autoradiography has been applied to the study of distributions of elements in geological and biological materials.

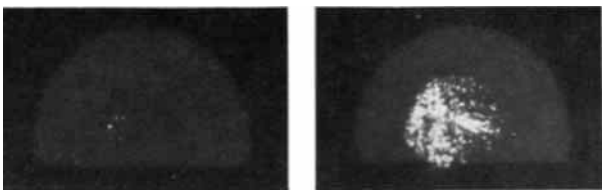


Fig. 20. Autoradiograms of silicon doped with iron, after neutron activation [30]. Left: beginning of iron deposition; right: pronounced iron deposition. Distance apart of the samples in the silicon rod was 5 cm.

In recent years the nuclear microprobe has been developed for investigating variations in concentrations of elements across a sample. A beam of accelerated charged particles can be focused by a quadropole magnet to a diamater of about 3 μm in such instruments[294–296]. The analytical measurement can be based on any of four principles: 1) on the conventional activation process, with the activity of the indicator radionuclide being measured, 2) on the measurement of new particles or gamma photons released in the nuclear reaction, 3) on the measurement of the elastically scattered primary particles, and 4) on the measurement of X-rays excited in the irradiation.

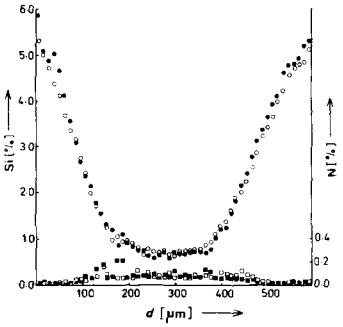


Fig. 21. Silicon and nitrogen profiles in a 20/25 niobium steel after contact with Si_3N_4 at 1000°C for 1173 hours, taken with a nuclear microprobe [169]. ○, ● silicon values, 1st and 2nd measurement; □, ■ nitrogen values, 1st and 2nd measurement. d = distance from the surface of the sample.

When this approach is applied to surface analysis[162,164,297–299], limits of detection of 0.01 μg cm^{-2} are attainable, with a resolution in depth of 10—20 μm, and all the light elements including hydrogen can be determined. Some examples are given in Table 17, and Figure 21 shows as an example a concentration profile determined by this means. Yet another example of this approach is given by the determination of concentration profiles of some elements in human teeth[300].

8.7. Industrial Applications

Many branches of industry are already making use of activation analysis, not only in research and development, but also on the production line, to monitor raw materials, intermediates, and finished products as well as environmental samples. The principal field of application of activation analysis is the metallurgical industry[301], although it plays a useful part in other areas of industry[302,303] including those concerned with electronics, oil processing, nuclear materials, building

Table 17. Examples of surface analysis by measurement of prompt radiation during bombardment with charged particles.

Element to be determined/ Target nuclide	Reaction	Particle energy [MeV]	Sample	Limit of detection
H/^{1}H	^{19}F,α	16.3–17.5	Lunar materials	Resolution in depth = 10 nm
N/^{14}N	d,p	1–3	Iron	0.01 μg/cm^2
O/^{16}O	d,p	1.2–3	Various metals	0.01 μg/cm^2
Al/^{27}Al	p,γ	2.5	Oxides	Resolution in depth = 10 nm
S/^{32}S	p,p′	3–4	GaSb	2×10^{18} atoms/m^2

materials, paper, textiles and foodstuffs, often for solving specific analytical problems, but sometimes also for automatic process control work. Many highly specialized problems have also been solved through activation methods, for example in an investigation of mass transfer on low-current contacts of electrical switches[304]. There are many irradiation facilities with associated laboratories in nuclear research centers which are available for use by industrial concerns (see Table 18),

Table 18. Radiation facilities with associated laboratories for use by industrial concerns in the European community [305].

Radiation source	Number available
Reactors	25
Isotope sources	15
14-MeV neutron generators	17
Cyclotrons	9
Low-energy particle accelerators	6
Linear accelerators	4

though a number of companies have purchased their own reactors specifically for analytical purposes (such as the mining and metallurgical complex at Noril'sk in the USSR[306] and the Dow Chemical Co in the USA[307]). While a reactor may be considered something of a luxury by most companies, many have invested in 14-MeV neutron generators, isotope neutron sources, and Van de Graff generators.

Received: April 3, 1978 [A 253 IE]
German version: Angew. Chem. *91*, 132 (1979)
Translated by Dr. *Iain Marr*, Aberdeen (Scotland)

[1] *N. B. Hannay* in *W. W. Meinke, B. F. Scribner:* Trace Characterization, Chemical and Physical. NBS Monograph No. 100, U.S. Government Printing Office, Washington 1967, p. 5.
[2] *M. Balarin*, Wiss. Fortschr. *21*, 111 (1971).
[3] *J. J. Dulka, T. H. Risby*, Anal. Chem. *48*, 640A (1976).
[4] *M. C. Lovell, A. J. Avery, M. W. Vernon:* Physical Properties of Materials. Van Nostrand Reinhold, New York 1976.
[5] *E. J. Underwood:* Trace Elements in Human and Animal Nutritions. 4th Edit. Academic Press, New York 1977.
[6] *J. Heinonen, O. Suschny*, J. Radioanal. Chem. *20*, 499 (1974); *G. Tölg*, Erzmetall *28*, 390 (1975).
[7] *Ph. D. LaFleur:* Accuracy in Trace Analysis: Sampling, Sample Handling, Analysis. NBS Spec. Publ. 422, Vol. II. U.S. Depart. of Commerce 1976.
[8] *Ph. Albert* in [7], p. 759.
[9] *T. Hirschfeld*, Anal. Chem. *48*, 16A (1976).
[10] *H. J. M. Bowen, D. Gibbson:* Radioactivation Analysis. Clarendon Press, Oxford 1963.
[11] *P. Kruger:* Principles of Activation Analysis. Wiley, New York 1971.
[12] *D. De Soete, R. Gijbels, J. Hoste:* Neutron Activation Analysis. Wiley, New York 1972.
[13] *S. S. Nargolwalla, E. P. Przybylowicz:* Activation Analysis with Neutron Generators. Wiley, New York 1973.
[14] *J. M. A. Lenihan, S. J. Thomson*, Advances in Activation Analysis, Vol. 1. Academic Press, London 1969.
[15] *J. M. A. Lenihan, S. J. Thomson, V. P. Guinn*, Advances in Activation Analysis, Vol. 2. Academic Press, London 1972.
[16] *F. F. Dyer, L. C. Bate:* Nuclear Data in Science and Technology. Proc. Symp., Vol. II, IAEA, Wien 1973, p. 386.
[17] *J. M. Bewers, G. J. Pearson:* Nuclear Data in Science and Technology. Proc. Symp., Vol. II, IAEA, Wien 1973, p. 229.
[18] *P. F. Schmidt, D. J. McMillan*, Anal. Chem. *48*, 1962 (1976).
[19] *V. Krivan:* Nuclear Data in Science and Technology. Proc. Symp., Vol. II, IAEA, Wien 1973, p. 193.
[20] *F. Girardi, G. Guzzi, J. Pauly*, Anal. Chem. *37*, 1085 (1965).
[21] *A. Alian, H.-J. Born, J. I. Kim*, J. Radioanal. Chem. *15*, 535 (1973).
[22] *A. Simonits, F. De Corte, J. Hoste*, J. Radioanal. Chem. *24*, 31 (1975).
[23] *A. Simonits, F. De Corte, J. Hoste*, J. Radioanal. Chem. *31*, 467 (1976).
[24] *M. Heurtebise, J. A. Lubkowitz*, Anal. Chem. *43*, 1218 (1971).
[25] *Y. Oka, T. Kato, H.-T. Tsai, K. Nomura*, Bull. Chem. Soc. Jpn. *41*, 329 (1968).
[26] *Y. Oka, T. Kato, H.-T. Tsai*, Bull. Chem. Soc. Jpn. *41*, 2427 (1968).
[27] *T. J. Murphy* in [7], p. 509.
[28] *M. Zief, J. W. Mitchell:* Contamination Control in Trace Element Analysis. Wiley Interscience, New York 1976.
[29] *G. Tölg*, Naturwissenschaften *63*, 99 (1976).
[30] *J. A. Martin, E. Haas, G. Fischer*, Z. Anal. Chem. *265*, 122 (1973).
[31] *B. Maziere, A. Gaudry, J. Gross, D. Comar*, Radiochem. Radioanal. Lett. *28*, 155 (1977).
[32] *L. J. Walters, Jr., J. W. Winchester*, Anal. Chem. *43*, 1020 (1971).
[33] *A. Schubiger, A. Wyttenbach*, Chem. Rundsch. *30*, No. 20, p. 16 (1977).
[33a] *R. E. Kay, J. W. Hilborn, P. D. Stevens-Guille, R. E. Jervis*, Int. J. Appl. Radiat. Isot. *24*, 509 (1973).
[34] *R. E. Jervis, J. J. Paciga, A. Chattopadhyay:* Measurement, Detection, and Control of Environmental Polutants. Proc. Symp., IAEA, Wien 1976, p. 125.
[35] *R. E. Jervis, B. Tiefenbach, A. Chattopadhyay*, J. Radioanal. Chem. *37*, 751 (1977).
[36] Handbook on Nuclear Activation Cross-Sections. Technical Report Series No. 156, IAEA, Wien 1974.
[37] *W. Marth:* Bestrahlungstechnik an Forschungsreaktoren. Thiemig, München 1969.
[38] *F. Rossitto, M. Terrani, S. Terrani*, Nucl. Instrum. Methods *103*, 77 (1972).
[39] *A. O. Brunfelt, E. Steinnes*, Anal. Chim. Acta *48*, 13 (1969).
[40] *M. Jannsens, B. Desmet, R. Dams, J. Hoste*, J. Radioanal. Chem. *26*, 305 (1975).
[41] *E. Steinnes*, Anal. Chem. *48*, 1440 (1976).
[42] *A. O. Brunfelt, I. Roelandts, E. Steinnes*, J. Radioanal. Chem. *38*, 451 (1977).
[43] *D. Brune*, Anal. Chim. Acta *46*, 17 (1969).
[44] *H. Al-Shahristani, K. Abbass*, J. Radioanal. Chem. *27*, 105 (1975).
[45] *N. V. Bagdavadze, L. M.* Mosulishvili, J. Radioanal. Chem. *24*, 65 (1975).
[46] *A. G. Hanna, H. Al-Shahristani*, J. Radioanal. Chem. *37*, 581 (1977).
[47] *J. Rowe, E. Steinnes*, J. Radioanal. Chem. *37*, 849 (1977).
[48] *S. M. Qaim*, Z. Naturforsch. *25*, 1977 (1970).
[49] *S. M. Qaim:* Nuclear Cross Sections and Technology. Vol. II, Proc. Conf., Washington, D.C., March 3—7, 1975, NBS Spec. Publ. 425, p. 664.
[50] *K. A. Schmidt, H. Dohrmann*, Atomkernenergie *27*, 159 (1976).
[51] *R. E. Wainerdi, R. Zeisler, E. A. Schweikert*, J. Radioanal. Chem. *37*, 307 (1977).
[52] *J. R. DeVoe, Ph. D. LaFleur:* Modern Trends in Activation Analysis. Proc. 1968 Intern. Conf., NBS Spec. Publ. 312, Vol. II, U.S. Depart. of Commerce 1969.
[53] *A. A. Fleischer* in [52], p. 868.
[54] *L. Hannappel, H. Schneider*, Kerntechnik *17*, 36 (1975).
[55] *V. Krivan, H. Münzel*, J. Radioanal. Chem. *15*, 575 (1973).
[56] *K. Schmidt, H. Münzel*, KFK-Bericht 1288, Kernforschungszentrum Karlsruhe 1970.
[57] *V. Krivan, H. Münzel*, J. Inorg. Nucl. Chem. *34*, 2093, 2989 (1972).
[58] *W. Bäuerle, V. Krivan, H. Münzel*, Anal. Chem. *48*, 1434 (1976).
[59] *C. Vandecastelle, A. Speecke, J. Hoste*, J. Radioanal. Chem. *37*, 255 (1977).
[60] *H. Münzel, F. Michel, M. R. Coetzee, V. Krivan*, J. Radioanal. Chem. *37*, 267 (1977).
[61] *K. Boddy, I. Robertson, J. E. Harrison*, J. Nucl. Med. *14*, 427 (1974).
[62] *T. B. Pierce:* ITE-Report No. 83. Commission of the European Communities, Euroisotop Office, 1975.
[63] Californium-252 Progr. *18*, 30 (1975).
[64] *G. J. Lutz:* Proceedings of an Education Seminar on the Uses of Californium-252 in Teaching and Research. Karlsruhe, April 14—18, 1975, IAEA, Wien 1976, p. 73.
[65] Californium-Progr. *18*, 27 (1976).
[66] Californium-Progr. *20*, 31 (1976).
[67] *N. A. Wogman, H. G. Rieck, J. C. Laul*, Nucl. Instrum. Methods *141*, 539 (1977).
[68] *J. R. Beyster, L. A. Kull*, Report BNL 50267 (T-596). Brookhaven National Laboratory, 1970.
[69] *N. D. Tyufyakov, L. A. Trykov, A. S. Shtan*, At. Energ. (UdSSR) *34*, 349 (1973).
[70] *L. Alaerts, J. Op de Beeck, J. Hoste*, Anal. Chim. Acta *69*, 1 (1974).
[71] *L. Alaerts, J. Op de Beeck, J. Hoste*, J. Radioanal. Chem. *38*, 205 (1977).
[72] *V. Krivan*, Z. Anal. Chem. *290*, 193 (1978).
[73] *Ch. Engelmann:* Radiochemical Methods of Analysis, Proc. Symp. Salzburg, Oct. 19—23, 1964, IAEA, Wien 1965, p. 405.
[74] *E. Ricci, R. L. Hahn*, Anal. Chem. *39*, 794 (1967).
[75] *B. Broderie, J. N. Barrandon, J. L. Debrun*, J. Radioanal. Chem. *37*, 297 (1977).
[76] *J. R. McGinley, L. Zikovsky, E. A. Schweikert*, J. Radioanal. Chem. *37*, 275 (1977).
[77] *P. P. Dmitriev, N. N. Krasnov, G. A. Molin, M. V. Panarin*, At. Energ. (USSR) *31*, 157 (1971).

[78] *Ch. Engelmann*, J. Radioanal. Chem. *7*, 89 (1971).
[79] *B. V. Zatolokin, I. O. Konstantinov, N. N. Krasnov*, Int. J. Appl. Radiat. Isot. *27*, 159 (1976).
[80] *K. Krivan, V. Krivan*, Z. Anal. Chem., in press.
[81] *D. L. Swindle, E. A. Schweikert*, Anal. Chem. *45*, 2111 (1973).
[82] *V. Krivan*, J. Radioanal. Chem. *26*, 251 (1975).
[83] *P. P. Dmitriev, Z. P. Dmitrieva, N. N. Krasnov, G. A. Molin, M. V. Panarin*, At. Energ. (UdSSR) *38*, 100 (1975).
[84] *P. P. Dmitriev, N. N. Krasnov, G. A. Molin, M. V. Panarin*, At. Energ. (USSR) *33*, 853 (1972).
[85] *M. S. Livingston, J. P. Blewett:* Particle Accelerators, McGraw-Hill, New York 1962.
[86] *G. J. Lutz*, Anal. Chem. *43*, 93 (1971).
[87] *G. J. Lutz*, Anal. Chem. *41*, 424 (1969).
[88] *L. I. Schiff*, Phys. Rev. *70*, 87 (1946).
[89] *P. Jost, P. Reimers, P. Weise:* BAM-Bericht Nr. 26. Bundesanstalt für Materialprüfung, Berlin 1974.
[90] *M. Yagi, K. Kondo*, J. Radioanal. Chem. *36*, 247 (1977).
[91] *V. Krivan, K. Krivan*, J. Radioanal. Chem. *29*, 145 (1976).
[92] *V. Krivan* in [7], p. 1189.
[93] *J. L. Debrun, J. H. Barrandon, Ph. Albert* in [52], p. 768.
[94] *J. S. Hewitt, K. G. McNeill, J. W. Jury*, Nucl. Instrum. Methods *80*, 77 (1970).
[95] *S. C. Mathur, G. Oldham*, Nucl. Energy *1967*, Sept./Oct., p. 136.
[96] *A. Kant, J. P. Cali, H. D. Thompson*, Anal. Chem. *28*, 1867 (1956).
[97] *J. P. Op de Beeck*, J. Radioanal. Chem. *3*, 431 (1969).
[98] *J. P. Op de Beeck*, J. Radioanal. Chem. *4*, 137 (1970).
[99] *W. Maenhaut, J. P. Op de Beeck*, J. Radioanal. Chem. *5*, 115 (1970).
[100] *V. K. Yurtchenko, E. N. Gilbert, G. V. Veriovkin, V. A. Mikhailov*, J. Radioanal. Chem. *41*, 137 (1977).
[101] *W. Gebauhr*, Z. Anal. Chem. *185*, 339 (1962).
[102] *P. F. Zweifel*, Nucleonics *18*, 174 (1960).
[103] *J. Gilat, Y. Gurfinkel*, Nucleonics *21*, 143 (1963).
[104] *O. T. Hogdal:* Radiochemical Methods of Analysis. Proc. Symp. Salzburg, Oct. 19—23, 1964, IAEA Wien 1965, p. 23.
[105] *E. Gruber*, Z. Anal. Chem. *263*, 194 (1973).
[106] *S. S. Nargolwalla, M. R. Crambers, J. A. DeVoe*, Anal. Chem. *40*, 666 (1968).
[107] *C. Vandecastelle, R. van Grieken, R. Gijbels, A. Speecke*, Anal. Chim. Acta *64*, 187 (1973).
[108] *G. J. Lutz* in [52], p. 829.
[109] *E. Ricci*, Act. Anal. *2*, 221 (1972).
[110] *C. E. Crouthamel:* Applied Gamma-Ray Spectrometry. 2nd Edit., Pergamon Press, New York 1970.
[111] *K. Siegbahn:* Alpha-, Beta- and Gamma-Ray Spectroscopy. 3rd Edit. North-Holland, Amsterdam 1974.
[112] *R. G. Helmer, J. E. Cline, R. C. Greenwood* in *W. D. Hamilton:* The Electromagnetic Interaction in Nuclear Spectroscopy. North-Holland, Amsterdam 1975, p. 775.
[113] *I. L. Fowler, R. J. Toone*, Nucl. Instrum. Methods *98*, 183 (1972).
[114] *H. Büker*, Nucl. Instrum. Methods *69*, 293 (1969).
[115] *D. A. Becker* in [7], p. 1143.
[116] *S. Wagner, R. Trammel, F. J. Walter*, IEEE Trans. Nucl. Sci. *NS-19*, 380 (1972).
[117] *W. E. Haas, R. Hofmann, J. A. Martin*, Radiochem. Radioanal. Lett. *19*, 207 (1974).
[118] *F. S. Goulding, D. A. Landis* in *J. Cerny:* Nuclear Spectroscopy and Reactions. Part A. Academic Press, New York 1974, p. 413.
[119] *P. W. Nicholson:* Nuclear Electronics. Wiley, New York 1974.
[120] *J. Bartosek, J. Masek, F. Adams, J. Hoste*, Nucl. Instrum. Methods *104*, 221 (1972).
[121] *L. Wielopolski, R. P. Gardner*, Nucl. Instrum. Methods *140*, 297 (1977).
[122] *G. P. Westphal*, Nucl. Instrum. Methods *136*, 271 (1976).
[123] *G. P. Westphal*, Nucl. Instrum. Methods *138*, 467 (1976).
[124] *J. Op de Beeck*, At. Energy Rev. *13*, 743 (1975).
[125] *H. Weigel, J. Dank*, J. Radioanal. Chem. *23*, 171 (1974).
[126] *G. W. Phillips, K. W. Marlow*, Nucl. Instrum. Methods *137*, 525 (1976).
[127] *P. J. M. Korthoven, M. De Bruin*, J. Radioanal. Chem. *35*, 127 (1977).
[128] *A. Speecke, B. De Soete:* Informationsheft des Büro EUROISOTOP 18. Serie: Monographien-4, Information und Dokumentation des Büro EUROISOTOP, 1972.
[129] *J. A. Cooper, R. W. Perkins*, Nucl. Instrum. Methods *99*, 125 (1972).
[130] *U. Rösick, P. Brätter*, Z. Anal. Chem. *286*, 336 (1977).
[131] *M. A. van Driel*, Dissertation, Universität Utrecht, September 1976.
[132] *A. Schroeder*, Dissertation, Universität Köln, February 1974.
[133] *V. R. Burmistrov, B. Koshenov, V. A. Shilin, V. A. Didorenko*, Zh. Anal. Chim. *31*, 81 (1976).
[133a] *S. Amiel, M. Mantel, Z. B. Alfassi*, J. Radioanal. Chem. *37*, 189 (1977).
[133b] *M. Mantel, Z. B. Alfassi, S. Amiel*, Anal. Chem. *50*, 441 (1978).
[134] *C. Ballaux, R. Dams, J. Hoste*, Anal. Chim. Acta *47*, 397 (1969).
[135] *F. Girardi, E. Sabbioni*, J. Radioanal. Chem. *1*, 169 (1968).
[136] *S. S. Krishnan, D. R. Crapper*, Radiochem. Radioanal. Lett. *20*, 287 (1975).
[137] *E. Sabbioni, R. Pietra, F. Girardi*, J. Radioanal. Chem. *4*, 289 (1970).
[138] *M. Heurtebise, W. J. Ross*, Anal. Chem. *44*, 596 (1972).
[139] *D. L. Massart*, J. Radioanal. Chem. *4*, 265 (1970).
[140] *J. Ruzicka, J. Stary*, Talanta *10*, 287 (1963).
[141] *J. Stary, J. Ruzicka*, Talanta *18*, 1 (1971).
[142] *R. A. Nadkarni*, J. Radioanal. Chem. *20*, 139 (1974).
[143] *K. Kudo, N. Suzuki*, J. Radioanal. Chem. *26*, 327 (1975).
[144] *J. W. Mitchell*, Radiochem. Radioanal. Lett. *24*, 123 (1976).
[145] *R. Keim*, Chem.-Ztg. *94*, 559 (1970).
[146] *E. A. Schweikert*, Talanta *15*, 883 (1968).
[147] *H. L. Rook, G. J. Lutz, P. D. LaFleur*, J. Radioanal. Chem. *15*, 557 (1973).
[147a] *N. Trautmann, G. Herrmann*, J. Radioanal. Chem. *32*, 533 (1976).
[147b] *M. Zendel, E. Stender, N. Trautmann, G. Herrmann*, Nucl. Instrum. Methods *153*, 149 (1978).
[148] *J. M. Rottschafer*, Talanta *19*, 163 (1972).
[149] *R. E. H. Reuter*, Dissertation, Universität Zürich 1977.
[150] *C. Lee, N. B. Kim, I. C. Lee, K. S. Chung*, Talanta *24*, 241 (1977).
[151] *B. M. Vanderborght, R. E. Van Grieken*, Anal. Chem. *49*, 311 (1977).
[152] *K. Samsahl, P. Wester, O. Landström*, Anal. Chem. *40*, 181 (1968).
[153] *R. O. Allen, L. A. Haskin, M. R. Anderson, O. Müller*, J. Radioanal. Chem. *6*, 115 (1970).
[154] *G. H. Morrison, J. T. Gerard, A. Traven, R. L. Currie, S. F. Peterson, N. M. Potter*, Anal. Chem. *41*, 1633 (1969); *44*, 839 (1972).
[155] *O. Brandstadter, F. Girsig, F. Grass, R. Klenk*, Nucl. Instrum. Methods *104*, 45 (1972).
[156] *H.-J. Kreiner*, Nucl. Instrum. Methods *141*, 119 (1977).
[157] *J. R. McGinley, E. A. Schweikert*, Anal. Chem. *47*, 2403 (1975).
[158] *R. Henkelmann, H.-J. Born*, J. Radioanal. Chem. *16*, 473 (1973).
[159] *V. Krivan*, Z. Anal. Chem. *262*, 1 (1972).
[160] *R. K. Jolly, H. B. White, Jr.*, Nucl. Instrum. Methods *97*, 299 (1971).
[161] *M. A. Wheeler*, Anal. Chem. *47*, 146 (1975).
[162] *P. Müller, G. Ischenko*, J. Appl. Phys. *47*, 2811 (1976).
[163] *F. Abel, G. Amsel, E. D'Artemare, M. Bruneaux, C. Cohen, B. Maurel, C. Ortega, S. Rigo, J. Siejka, M. Croset, D. Dieumegard*, J. Radioanal. Chem. *16*, 567 (1973).
[164] *J. R. Bird, B. L. Campbell, P. B. Price*, At. Energy Rev. *12*, 275 (1974).
[165] *L. Shabason, B. L. Cohen*, Anal. Chem. *45*, 284 (1973).
[166] *R. B. Boulton, G. T. Ewan*, Anal. Chem. *49*, 1297 (1977).
[167] *G. Deconninck, N. Longequeue*, Phys. Rev. Lett. *30*, 863 (1973).
[168] *G. Deconninck, G. Demortier, F. Bodart*, At. Energy Rev. *13*, 367 (1975).
[169] *J. W. McMillan, F. C. W. Pummery*, J. Radioanal. Chem. *38*, 51 (1977).
[170] *G. J. Lutz, R. J. Boreni, R. S. Maddock, W. W. Meinke:* Activation Analysis—A Bibliography. NBS Techn. Note 467, U.S. Depart. of Commerce 1972.
[171] *J. W. Mitchell, J. E. Riley*, J. Radioanal. Chem. *38*, 79 (1977).
[172] *K. Kudo, K. Kobayashi, T. Shigematsu*, J. Radioanal. Chem. *27*, 329 (1975).
[173] *G. Beurton, B. Beyssier, Y. Angella*, J. Radioanal. Chem. *38*, 257 (1977).
[174] *R. Neirinckx, F. Adams, J. Hoste*, Anal. Chim. Acta *43*, 369 (1968).
[175] *E. N. Gilbert, G. V. Veriovkin, V. I. Semenov, V. A. Mikhailov*, J. Radioanal. Chem. *38*, 229 (1977).
[176] *S. Agarwal, G. Pinte, S. May*, J. Radioanal. Chem. *38*, 165 (1977).
[177] *N. V. Filippova, L. A. Smakhtin, N. V. Miglina*, Zh. Anal. Chim. *25*, 2001 (1970).
[178] *J. W. Mitchell, C. L. Luke, W. R. Northover*, Anal. Chem. *45*, 1503 (1973).
[179] *H. D. Buenofama, J. A. Lubkowitz*, Anal. Chim. Acta *96*, 285 (1978).
[179a] *W. Faix, V. Krivan*, results to be published.
[180] *V. Krivan*, Talanta *23*, 621 (1976).
[180a] *V. Krivan, D. L. Swindle, E. A. Schweikert*, Anal. Chem. *46*, 1626 (1974).
[180b] *J. L. Debrun, J. N. Barrandon, P. Benaben, Ch. Rouxel*, Anal. Chem. *47*, 637 (1975).
[180c] *J. L. Debrun, J. N. Barrandon*, J. Radioanal. Chem. *17*, 291 (1973).
[180d] *E. A. Schweikert, J. R. McGinley, G. Francis, D. L. Swindle*, J. Radioanal. Chem. *19*, 89 (1974).
[181] *V. Krivan*, Anal. Chem. *47*, 469 (1975).
[181a] *W. Faix, J. W. Mitchell, V. Krivan*, results to be published.
[182] *Ch. Engelmann, B. Fritz, J. Gosset, P. Graeff, M. Locuillet:* Proc. Conf. on Practical Aspects of Activation Analysis with Charged Particles. Liège, Sept. 21—22, 1967, Report EUR 3896, p. 319.
[183] *H. L. Rook, E. A. Schweikert, R. E. Wainerdi*, Anal. Chem. *40*, 1194 (1968).
[184] *C. Vandecasteele, F. Adams, J. Hoste*, Anal. Chim. Acta *71*, 67 (1974).
[185] *G. Y. Weber, D. David, L. Quaglia, J. Pauwels, J. Vanaudenhove*, J. Radioanal. Chem. *39*, 343 (1977).
[186] *R. Cornelis, J. Hoste, A. Speecke, C. Vandecasteele, J. Versieck, R. Gijbels* in *T. S. West:* Analytical Chemistry – Part I. Butterworths, London 1976, p. 137.

[187] *Ch. Engelmann:* Bericht Nr. 69, Euroisotop, 1971.
[188] *Ch. Engelmann* in *J. M. A. Lenihan, S. J. Thomson, V. P. Guinn:* Advances in Activation Analysis, Vol. 2, Academic Press 1972, p. 1.
[189] *R. Van Grieken, J. Hoste:* Annotated Bibliography on 14-MeV Neutron Activation Analysis. Euroisotop Office 65–8, 1972.
[190] *C. Vandecasteele, A. Speecke, J. Hoste:* Euroisotop Office Information Booklet 68. Series: Monographs-22, Commission of the European Communities, 1972.
[191] *J. Op de Beeck, J. Hoste,* Analyst *99*, 973 (1974).
[192] *G. H. Morrison,* J. Radioanal. Chem. *18*, 9 (1973).
[193] *P. Dulski, P. Möller:* HMI-B177. Hahn-Meitner-Institut für Kernforschung, Berlin 1975.
[194] *H. Onishi* in [7], p. 773.
[195] *R. Cornelis, J. Hoste, A. Speecke, C. Vandecasteele, R. Gijbels* in *T. S. West,* Analytical Chemistry – Part 1. Butterworths, London 1976, p. 71.
[196] *H. J. M. Bowen* in *D. I. Coomber:* Radiochemical Methods in Analysis. Plenum Press, New York 1975, p. 288.
[197] *R. Gijbels, A. Govaerts,* J. Radioanal. Chem. *16*, 7 (1973).
[198] *A. O. Brunfelt,* Talanta *18*, 1197 (1971).
[199] *A. O. Brunfelt, B. Sundvoll,* Radiochem. Radioanal. Lett. *28*, 181 (1977).
[200] *E. G. Gordon, K. Randle, G. G. Goles, J. B. Gorliss, M. H. Beeson, S. S. Oxley,* Geochim. Cosmochim. Acta *32*, 169 (1968).
[201] *J. I. Watterson, J. P. F. Sellschop,* J. Radioanal. Chem. *38*, 301 (1977).
[202] *H. H. Schock,* J. Radioanal. Chem. *38*, 327 (1977).
[203] *A. M. Davis, R. Ganapathy, L. Grossman,* Earth Planet. Sci. Lett. *35*, 19 (1977).
[204] *R. L. Caldwell, K. P. Desai, W. R. Mills, Jr.,* in: Nuclear Techniques in Geochemistry and Geophysics. IAEA, Wien 1976, p. 3.
[205] *W. W. Givens, W. R. Mills, C. L. Dennis, R. L. Caldwell,* Geophysics *41*, 468 (1976).
[206] *F. E. Senftle, R. M. Moxham, A. B. Tanner, B. R. Boynton, P. W. Philbin,* Nucl. Instrum. Methods *138*, 371 (1976).
[207] *F. E. Senftle, R. M. Moxham, A. B. Tanner, P. W. Philbin, G. R. Boynton, R. E. Wagner,* Geoexploration *15*, 121 (1977).
[208] *R. M. Moxham, A. B. Tanner, F. E. Senftle,* MTS Journal *11*, 14 (1976).
[209] *F. E. Senftle, P. W. Philbin, R. M. Moxham, G. R. Boynton,* Nucl. Instrum. Methods *117*, 435 (1974).
[210] *R. Pretorius, F. Odendaal, M. Peisach,* J. Radioanal. Chem. *12*, 139 (1972).
[211] *R. Delmas, J. N. Barrandon, J. L. Debrun,* Analusis *4*, 339 (1976).
[212] *A. Chattopadhyay, R. E. Jervis,* Anal. Chem. *46*, 1630 (1974).
[213] *R. Dams, J. A. Robbins, K. A. Rahn, J. W. Winchester,* Anal. Chem. *42*, 861 (1970).
[214] *W. H. Zoller, G. E. Gordon,* Anal. Chem. *42*, 257 (1970).
[215] *K. K. Pillay, C. C. Thomas, Jr.,* J. Radioanal. Chem. *7*, 107 (1971).
[216] *O. J. Kronborg, E. Steinnes,* Radiochem. Radioanal. Lett. *21*, 379 (1975).
[217] *A. Mizohata, T. Matsunami, T. Mamuro,* Annu. Rep. Radiat. Cent. Osaka Prefect. *17*, 1 (1976).
[218] *L. C. Bate, S. E. Lindberg, A. W. Andren,* J. Radioanal. Chem. *32*, 125 (1976).
[219] *W. Maenhaut, W. H. Zoller,* J. Radioanal. Chem. *37*, 637 (1977).
[220] *P. E. Wilkins, D. J. Bressan, W. H. Cullen, F. K. Lepple, G. W. Phillips, K. W. Marlow,* J. Radioanal. Chem. *37*, 661 (1977).
[221] *H. Vogg, R. Härtel,* J. Radioanal. Chem. *37*, 857 (1977).
[221a] *I. Othman, N. M. Spyrou:* Nuclear Activation Techniques in the Life Sciences, Proc. Symp., IAEA, Wien 1978, SM-227, 33.
[222] *K. H. Lieser, V. Neitzert,* J. Radioanal. Chem. *31*, 397 (1976).
[223] *B. Salbu, E. Steinnes,* J. Radioanal. Chem. *47*, 1011 (1975).
[224] *J. Schneider, R. Geisler,* Z. Anal. Chem. *267*, 270 (1973).
[225] *J. B. Luten,* J. Radioanal. Chem. *37*, 897 (1977).
[226] *H. A. van der Sloot, J. B. Luten:* Measurement, Detection, and Control of Environmental Polutants. Proc. Symp., IAEA, Wien 1976, p. 435.
[227] *R. I. Draskovic, R. Radosavljevic, T. Tasovac,* J. Radioanal. Chem. *28*, 231 (1975).
[228] *C. Schnier, L. Karbe:* Measurement, Detection, and Control of Environmental Polutants. Proc. Symp., IAEA, Wien 1976, p. 415.
[229] *G. Grancini, M. B. Stievano, F. Girardi, G. Guzzi, R. Pietra,* J. Radioanal. Chem. *34*, 65 (1976).
[230] *I. Obrusnik, B. Starkova, J. Blazek,* J. Radioanal. Chem. *31*, 495 (1976).
[231] *C. Block, R. Dams, J. Hoste:* Measurement, Detection, and Control of Environmental Polutants. Proc. Symp., IAEA, Wien 1976, p. 101.
[232] *J. J. Rowe, E. Steinnes,* Talanta *24*, 433 (1977).
[233] *T. W. Oakes, A. K. Furr, D. J. Adair, T. F. Parkinson,* J. Radioanal. Chem. *37*, 881 (1977).
[234] *Z. Abedinzadeh, M. Razeghi, B. Parsa,* J. Radioanal. Chem. *35*, 373 (1977).
[235] *N. K. Aras, W. H. Zoller, G. E. Gordon, G. J. Lutz,* Anal. Chem. *45*, 1481 (1973).
[236] *G. J. Lutz, N. K. Arasm, W. H. Zoller, G. Gordon,* J. Radioanal. Chem. *16*, 609 (1973).
[237] *T. Kato, N. Sato, N. Suzuku,* Talanta *23*, 517 (1976).
[238] *A. Chattopadhyay,* J. Radioanal. Chem. *37*, 785 (1977).
[239] *S. F. Bankert, S. D. Bloom, G. D. Santer,* Anal. Chem. *45*, 692 (1973).
[240] *D. C. Riddle, E. A. Schweikert,* Anal. Chem. *46*, 395 (1974).
[241] *B. Parsa, S. S. Markowitz,* Anal. Chem. *46*, 186 (1974).
[242] *R. D. Vis, H. Verheul,* J. Radioanal. Chem. *25*, 293 (1975).
[243] *B. Maziere, A. Gaudry, W. Stanilewicz, D. Comar,* J. Radioanal. Chem. *16*, 281 (1973).
[244] *R. A. Nadkarni, G. H. Morrison,* Anal. Chem. *45*, 1957 (1973).
[245] *J. A. Valendia, A. K. Perkons,* J. Radioanal. Chem. *20*, 715 (1974).
[246] *J. M. A. Lenihan,* Pure Appl. Chem. *44*, 509 (1975).
[247] *B. Maziere,* Bull. Inf. Sci. Tech. Commis. Energ. At. (Fr.) No. 220, 61 (1976).
[248] *F. Girardi, R. Pietra,* At. Energy Rev. *14*, 521 (1976).
[249] *A. Mizohata, T. Matsunami, T. Mamuro,* Annu. Rep. Radiat. Cent. Osaka Prefect *17*, 1 (1976).
[250] *R. A. Nadkarni, G. H. Morrison,* Radiochem. Radioanal. Lett. *24*, 103 (1976).
[251] *R. Cornellis, A. Speecke, J. Hoste,* Anal. Chim. Acta *78*, 317 (1975).
[252] *R. E. J. Porritt, C. J. Bowles, J. W. Kelly,* Radiochem. Radioanal. Lett. *26*, 27 (1976).
[253] *P. Lievens, J. Versieck, R. Cornelis, J. Hoste,* J. Radioanal. Chem. *37*, 483 (1977).
[254] *H. Schicha, L. E. Feinendegen, K. Kasperek, H. J. Klein, V. Siller,* Beitr. Pathol. *146*, 55 (1972).
[255] *P. Brätter, D. Gawlik, J. Lausch, V. Rösick,* J. Radioanal. Chem. *37*, 393 (1977).
[256] *G. C. Verghese, R. Kishon, V. P. Guin,* J. Radioanal. Chem. *15*, 329 (1973).
[257] *I. H. Qureshi, M. N. Cheema:* Trace Element Analysis: A Diagnostic Tool. NCD-2 (ACG), Pakistan Inst. of Nuclear Technology, Rawalpindi 1976.
[258] *G. V. Iyengar,* Radiochem. Radioanal. Lett. *24*, 35 (1976).
[259] *S. Speecke, J. Hoste, J. Versieck* in [7], p. 299.
[259a] *B. Sansoni, V. Iyengar:* Nuclear Activation Techniques in the Life Sciences. Proc. Symp., IAEA, Wien 1978, SM-227/107.
[260] *E. P. Mignonsin,* Radiochim. Acta *22*, 183 (1975).
[261] *E. J. Underwood,* At. Energy Rev. *14*, 591 (1976).
[262] *B. Maziere, C. Loc'h, O. Stulzaft, A. Gaudry, D. Comar,* J. Radioanal. Chem. *37*, 617 (1977).
[263] *J. Turbstra, A. M. Harthoorn, P. J. L. Beukes, R. J. N. Brits,* J. Radioanal. Chem. *37*, 473 (1977).
[264] *P. J. Peterson,* Sci. Prog. (Oxford) *59*, 505 (1971).
[265] *R. E. Tout, W. B. Gilboy, N. N. Spyrou,* J. Radioanal. Chem. *37*, 705 (1977).
[266] *J. F. Diehl, R. Schelenz,* Lebensm.-Wiss. Technol. *8*, 154 (1975).
[267] *S. Meloni, V. Caramella-Crespi, G. Fassi,* J. Radioanal. Chem. *34*, 113 (1976).
[268] *J. T. Tanner, M. H. Friedman,* J. Radioanal. Chem. *37*, 529 (1977).
[269] *R. Schelenz,* J. Radioanal. Chem. *37*, 539 (1977).
[270] *G. F. Clemente,* J. Radioanal. Chem. *32*, 25 (1976).
[271] *K. Broddy, D. Claros,* Int. J. Appl. Radiat. Isot. *24*, 179 (1973).
[272] *B. Maziere, D. Comar, D. Kuntz,* J. Radioanal. Chem. *37*, 357 (1977).
[273] *K. J. Ellis, S. H. Cohn, A. Vaswani, I. Zanzi, M. Roginsky, J. Alvia,* J. Radioanal. Chem. *37*, 333 (1977).
[274] *J. R. Mernagh, J. E. Harrison, K. G. McNeil,* Phys. Med. Biol. *22*, 831 (1977).
[275] *K. Boddy, I. Holloway, A. Elliot,* Int. J. Appl. Radiat. Isot. *24*, 428 (1973).
[276] *M. I. Chamberlain, J. H. Fremlin, I. Holloway, D. K. Peters,* Int. J. Appl. Radiat. Isot. *21*, 725 (1970).
[277] *C. D. Bond, R. B. Theus, L. S. August, P. Shapiro, C. C. Rogers,* Med. Phys. *3*, 248 (1976).
[278] *T. J. Spinks, D. K. Bewley, A. S. O. Ranicar, G. F. Joplin,* J. Radioanal. Chem. *37*, 345 (1977).
[278a] *E. D. Williams, K. Boddy, I. Harvey, J. K. Haywood,* Phys. Med. Biol. *23*, 405 (1978).
[279] *T. Kato, N. Sato, N. Suzuki,* Anal. Chim. Acta *81*, 337 (1976).
[280] *D. Gawlik, J. Möller,* Z. Anal. Chem. *283*, 121 (1977).
[281] *L. Zikovsky, E. A. Schweikert,* J. Radioanal. Chem. *37*, 571 (1977).
[282] *J. H. Fremlin, W. Tanti-Wipawin,* Proc. Anal. Div. Chem. Soc. *13*, 195 (1976).
[283] *R. G. V. Hancock,* Anal. Chem. *48*, 1443 (1976).
[284] *E. V. Sayre, P. Meyers,* Art Archaeol. Tech. Abstr. *8*, 115 (1971).
[285] *P. Meyer* in *E. T. Hall, D. M. Metcalf:* Methods of Chemical and Metallurgical Investigation of Ancient Coinage. Spec. Publ. No. 8. Royal Numismatic Society, University Press, Oxford 1972, p. 183.
[286] *E. V. Sayre,* Act. Anal. *2*, 157 (1972).
[287] *G. Harbottle,* Radiochemistry (London) *3*, 33 (1976).
[288] *V. P. Guinn,* Annu. Rev. Nucl. Sci. *24*, 561 (1974).

[289] *R. A. Wood, K. A. Nagy, N. S. MacDonald, S. T. Wakakuwa, R. J. Beckman, H. Kaaz*, Anal. Chem. *47*, 646 (1975).
[290] *C. Engelmann, G. Filippi, J. Gosset, F. Moreau*, J. Radioanal. Chem. *37*, 559 (1977).
[291] *H. Rausch*, J. Radioanal. Chem. *33*, 201 (1976).
[292] *H. Jaskolska, L. Rowinska, L. Wah's*, J. Radioanal. Chem. *38*, 29 (1977).
[293] *J. A. Martin, M. Angenendt, E. Haas*, Lecture at 4th Symposium on the Recent Developments in Neutron Activation Analysis. Aug. 4 - 7, 1975, Cambridge, Commission of the European Communities, Euroisotope, Brussels.
[294] *J. A. Cookson, A. T. G. Ferguson, F. D. Pilling*, J. Radioanal. Ch3m. *12*, 39 (1972).
[295] *C. Olivier, T. B. Pierce*, J. Radioanal. Chem. *24*, 21 (1975).
[296] *T. B. Pierce*, J. Radioanal. Chem. *37*, 285 (1977).
[297] *E. A. Wolicki*: NRL Report 7477. Naval Research Laboratories, 1972.
[298] *R. P. Meshcheryakov, I. P. Chernow, A. N. Oblivantsev, B. I. Kuznetsov, G. I. Tronov, A. G. Rybasov*, J. Radioanal. Chem. *16*, 427 (1973).
[299] *G. Baudin*, Analusis *4*, 320 (1976).
[300] *J. Baijot-Stroobants, G. Debras, G. Demortier*, Radiochem. Radioanal. Lett. *27*, 271 (1976).
[301] *J. Holzhey*: Aktivierungsanalyse – Anwendung in der Metallurgie. VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1975.
[302] *J. Pauwels, G. Pröbstl*: Technical and Economic ITE-Report No. 68. Commission of the European Communities, Euroisotope, Brussels 1973.
[303] *J. A. Heslop*, Radiochemistry (London) *3*, 1 (1976).
[304] *W. Dehnke*, Isotopenpraxis *13*, 362 (1977).
[305] *J. Pauwels*: Euroisotop Office Information Booklet No. 99. Series: Data-2. Commission of the European Communities, Euroisotope, Brussels 1975.
[306] *V. N. Nikitin, V. N. Pavlova, A. I. Petrov, A. M. Shchetinin*, At. Energ. (UdSSR) *40*, 11 (1976).
[307] *G. L. Jewett, R. P. Himes, O. V. Anders*, J. Radioanal. Chem. *37*, 813 (1977).

COMMUNICATIONS

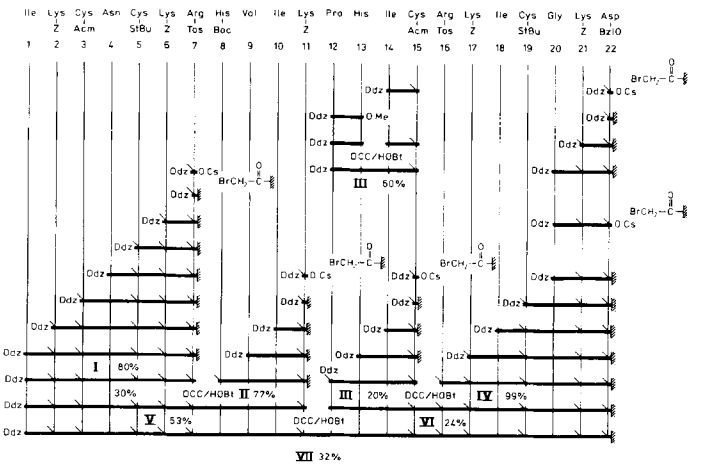
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying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

Synthesis of the Mast Cell Degranulating (MCD) Peptide from Bee Venom[**]

By *Christian Birr* and *Margot Wengert-Müller*[*]

The mast cell degranulating peptide (MCD peptide) is a minimal component (1—3 %) of bee venom[1]. The single-stranded sequence consisting of 22 amino acids[2] (Scheme 2) has two disulfide bridges and contains 5 lysine, 2 arginine, and 2 histidine residues; the isoelectric point lies near pH 12. At low dosage (<0.1 mg/kg) the natural product effects release of histamine (degranulation) in mast cells[1] which is overcompensated at higher dosages (1 mg/kg) by an anti-inflammatory effect[3]. The MCD peptide appears to have an anti-inflammatory activity exceeding that of all known pharmaceuticals without being neurotoxic. This property endows the compound with therapeutic interest in the case of rheumatic processes[4], and also for allergic reactions, and kindled our interest in the total synthesis of this compound.

In order to synthesize the MCD peptide (see Scheme 1), four fragments (I—IV) were produced by an extensively modified Merrifield method[5] on a polystyrene gel phase (<0.5 % crosslinked): thanks to the spectroscopic properties of the acid-labile Ddz protecting group, each operation could be continuously monitored by photometry for complete reaction and plotted visually[6]. None of the fragment syntheses was programmed with regard to sequence length. Rather, the automatic synthetic process was stopped when the reactions on the polystyrene gel phase fell below 70 % average yield. This gave heptapeptides as the longest sequences. As a result of the ready basic cleavage of the 2-oxo ethyl ester bond —O—CH_2—CO-Polymer of the peptides on the polystyrene phase (0.1 N benzyltrimethylammonium hydroxide in dry methanol/dioxane 1:3, v/v) the peptides could be removed from the support for intermediate purification and subsequently condensed on the solid phase to give larger fragments. Thus



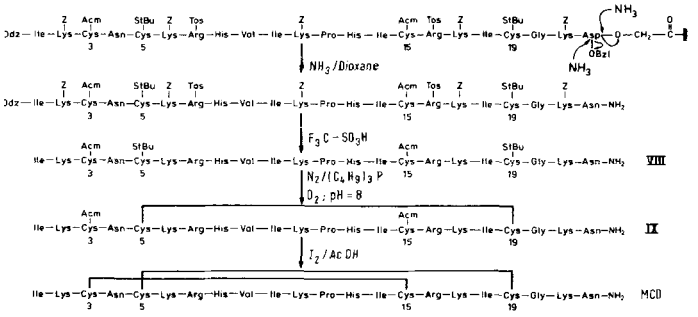
Scheme 1. Synthesis of the fragments and carrier-bound completely protected MCD peptide (fragment VII). The yields of I—IV are based on the initial loading of the gel phase. The fragment III obtained in 60 % yield was additionally produced in solution. Protecting groups: Acm, acetamidomethyl; Boc, *tert*-butyloxycarbonyl; Bzl, benzyl; Ddz, 3,5-dimethoxy-α,α-dimethylbenzyloxycarbonyl; StBu, *tert*-butylthio; Tos, toluenesulfonyl; Z, benzyloxycarbonyl.

[*] Priv.-Doz. Dr. Ch. Birr, Dr. M. Wengert-Müller
Max-Planck-Institut für Medizinische Forschung
Abteilung Naturstoff-Chemie
Jahnstrasse 29, D-6900 Heidelberg 1 (Germany)

[**] *Ch. Birr*, Lecture at German-Soviet Peptide Symposium, Eibsee 1978. We are grateful to Prof. Dr. *E. Habermann*, Giessen, for a sample of MCD peptide.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*
0570-0833/79/0202-0147 $ 01.00/0

I and II reacted on the carrier to form V (53 % based on II-gel polymer) and III and IV reacted on the carrier to give VI (24 % based on IV-gel polymer). V was again released from the carrier, purified, and combined with VI on the carrier to give the fully protected final product VII (32% based on VI-gel polymer). The scheme of fragment syntheses and the formation of the fully protected sequence VIII has already been briefly described[7].



Scheme 2. Liberation of the MCD peptide from carrier-bound final product VII.

The product VII of the Merrifield synthesis was released from the carrier as the diamide by treatment with ammonia-saturated dioxane (Scheme 2). The release of VII from polystyrene gel was practically complete (98.5 %) and after chromatography on Sephadex LH 20/DMF resulted in completely protected MCD peptide (MW 4067). All the benzyloxycarbonyl and toluenesulfonyl groups were removed with trifluoromethanesulfonic acid, the sulfur-protecting groups being left intact in positions 3, 5, 15, and 19. No aromatic protons were detected in the ^{1}H-NMR spectrum, while the signals of the sulfur-protecting groups remained unchanged.

After ion exchange and gel chromatography, 507 mg of Cys(Acm)^{3,15},Cys(StBu)^{5,19}-MCD peptide (VIII) was obtained (71 % based on the amount of VII released from the carrier).

Reduction with tributylphosphane[8] selectively removed the StBu protecting groups in positions 5 and 19, and the disulfide bridge 5—19 was formed by air oxidation at pH 8; there resulted 276 mg of Cys(Acm)^{3,15}-MCD peptide (IX) (61 % based on VIII).

In order to bring about selective linkage of the 3—15 disulfide bridge, the Acm protecting groups were removed from 126 mg of IX by iodine in acetic acid solution[9]. Oxidation was halted with ascorbic acid and the final product immediately chromatographed on Sephadex G25 with 0.1 N acetic acid. The fraction containing the most synthetic MCD peptide initially gave 16 mg of pure product after purification. It was shown by electrophoresis (paper, polyacrylamide normal and SDS gel) and chromatography (HPLC, Zorbax ODS; acetonitrile/water 35/65, isocratic) to be identical with the natural product. Amino acid analysis (calculated values given in parentheses): Cys 4.2(4); Ile 4.0(4); Lys 5.0(5); Arg 2.3(2); His 1.8(2); Val 0.8(1); Pro 1.4(1); Gly 1.5(1); Asp 2.4(2).

In the CD spectrum, the synthetic MCD peptide shows the same four bands between 190 and 240 nm as the natural product; however, the spectra are not congruent. This suggests gradual racemization of particularly endangered sites (histidine, cysteine). The degranulating effect of the synthetic product was tested on rat mast cells. The synthetic MCD peptide exhibited 35 % of the histamine-releasing activity of the natural product.

Received: December 18, 1978 [Z 139 IE]
German version: Angew. Chem. 91, 156 (1979)

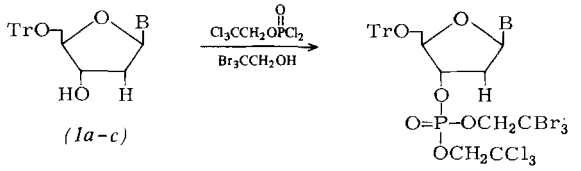
[1] *H. Breithaupt, E. Habermann*, Naunyn-Schmiedebergs Arch. Pharmakol. Exp. Path. *261*, 252 (1968).
[2] *P. Haux*, Hoppe-Seylers Z. Physiol. Chem. *350*, 536 (1969).
[3] *M. J. E. Billingham, J. Morley, J. M. Hanson, R. A. Shipolini, C. A. Vernon*, Nature *245*, 163 (1973).
[4] *B. E. C. Banks, F. D. Rumjanek, N. M. Sinclair, C. A. Vernon*, Bull. Inst. Pasteur *74*, 137 (1978).
[5] *Ch. Birr*: Aspects of the Merrifield Peptide Synthesis. Springer, Berlin 1978; *B. W. Erickson, R. B. Merrifield* in *H. Neurath, R. L. Hill*: The Proteins. Vol. 2. 3rd Edit. Academic Press, New York 1976.
[6] *Ch. Birr* in *Y. Wolman*: Peptides 1974. Halsted Press, New York 1975, pp. 117ff.
[7] *Ch. Birr, M. Wengert-Müller, A. Buku* in: *M. Goodman, J. Meienhofer*: Peptides. Halsted Press, New York 1977, pp. 510ff.
[8] *J. van Rietschoten, C. Granier, H. Rochat, S. Lissitzky, F. Miranda*, Eur. J. Biochem. *56*, 35 (1975).
[9] *P. Sieber, B. Kamber, A. Hartmann, A. Jöhl, B. Riniker, W. Rittel*, Helv. Chim. Acta *60*, 27 (1977).

Selective Electrochemical Removal of Protecting Groups in Nucleotide Synthesis

By *Joachim Engels*[*]

In the synthesis of nucleotides by the triester method[1] a completely protected nucleoside-3′-phosphate in the triester form *(2)* can be used as synthon for construction of the oligonucleotide chain. A major problem in the synthesis is the selective cleavage of an ester moiety. We report here on the selective deprotection of such synthons by controlled potential electroreduction[2]. Two important advantages make this approach attractive: Firstly, the 2,2,2-trichloro- and -bromoalkyl esters of phosphoric acid are quite stable towards both basic and acidic hydrolysis[3], so that a wide range of acid- and alkali-labile protecting groups can be used on the sugar and on the base. Secondly, owing to the reaction mechanism[4], the danger of an isomerization during cleavage of an ester function is far less than during attack of the reagent at phosphorus.

The protected nucleosides *(1a—c)* were allowed to react with 2,2,2-trichloroethylphosphoric dichloride[5] and then with 2,2,2-tribromoethanol. The triesters *(2a—c)* can be isolated in 85—90 % yield by chromatography on silica gel.



(1a-c) *(2a-c)*

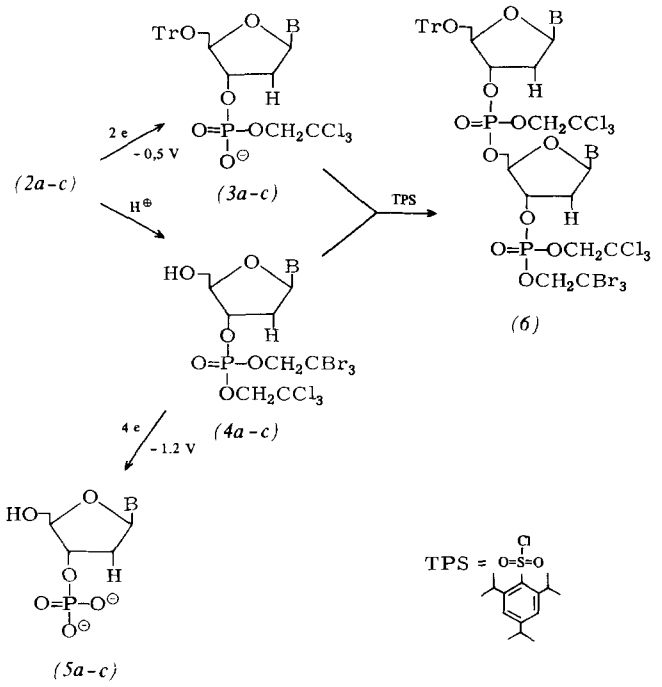
(a), B = Thyminyl
(b), B = N^4-Benzoylcytosyl
(c), B = N^6-Benzoyladenyl

Tr = Trityl or monomethoxytrityl

The detritylation of *(2a—c)* was achieved with 1% trifluoroacetic acid in CH_2Cl_2 or with BF_3Et_2O/MeOH in CH_2Cl_2[6]; the resulting crystalline esters *(4a—c)* are stable and can be lengthened in the 5′-direction. It is possible to cleave the tribromoethyl protecting group quantitatively from *(2a—c)* by controlled potential electroreduction[7] at a mercury cathode at −0.5 to −0.6 V. The reaction is carried out in acetonitrile/pyridine with $LiClO_4$ as supporting electrolyte; the diesters *(3a—c)* which are formed can be used for the condensation reaction directly after extraction with $CHCl_3$. Reaction of TPS with the triesters *(4a—c)* afforded *(6)*. The reactions proceed very smoothly. The nine possible combinations of

[*] Dr. J. Engels
Fachbereich Chemie der Universität
Universitätsstrasse 10, D-7750 Konstanz (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0148 $ 01.00/0*



(6) can then be cleaved by selective electroreduction and lengthened in the 3'-direction or be used for block condensation after acid cleavage at the 5'-terminal. Complete electrochemical deprotection to give the free phosphates was carried out on the diesters *(4a—c)*. On reduction in dimethylformamide (DMF) with tetrabutylammonium tetrafluoroborate as supporting electrolyte, *(4a)* and *(4c)* can be smoothly reduced at -1.2 to -1.4 V to *(5a)* and *(5c)* respectively in 90% yield. The dichloroethyl ester, *i.e.* the byproduct cited in [4], is formed to the extent of 2% at most and is virtually inseparable from the trichloroethyl ester (reactant).

Experimental

Reduction of *(2a—c)*: The reduction is carried out at room temperature under nitrogen in a partitioned electrolytic cell[8] (Pt-anode, Hg-cathode, Ag-wire; Nafion 125 membrane) using a 0.5 M solution of $LiClO_4$ in pyridine/CH_3CN (1:5) and 0.5—1 mmol *(2a—c)* as catholyte and 0.5 M $LiClO_4$ and 1—2 mmol pyridine as anolyte. The cathode potential is potentiostatically adjusted to -0.5 V (Ag-wire) and the uptake of electrons monitored coulometrically. When the current has reached its residual value the reaction is complete. After removal of solvent, partition of the residue between water and chloroform, extraction with chloroform, and drying of the chloroform phase with Na_2SO_4 followed by filtration and removal of solvent, *(3a—c)* is obtained and can be used directly for further reaction in pyridine.

Reduction of *(4a—c)*: The reduction is carried out at room temperature under nitrogen in the same type of cell as described above using 0.5 M tetrabutylammonium tetrafluoroborate in DMF/CH_3CN (1:1) and 0.5—1 mmol *(4a—c)* as catholyte and the same anolytes as above plus an additional 1—2 mmol 2,6-lutidine. The cathode potential is adjusted to -1.2 V (Ag-wire). On completion of reaction, extraction of the supporting electrolyte with chloroform and chromatography of the aqueous phase on RP8 or RP18 silica gel with water or water/ethanol as eluent affords *(5a—c)*.

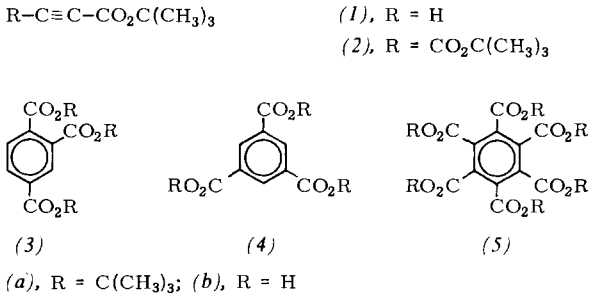
Received: December 11, 1978 [Z 136 IE]
German version: Angew. Chem. *91*, 155 (1979)

[1] *V. Amarnath, A. D. Broom*, Chem. Rev. *77*, 183 (1977).
[2] *J. Engels*, Nucl. Acid Res. Spec. Publ. *4*, s31 (1978); Chem. Ber., in press.
[3] *E. Cherbuliez, A. Gabriel, H. Probst, A. Yazgi, J. Rabinowitz*, Helv. Chim. Acta *45*, 2282 (1962).
[4] *M. F. Semmelhack, G. E. Heinsohn*, J. Am. Chem. Soc. *94*, 5139 (1972).
[5] *P. Cashion, K. Porter, T. Cadger, G. Sathe, T. Tranquilla, H. Notman, E. Jay*, Tetrahedron Lett. *1976*, 3769.
[6] *K. Dax, W. Wolflehner, H. Weidmann*, Carbohydr. Res. *65*, 132 (1978).
[7] *V. G. Mairanovsky*, Angew. Chem. *88*, 283 (1976); Angew. Chem. Int. Ed. Engl. *15*, 281 (1976).
[8] *R. Gottlieb, W. Pfleiderer*, Chem. Ber. *111*, 1753 (1978).

Di-*tert*-Butyl Acetylenedicarboxylate and Its Cyclotrimerization

By *Wolfgang Sucrow* and *Fritz Lübbe*[*]

For the synthesis of ene-hydrazines[1] we required as starting material di-*tert*-butyl acetylenedicarboxylate *(2)*, which, surprisingly, had previously not been described in the literature. Following the procedure used for the preparation of tert-*butyl* propiolate *(1)*[2] we have now been able to obtain *(2)* as a crystalline product, m.p. 35—36°C [^{1}H-NMR (90 MHz, $CDCl_3$): singlet, $\delta = 1.50$] from acetylenedicarboxylic acid and isobutene.



In spite of the bulky *tert*-butyl residue the esters *(1)* and *(2)* can be trimerized with dicarbonylbis(triphenylphosphane)nickel(0)[3]. *(1)* furnishes tri-*tert*-butyl trimellitate *(3a)* [oil, b.p. 165—170°C (bath)/0.03 torr, Kugelrohr] and tri-*tert*-butyl trimesitate *(4a)* [from petroleum ether, m.p. 218°C (dec)] in the ratio 6:1, while, according to the NMR spectrum, the known trimethyl esters are formed in the ratio 12:1. The total yield of *(3a)* and *(4a)* after chromatographic separation is 55%.—Under somewhat more severe conditions, *(2)* trimerizes to hexa-*tert*-butyl mellitate *(5a)* in 44% yield [^{1}H-NMR (90 MHz, $CDCl_3$): singlet, $\delta = 1.59$]. The crystals obtained from petroleum ether/chloroform decompose without melting above 180°C into mellitic acid *(5b)* and isobutene. In the case of the ester *(4a)* complete decomposition to *(4b)* takes place following previous melting.

In contrast to *(1)*, compounds *(2)* and *(3a)* also decompose to acetylenedicarboxylic acid and *(3b)*, respectively, on attempted distillation above 165°C and 204°C under normal pressure.—The new compounds *(2)*, *(3a)*, *(4a)*, and *(5a)* gave correct elemental analyses.

As shown by the cyclotrimerization, the *tert*-butyl groups in *(2)* do not give rise to much steric hindrance. The numerous reactions realizable with dimethyl acetylenedicarboxylate can thus presumably also be carried out with the di-*tert*-butyl ester *(2)*. This offers advantages, *e.g.* easy cleavage of the ester without use of bases.

[*] Prof. Dr. W. Sucrow, Dr. F. Lübbe
Fachbereich Naturwissenschaften II der Gesamthochschule
Warburger Strasse 100, D-4790 Paderborn (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*
0570-0833/79/0202-0149 $ 01.00/0

Procedure

Synthesis of *(2)*: Conc. sulfuric acid (0.15 ml) is added dropwise under nitrogen at −10 °C to a stirred mixture of acetylenedicarboxylic acid (2.0 g, 17.5 mmol), ether (10 ml), and isobutene (55 ml) in an ampoule. The ampoule is sealed at −195 °C and then allowed to stand for 4 days at room temperature. After removal of solvent *in vacuo* the residue is chromatographed with petroleum ether/6 % ether on 50 g silica gel and the product distilled at 80—82 °C (bath)/0.05 torr in a Kugelrohr [2.9 g (73 %), m.p. 35—36 °C].

Synthesis of *(5a)*: A solution of *(2)* (0.25 g, 1.1 mmol) in benzene (0.4 ml) is added dropwise at 70 °C to a suspension of $[(C_6H_5)_3P]_2Ni(CO)_2$ (0.10 g) in benzene (0.5 ml). The benzene is then removed by distillation (almost complete when the temperature reaches 115 °C), a further 0.05 g of catalyst is added to the product, and the resultant mixture stirred for 2 h at 115 °C. Chromatographic separation with petroleum ether/30 % ether on 30 g of silica gel and crystallization from petroleum ether/5 % $CHCl_3$ affords 0.11 g (44 %) of *(5a)* as colorless platelets.

Received: November 15, 1978 [Z 134 IE]
German version: Angew. Chem. *91*, 157 (1979)

CAS Registry numbers:
(1), 13831-03-3; *(2)*, 66086-33-7; *(3a)*, 69225-38-3; *(3b)*, 528-44-9; *(4a)*, 69225-39-4; *(4b)*, 554-95-0; *(5a)*, 69257-97-2; *(5b)*, 517-60-2; acetylenedicarboxylic acid, 142-45-0; isobutene, 115-11-7

[1] *A. Fehlauer, K.-P. Grosz, M. Slopianka, W. Sucrow, W. J. S. Lockley, W. Lwowski*, Chem. Ber. *109*, 253 (1976).
[2] *F. Sondheimer, N. Stjernström, D. Rosenthal*, J. Org. Chem. *24*, 1280 (1959).
[3] *W. Reppe, N. von Kutepow, A. Magin*, Angew. Chem. *81*, 717 (1969); Angew. Chem. Int. Ed. Engl. *8*, 727 (1969).

Synthesis and Properties of Tetrabutylammonium Octaiododirhenate(III), $[(n\text{-}C_4H_9)_4N]_2[Re_2I_8]$

By *Wilhelm Preetz* and *Lutz Rudzik*[*]

Dinuclear complexes $[Re_2X_8]^{2-}$ (X = Cl, Br) containing a Re···Re quadrupole bond were first prepared by *Cotton et al.*[1] as long ago as 1965. Compounds of Mo and Tc having the same type of structure have also been reported[2]. They can also contain organic moieties as ligands[3]. Detailed spectroscopic and X-ray crystallographic investigations have already been carried out on the alkali-metal and tetraalkylammonium salts of the octachloro- and octabromo-complexes[4].

We have now been able to prepare for the first time the previously unreported[7] octaiodo-complex *via* a simple route, namely by reaction of the tetrabutylammonium salt with hydrogen iodide in dichloromethane:

$$[(n\text{-}C_4H_9)_4N]_2[Re_2X_8] + 8\,HI \xrightarrow[CH_2Cl_2]{20\,^\circ C} [(n\text{-}C_4H_9)_4N]_2[Re_2I_8] + 8\,HX$$

The new compound[7], owing to the large I-ligand, is of interest from the point of view of its structural chemistry and bonding. It is immediately hydrolyzed in aqueous media, but is stable in organic solvents and in the solid state. On reaction with the corresponding tetrabutylammonium halides in CH_2Cl_2 it is reconverted into the octachloro- or octabromo-compound. It is also suitable for the preparation of other already known derivatives.

The absorption spectra[5] (Fig. 1) measured at about 10 K show systematic band shifts for the three homologous compounds. The $\delta \rightarrow \delta^*$ transition, which in the case of the chloro- (*ca.* 14500 cm^{-1}) and bromo-compound (*ca.* 14100 cm^{-1}) displays a vibration fine structure of the Re_2 group, appears at 12800 cm^{-1}. The ReRe bond length in the octaiodocomplex is thus estimated to be 2.27 Å[6].

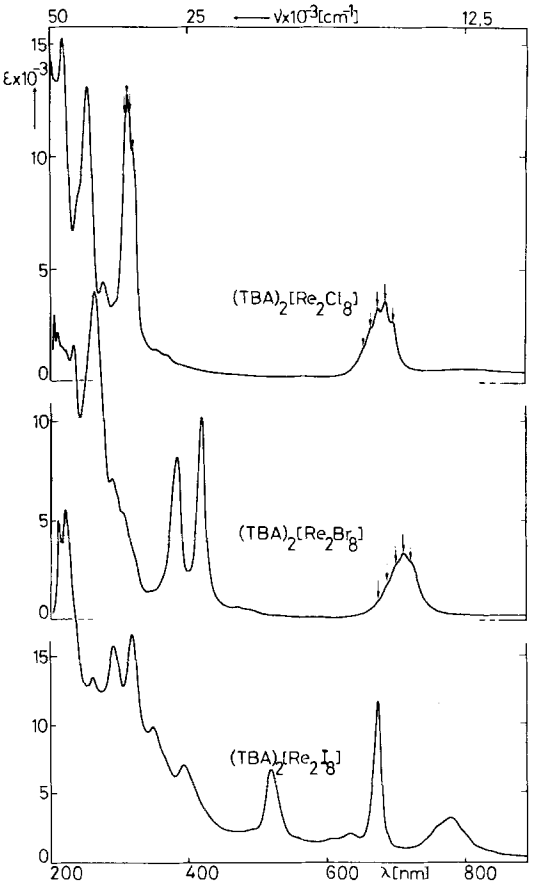


Fig. 1. UV/VIS spectra of the tetrabutylammonium octahalodirhenates(III), recorded on tablets of the corresponding rubidium halides at 10 K.

The IR spectrum shows only one intense Re—I stretching vibration at 184 cm^{-1}. In the Raman spectrum the Re—Re stretching vibration at 257.7 cm^{-1} is by far the most intense. It can be determined very accurately since on excitation in the region of the charge-transfer band at 522 nm several overtones occur as a result of the resonance-Raman-effect as well as a series of combination tones with the symmetric Re—I stretching vibration at 153 cm^{-1}. The Re—Re vibrations of the octachloro- (277 cm^{-1}) and octabromo-complex (279 cm^{-1}) appear distinctly higher. Weak skeletal and lattice vibrations occur at 195, 119, 107 and 98 cm^{-1}.

Experimental

Anhydrous, iodine-free hydrogen iodide is passed into a solution of about 500 mg of $[(n\text{-}C_4H_9)_4N]_2[Re_2Cl_8]$ in 250 ml of freshly distilled CH_2Cl_2, previously dried over a molecular sieve. The color of the solution immediately changes from light blue to deep violet. On removal of solvent by evaporation $[(n\text{-}C_4H_9)_4N]_2[Re_2I_8]$ precipitates in the form of dark-violet to black crystals. Double recrystallization from CH_2Cl_2 affords the very pure compound in 50—70 % yield. On elemental

[*] Prof. Dr. W. Preetz, Dipl.-Chem. L. Rudzik
Institut für Anorganische Chemie der Universität
Olshausenstrasse 40—60, D-2300 Kiel (Germany)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79 0202-0150 $ 01.00/0

analysis the sum of the contents of C, H, N, I and Re amounted to 99.35%. The solid complex salt thermally decomposes at *ca.* 200°C. It is moderately soluble in benzene, toluene, and ethanol, and readily soluble in dichloromethane and acetone.

Received: October 6, 1978 [Z 144a IE]
German version: Angew. Chem. *91*, 159 (1979)

[1] *F. A. Cotton, N. F. Curtis, B. F. G. Johnson, W. R. Robinson*, Inorg. Chem. *4*, 326 (1965).
[2] *J. V. Brencic, F. A. Cotton*, Inorg. Chem. *9*, 351 (1970); *W. K. Bratton, F. A. Cotton, ibid. 9*, 789 (1970); *K. Hedwig, K. H. Linse, K. Schwochau*, Inorg. Nucl. Chem. Lett. *13*, 77 (1977).
[3] *F. A. Cotton, C. Oldham, W. R. Robinson*, Inorg. Chem. *5*, 1798 (1966).
[4] *R. J. H. Clark, M. L. Franks*, J. Am. Chem. Soc. *98*, 2763 (1976); *F. A. Cotton, W. T. Hall*, Inorg. Chem. *16*, 1867 (1977); *W. C. Trogler, E. I. Solomon, H. B. Gray, ibid. 16*, 3031 (1977); *W. C. Trogler, C. D. Cowman, H. B. Gray, F. A. Cotton*, J. Am. Chem. Soc. *99*, 2993 (1977); *F. A. Cotton, B. A. Frenz, B. R. Stults, T. R. Webb, ibid. 98*, 2768 (1976).
[5] *W. Preetz, H. Homborg*, Z. Anorg. Allg. Chem. *415*, 8 (1975).
[6] *R. J. H. Clark, N. R. D'Urso*, J. Am. Chem. Soc. *100*, 3088 (1978).
[7] Note added in proof: Another, albeit less productive method for the synthesis of the title compound has just been published: *H. D. Glicksmann, R. A. Walton*, Inorg. Chem. *17*, 3179 (1978).

Long-Chain Alkylammonium Ions as Phase Transfer Reagents for the Synthesis of Mixed-Ligand Complexes of the Platinum Metals

By *Ashok Kumar Shukla* and *Wilhelm Preetz*[*]

The transfer of anionic reactants from a polar phase into an apolar phase by lipophiles has recently gained increasing importance in synthetic chemistry. In two-phase liquid/liquid or solid/liquid systems, complete reaction of organic compounds with inorganic anions can be achieved merely with the aid of a few mol-percent of transfer reagent, a process now commonly referred to as phase transfer catalysis (PTC)[1]. Crown ethers were first used for this purpose, but the more readily accessible quaternary alkylammonium salts are equally suitable reagents[2]. To our knowledge the application of PTC to "inorganic reactions" has so far not been reported in the literature.

In the case of kinetically inert hexahaloosmates(IV) ligand exchange processes take place 10^2 to 10^4 times more rapidly in weakly polar or apolar solvents than in aqueous systems[3]. Exploiting this fact in the application of phase transfer processes it is possible to carry out substitution reactions under mild conditions. Though only the heavier halogen ligands X = Cl, Br, I can be mutually substituted in complexes of the type $[MX_6]^{2-}$, M = Os, Ir, Pt, (Re), in aqueous acidic media[4], we have now been able to prepare the first fluorine-containing mixed-ligand complexes of the type $[MF_nX_{6-n}]^{2-}$, $n = 1-5$, in organic solvents. Hitherto, platinum metal complexes could be fluorinated only with BrF_3 or XeF_2 and in KHF_2 melts[5]. But all Br and I ligands are cleaved under such reaction conditions.

Tridodecylammonium, $[(C_{12}H_{25})_3NH]^+$ (A^+), the hydrogen sulfate of which is readily available in very pure crystalline form, has proven to be a suitable lipophilic phase-transfer reagent. Substitution can be carried out both in homogeneous organic phases as well as in two phases using the PTC method. The principle steps of such substitutions are as follows:

1. *Ion-pair extraction.* The complex anions and the halide ions are transferred separately or together from the aqueous solution or the solid salt into the organic phase (benzene or toluene) with the aid of A^+.

$$2A^+HSO_{4\,org}^- + [MX_6]_{aq}^{2-} \rightleftharpoons A_2^+[MX_6]_{org}^{2-} + 2HSO_{4\,aq}^-$$

$$A^+HSO_{4\,org}^- + NaY_{solid\ or\ aq} \rightleftharpoons A^+Y_{org}^- + NaHSO_{4\,solid\ or\ aq}$$

2. *Ion-pair reaction.* The ion pairs undergo stepwise ligand substitution. An equilibrium between several mixed-ligand complexes ensues in dependence of their concentrations. The presence of solid NaY favors the ligand exchange if X is a lighter halide then Y; owing to the high lattice energy solid NaX is formed by PTC.

$$A_2^+[MX_6]_{org}^{2-} + nA^+Y_{org}^- \rightleftharpoons A_2^+[MY_nX_{6-n}]_{org}^{2-} + nA^+X_{org}^-$$

3a. *Precipitation as sparingly soluble complex salt.* Benzene forms a homogeneous organic phase with a solution of potassium acetate in glacial acetic acid. The ion pairs undergo double conversion with precipitation of the complex potassium salts, which are readily soluble in water.

$$A_2^+[MY_nX_{6-n}]_{org}^{2-} + 2K^+AcO_{org}^- \xrightarrow{C_6H_6/AcOH} K_2[MY_nX_{6-n}]\downarrow_{solid} + 2A^+AcO_{org}^-$$

3b. *Complex-ion extraction* ("stripping"). The complex anions can be extracted into an aqueous phase in exchange with larger, less hydrolyzed anions (*e.g.* ClO_4^-, CCl_3COO^-).

$$A_2^+[MY_nX_{6-n}]_{org}^{2-} + 2ClO_{4\,aq}^- \xrightarrow{C_6H_6/H_2O} [MY_nX_{6-n}]_{aq}^{2-} + 2A^+ClO_{4\,org}^-$$

4. *Separation of mixtures of complexes.* Hexahalo complexes of tetravalent platinum metals, whether containing the same or different ligands, are kinetically inert in aqueous acidic solutions at low temperatures. The individual species of the $[MY_nX_{6-n}]^{2-}$ mixtures can be isolated in pure form by separation on cellulose ion-exchangers[6]. Of the many mixed-halo complexes accessible in this way, the new fluorine-containing compounds are of special interest. The reaction conditions for a selection of such compounds are listed in Table 1.

Table 1. Synthesis of fluorine-containing hexahalo complexes by ion-pair reactions in benzene.

Reactants	T [°C]	t [min]	Main product (yield %) [a]
$A_2^+[OsCl_6]^{2-}$, A^+F^-	80	60	$[OsFCl_5]^{2-}$ (40), $[OsF_2Cl_4]^{2-}$ (30)
$A_2^+[OsCl_6]^{2-}$, A^+F^-	80	180	$[OsF_2Cl_4]^{2-}$ (40), $[OsF_3Cl_3]^{2-}$ (20)
$A_2^+[OsBr_6]^{2-}$, A^+F^-	80	10	$[OsFBr_5]^{2-}$ (40), $[OsF_2Br_4]^{2-}$ (40)
$A_2^+[OsBr_6]^{2-}$, A^+F^-	80	60	$[OsF_3Br_3]^{2-}$ (50), $[OsF_4Br_2]^{2-}$ (20)
$A_2^+[OsI_6]^{2-}$, A^+F^-	20	10	$[OsF_2I_4]^{2-}$ (20), $[OsF_3I_3]^{2-}$ (10) [b]
$A_2^+[OsCl_5I]^{2-}$, A^+F^-	80	30	$[OsFCl_4I]^{2-}$ (60), $[OsF_2Cl_3I]^{2-}$ (30)

[a] Low yields of other mixed-ligand complexes; [b] losses by hydrolysis.

The hexahalometalates(IV) of Ir, Pt and Re react similarly. The method is not restricted to the mutual exchange of F,

[*] Prof. Dr. W. Preetz, Dipl.-Chem. A. K. Shukla
Institut für Anorganische Chemie der Universität
Olshausenstr. 40–60, D-2300 Kiel (Germany)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979
0570-0833/79/0202-0151 $ 01.00/0

Cl, Br and I; it can also be utilized for the stepwise insertion of NO_2^-, CN^-, SCN^- and $C_2O_4^{2-}$ in hexahalo complexes.

Received: November 20, 1978 [Z 144b IE]
German version: Angew. Chem. 91, 160 (1979)

[1] *W. P. Weber, G. W. Gokel:* Phase Transfer Catalysis in Organic Synthesis. Springer-Verlag, Berlin 1977; *E. V. Dehmlow*, Angew. Chem. *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *16*, 493 (1977); *G. W. Gokel, W. P. Weber*, J. Chem. Educ. *55*, 350, 430 (1978).
[2] *A. Jończyk, M. Ludwikow, M. Mąkosza*, Angew. Chem. *90*, 58 (1978); Angew. Chem. Int. Ed. Engl. *17*, 62 (1978).
[3] *W. Preetz, A. K. Shukla*, Z. Anorg. Allg. Chem. *433*, 140 (1977).
[4] *W. Preetz, H. J. Walter*, Z. Anorg. Allg. Chem. *402*, 169 (1973); *W. Preetz, H. Homborg, ibid. 407*, 1 (1974).
[5] *K. R. Dixon, D. W. A. Sharp, G. A. Sharpe*, Inorg. Synth. *12*, 232 (1970); *W. Preetz, H. Kühl*, Z. Anorg. Allg. Chem. *425*, 97 (1976).
[6] *G. Barka, W. Preetz*, Z. Anorg. Allg. Chem. *433*, 147 (1977); *L. Rudzik, W. Preetz, ibid. 443*, 118 (1978).

Detection of Large-Ring Sulfur Molecules in Liquid Sulfur: Simple Preparation of S_{12}, α-S_{18}, and S_{20} from S_8[1]

By *Ralf Steudel* and *Hans-Joachim Mäusle*[*]

On melting at 120°C, *cyclo*-octasulfur is slowly converted into an equilibrium mixture of S_8 and π-sulfur (S_π); the solidification temperature (triple point) is therefore *ca.* 5°C lower than the melting temperature; the S_π content increases from 5.5 wt-% at 115°C to 12% at 159°C[2]. It has already been shown by vibrational spectroscopic analysis that S_π contains S_6, S_7, and S_{12}[3a], and S_7 can be preparatively isolated from quenched sulfur melts[3b]. We now report the simple preparation of pure S_{12}, α-S_{18}, and S_{20} from liquid sulfur, in yields comparable with those obtained[6] in the condensation reactions[4, 5] previously employed for the synthesis of these rings. The separation of S_{12}, α-S_{18}, and S_{20} from excess S_8 was accomplished by flotation (in the case of S_{12}) and by fractional crystallization (solutions of S_{18} and S_{20} in CS_2 tend to supersaturation).

S_{12} was identified by its crystal shape, melting point, and Raman spectrum[7], α-S_{18} and S_{20} by their melting points, color, crystal shape, densities, and lattice constants (both crystallize orthorhombically). The α-S_{18} isolated was free from β-S_{18}. The hitherto unrecorded vibrational spectra of α-S_{18} and S_{20}, which are best suited for the rapid characterization and differentiation of these species from other sulfur modifications, are given in Table 1. Owing to the low molecular symmetry (α-S_{18}: C_{2h}; S_{20}: C_2[4b]) the spectra show many lines.

Table 1. Raman and IR spectra of solid α-S_{18} and S_{20} (in cm^{-1}; Cary 82 Raman spectrometer with krypton laser, 647.1 nm, sample temperature −80°C, slit 1.5 cm^{-1}, relative intensities in brackets; Perkin Elmer 325 IR spectrometer, range 200—600 cm^{-1}, CsI pellets, 25°C).

α-S_{18}			S_{20}		
Raman		IR	Raman		IR
478 (72)	136 (43)	465 s	470.5 (41)	188 (12)	460 m, br
469 sh	131 sh	456 m	466 (100)	173 (5)	
462 (25)	99 (21)	427 m	462 sh	167 (16)	423 vw
458 (100)	85 (26)	271 m	454 (9)	136 (73)	278 m
445 (45)	80 (10)	263 vs	444 (17)	113 (4)	270 m
420 (2)	69 (>100)	253 s	428 (8)	93 (63)	260 s
276 (14)	59 (52)	224 w	416 (3)	66 (46)	252 s
257 (16)	50 (7)		411 (3)	54 (31)	
250 (18)	45 (24)		270 (26)	48 (17)	
234 (6)	36 (51)		254 sh	40 sh	
228 (45)	30 (10)		250 (24)	32 (34)	
166 (74)	20 (12)		213 (5)	29 sh	
153 (34)			207	18 (7)	

Apart from the three above-mentioned components, which are stable at 25°C, we have now isolated for the first time an orange-yellow resin-like substance from S_π which may be regarded as a mixture of large S_x rings. S_x is very soluble in CS_2 at 25°C; at −78°C the solubility is 4 g/100 g CS_2. This solution can be stored for weeks at 25°C, whereas neat S_x decomposes within a matter of days at 25°C into polymeric sulfur (*ca.* 60%), S_8 (*ca.* 40%), and traces of S_{12}; no decomposition occurs at −78°C. S_x is practically insoluble in benzene toluene, trichloro-, dichloro-, and dibromomethane. The relative molecular mass of S_x, determined osmometrically in CS_2, corresponds to 25 atoms per molecule; however the Raman spectrum is consistent with a complex mixture of homocycles, since a continuum (due to numerous closely adjacent lines) instead of discrete lines is observed in the region of the SSS deformation vibrations (285—100 cm^{-1}) while, on the other hand, only few SS stretching vibrations occur. Column chromatography on silica gel 60 at −40°C, with partial (10%) decomposition of S_x to S_8, gave only partial separation into six S_8-free fractions with relative molecular masses corresponding to $x = 23$ to 34 (column length 120 cm, solvent CS_2). Under the same conditions, S_6/S_{12} mixtures were separated almost quantitatively.

These findings confirm earlier presumptions[2] that liquid sulfur contains both smaller as well as larger S_n rings ($n = 6$, 7, 12, 18, 20, >20) besides S_8; however, there is no evidence available as yet for the presence of S_9, S_{10} and other medium sized sulfur rings ($n = 13$—17). The view expressed in recent work[8] that S_π consists of S_8 rings in a conformation deviating from that of the normal (D_{4d}) conformation is thus refuted.

Experimental

Preparation of S_x: 400 g of a sulfur melt previously heated to 155—159°C for 3 h and then quenched by pouring into liquid nitrogen is extracted with 250 ml of CS_2 for 1 h at 25°C, and the filtered extract allowed to stand for 20 h at −78°C. The solution is separated from precipitated S_8 and S_{12} by rapid decantation, warmed to 25°C, and treated with an equal volume of *n*-pentane. After 10 min the solution is carefully decanted from the oily S_x. Reprecipitation of the CS_2-containing S_x five times—by dissolution in 40 ml CS_2, treatment with 40 ml *n*-pentane and careful decantion—affords the resin-like product free from S_8, S_7 and S_6. Yield 1.2 g.

Preparation of α-S_{18} and S_{20}: The 5 × 80 ml CS_2/pentane mixture remaining after reprecipitation of the S_x is stored for 3 d in a closed flask at 25°C. The lemon-yellow precipitate is recovered by decantation and extracted with 50 ml CS_2 for 30 min at 25°C. The extract is concentrated to 5 ml and allowed to stand for 1 h. The precipitated sulfur is recrystallized by dissolution in 40 ml CS_2 and concentration of the resulting solution to 3 ml. After 3 h, 150 mg of a mixture of α-S_{18} (intense yellow rhombic platelets) and S_{20} (pale yellow prismatic rods) crystallize out. For separation a small portion of the roughly ground mixture is added to a mixture of 14 ml $CHBr_3$ and 20 ml $CHCl_3$ in a separating funnel and the density of the mixed solvent adjusted by dropwise addition of further $CHBr_3$ (*ca.* 0.25 ml) so that S_{20} ($\rho = 2.01$ g·cm^{-3}) floats on the solution and α-S_{18} ($\rho = 2.09$ g·cm^{-3}) sinks, while small amounts of S_{18} and S_{20} (*e.g.* intergrown crystals) remain suspended in the liquid. On addition of all the remaining

[*] Prof. Dr. R. Steudel, Dipl.-Chem. H.-J. Mäusle
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979
0570-0833/79/0202-0152 $ 01.00/0

S_{18}/S_{20} mixture, the α-S_{18} separates from S_{20} and each fraction is recrystallized from CS_2. Yields: 80 mg α-S_{18}, 40 mg S_{20}.

Preparation of S_{12}: 400 g of S_8 is heated to *ca.* 200 °C for 5—10 min in a 500 ml flask. The melt is then allowed to cool within 15 min to 140 °C, poured into liquid nitrogen and the product recovered after decantation extracted with 250 ml CS_2 for 1 h at 25 °C. The filtered solution is stored for *ca.* 20 h at −78 °C and then rapidly decanted. The precipitate of S_8 and $S_{12}\cdot CS_2$ is warmed to 25 °C, vigorously shaken with 50 ml CS_2 and the solution rapidly decanted off; the suspended, colorless powdery $S_{12}\cdot CS_2$ is carried over with the solution and is thus separated from the large S_8 crystals. The $S_{12}\cdot CS_2$ is recovered from the solution by filtration, and the filtrate returned to the S_8/S_{12} mixture for further recovery of $S_{12}\cdot CS_2$ by extraction, decantation, and filtration. This procedure is repeated a further three times. The crude product is dissolved in 200 ml CS_2 at 25 °C and recrystallized at −78 °C. Yield: 1.0 g $S_{12}\cdot CS_2$, after prolonged exposure to air 0.85 g S_{12} of m.p. 146—148 °C.—If the sulfur melt is not heated to 200 °C and then cooled to 140 °C but allowed to reach equilibrium at 140 °C within 3 h, the yield of S_{12} is only 0.25 g.

Received: November 10, 1978 [Z 140 IE]
German version: Angew. Chem. *91*, 165 (1979)

[1] Part 60 of Sulfur Compounds. This work was supported by the Deutsche Forschungsgemeinschaft. We thank Dipl.-Chem. *J. Steidel* and Dipl.-Chem. *K. Erekul* for carrying out the X-ray crystallographic measurements, and *G. Gökmen* for experimental assistance.—Part 59: *J. Steidel, J. Pickardt, R. Steudel*, Z. Naturforsch. *B 33*, 1554 (1978).

[2] *R. E. Harris*, J. Phys. Chem. *74*, 3102 (1970); and references cited therein.

[3] a) *R. Steudel, H.-J. Mäusle*, Angew. Chem. *89*, 114 (1977); Angew. Chem. Int. Ed. Engl. *16*, 112 (1978); b) *ibid. 90*, 54 (1978) and *17*, 56 (1978).

[4] a) *M. Schmidt, G. Knippschild, E. Wilhelm*, Chem. Ber. *101*, 381 (1968); b) *M. Schmidt, E. Wilhelm, T. Debaerdemaeker, E. Hellner, A. Kutoglu*, Z. Anorg. Allg. Chem. *405*, 153 (1974). In Fig. 1 of this publication, S_{18} and S_{20} are interchanged; S_{18} has C_{2h}- not C_{2v}-symmetry.

[5] We suggest that the S_{18} described by *Schmidt et al.* [4b] should be designated as α-S_{18} to distinguish it from the conformer β-S_{18} [*T. Debaerdemacker, A. Kutoglu*, Cryst. Struct. Commun. *3*, 611 (1974)]. α-S_{18} is not transformed into β-S_{18} on boiling in toluene for 6 h.

[6] The isolation of S_{12} ("yield" 0.1 %) from sulfur melts as first reported by *M. Schmidt* and *H.-D. Bock* [Angew. Chem. 79, 944 (1967); Angew. Chem. Int. Ed. Engl. *6*, 955 (1967)] could not be reproduced in our laboratory, even after several attempts by different co-workers.

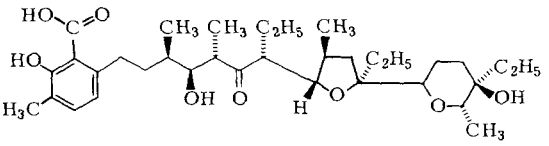
[7] *R. Steudel, H.-J. Mäusle*, Z. Naturforsch. *A 33*, 951 (1978).

[8] *M. F. Churbanov, I. V. Skripachev, G. G. Devyatykh*, Russ. J. Inorg. Chem. *21*, 439 (1976) and references cited therein. *M. E. Baur, D. A. Horsma*, J. Phys. Chem. *78*, 1670 (1974).

^{23}Na-NMR Study of the Competition of Biogenic Amines with Sodium Ion for Binding to Lasalocid (X-537A)[**]

By *Jean Grandjean* and *Pierre Laszlo*[*]

Lasalocid (X-537A) *(1)*[1], a linear carboxylic polyether antibiotic ionophore, is remarkable for its multiple functions. Not only does it complex and transport a wide variety of ions (alkali and alkaline earth[2], rare earth, transition metal ions) across membranes but has the same action on biogenic amines[3]. Furthermore, it also stimulates thromboxane or prostaglandin synthesis and thus affects calcium metabolism[4].



(1)

Through direct observation of the sodium ion, we have demonstrated competitive binding of Na^+ and biogenic amines (cf. Table 1) with lasalocid *(1)*. This conclusion is in accord with the very similar structures found for both types of complexes (cf.[7]). Given the significantly greater binding constants of the amines with *(1)* in a membrane-like environment[3c, 6b], the transport of the amines across biological membranes can be rationalized as follows: after crossing the membrane, *(1)* disgorges its organic load at the water interface as it recomplexes with alkali and alkaline earth cations, whose physiological concentrations are far greater than those of the catecholamines.

Solvent polarity is an important parameter: whereas one molecule of lasalocid complexes one ion in polar solvents[2b, 2e, 5], two molecules of lasalocid sandwich the alkali or alkaline earth ion in nonpolar media[2a, 2c, 2d] and in the crystal. In such nonpolar environments, the free acid *(1)* assumes a hydrogen-bonded cyclic structure virtually identical to that of the Na^+ complex[2d, 6a]. The binding constants for biogenic amines drop by one or two orders of magnitude when the solvent is changed from isooctane to octanol, and become negligible in methanol solution[6b].

We have chosen a binary mixture of methanol and *n*-hexane (71 : 29 v/v) as solvent in order to mimic the lipid membrane-aqueous solution interface, and to ensure formation of 1 : 1 complexes between *(1)* and Na^+[2e] or the biogenic amines[7]. The ^{23}Na-NMR data[8a] were evaluated in the manner already described[8b].

Addition of biogenic amines to 10^{-2} M solutions of *(1)* as the sodium salt (= 1 : 1 complex of *(1)* and Na^+) induces a narrowing of the observed ^{23}Na resonance. In the absence of amines, the band width decreases upon raising the temperature, as befits fast chemical exchange of the sodium cation between the free state in solution and the bound state in the Na^+/*(1)* complex. The sodium chemical shift does not depend upon the amine concentration. Therefore, the observed relaxation rate $1/T_2$ is simply the weighted average of the relaxation rates in the free (F) and in the bound (B) state, respectively:

$$\frac{1}{T_2} = \frac{p_F}{T_{2F}} + \frac{p_B}{T_{2B}}, \quad \text{with} \quad \frac{1}{T_{2F}} \ll \frac{1}{T_{2B}}$$

The calculated stability constant K_{Na} of the sodium complex is $500 \pm 100\ l\,mol^{-1}$, a value in agreement with the expected solvent effect[2c, 6b]. Addition of the biogenic amines, by displacement of sodium cations from the 1 : 1 complex they form with *(1)*, increases the mole fraction p_F at the expense of p_B, leading to the observed narrowing of the linewidth. The stability constants K_{amine} of the amine complexes (Table 1) have been determined from the following equation:

$$K_{amine} = \frac{[\text{amine}]_F[Na^+]_B}{[\text{amine}]_B[Na^+]_F} K_{Na}$$

[*] Prof. Dr. P. Laszlo, Dr. J. Grandjean
Institut de Chimie Organique êt de Biochimie (B 6)
Université de Liège
Sart-Tilman par 4000 Liège (Belgium)

[**] We thank Dr. *D. Valentine* (Hoffmann-Laroche, Nutley, N. J.) for the kind gift of a sample of lasalocid, and Dr. *J. Y. Lallemand* (Ecole Normale Supérieure, Paris) for helping us with spectrometer time.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* 0570-0833/79/0202-0153 $ 01.00/0

Table 1. Stability constants K_{amine} and K_{Na} of complexes with lasalocid (*1*).

T(K)	Amine or ion	K, [l mol^{-1}] ($\pm 2\sigma$)
299	Serotonin bimaleate	450 ± 80 [a]
297	3-Hydroxytyramine	260 ± 60 [a]
297	L-Norepinephrine	280 ± 60 [a]
298	Na^+	500 ± 100

[a] Assuming $K_{Na} = 500$ l mol^{-1}.

Received: November 7, 1978 [Z 133 IE]
German version: Angew. Chem. *91*, 166 (1979)

[1] *S. M. Johnson, J. Herrin, S. J. Liu, I. C. Paul*, Chem. Commun. *1970*, 72.
[2] a) *S. R. Alpha, A. H. Brady*, J. Am. Chem. Soc. *95*, 7043 (1973); b) *G. Cornélius, W. Gartner, D. H. Haynes*, Biochemistry *13*, 3052 (1974); c) *H. Degani, H. L. Friedman, ibid. 13*, 5022 (1974); d) *D. J. Patel, C. Shen*, Proc. Nat. Acad. Sci. USA *73*, 1786 (1976); e) *C. Shen, D. J. Patel, ibid. 73*, 4277 (1976).
[3] See, *e.g.*, a) *B. C. Pressman*, Fed. Proc. *32*, 1698 (1973); b) *J. C. Foreman, J. L. Mongar, B. D. Gomperts*, Nature *245*, 249 (1973); c) *B. C. Pressman, N. T. de Guzman*, Ann. N. Y. Acad. Sci. *227*, 380 (1974); *264*, 373 (1975); d) *H. Pasantes-Morales, R. Salced, A. Gomez-Puyov*, Biochem. Biophys. Res. Commun. *58*, 847 (1974); e) *J. J. Nordmann, G. A. Currell*, Nature *253*, 646 (1975).
[4] *H. R. Knapp, O. Oelz, L. J. Roberts, B. J. Sweetman, J. A. Oates, P. W. Reed*, Proc. Nat. Acad. Sci. USA *74*, 4251 (1977).
[5] *C. C. Chiang, I. C. Paul*, Science *196*, 1441 (1977).
[6] a) *M. J. O. Anteunis*, Bioorg. Chem. *5*, 327 (1976); *J. M. Friedman, D. L. Rousseau, C. Shen, I. C. Paul*, J. Chem. Soc. Chem. Commun. *1977*, 684; b) *S. Lindenbaum, L. Sternson, S. Rippel, ibid. 1977*, 268.
[7] a) *C. Shen, D. J. Patel*, Proc. Nat. Acad. Sci. USA *74*, 4734 (1977); b) *J. W. Westley, R. H. Evans, J. F. Blount*, J. Am. Chem. Soc. *99*, 6057 (1977).
[8] a) *P. Laszlo*, Angew. Chem. *90*, 271 (1978); Angew. Chem. Int. Ed. Engl. *17*, 254 (1978); b) *J. Grandjean, P. Laszlo, F. Vögtle, H. Sieger, ibid. 90*, 902 (1978) and *17*, 856 (1978), respectively.

Reversal of the Selectivity Principle in Free-Radical Additions to Alkenes[**]

By *Bernd Giese* and *Jürgen Meixner*[*]

It has previously been assumed that the nucleophilic properties of alkyl radicals in additions to alkenes[1] and arenes[2] can be described in terms of the dominant interaction between

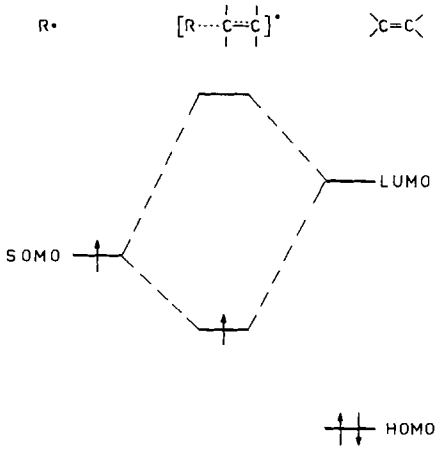
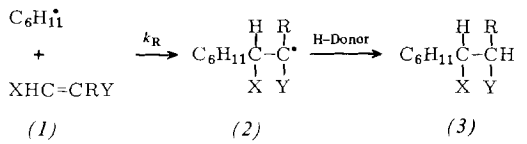


Fig. 1. Frontier orbital interaction between the singly occupied orbital (SOMO) of a radical and the unoccupied orbital (LUMO) of an alkene.

[*] Prof. Dr. B. Giese, Dipl.-Chem. J. Meixner
Institut für Organische Chemie und Biochemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)
[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

the singly occupied orbitals (SOMO) of the radicals and the lowest unoccupied orbitals (LUMO) of alkenes[3].

Substituents which lower the difference in energy between the SOMO and LUMO ought to increase both the reactivity as well as the selectivity of the radicals and the alkenes, owing to the better frontier orbital interaction. We have now observed this contradiction of the selectivity principle[4] in the reaction of the cyclohexyl radical with the alkenes (*1*): If generation of the C_6H_{11} radical from $C_6H_{11}HgOAc$ and $NaBH_4$ is carried out in the presence of (*1*) the adduct radicals (*2*) capture H to give the product (*3*) in almost quantitative yield[1a, 5].



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

In reactions with pairs of alkenes the relative rate constants k_H (R = H) and k_{CH_3} (R = CH_3) can be measured[5].

Table 1. Relative rate constants k_H (R = H) and k_{CH_3} (R = CH_3) (mean error ± 10 %) and competition constants k_H/k_{CH_3} of the cyclohexyl radical with the alkenes (*1*) at 293 K [a] in $CHCl_3$.

Alkene	k_H [b]	k_{CH_3}	k_H/k_{CH_3}
Styrene	≡ 1.0		1.1
α-Methylstyrene		0.92	
Methyl acrylate	6.7		1.3
α-Methyl methacrylate		5.0	
Acrylonitrile	24		1.8
Methylacrylonitrile		13	
Fumarodinitrile	310		4.4
Methylfumarodinitrile		70	
Maleic anhydride	730		5.0
Methylmaleic anhydride		145	

[a] Preliminary experiments show that the reactivity sequence does not alter on varying the temperature.
[b] The k_H values are rate constants per attacked vinylic C-atom. The reactivity of fumarodinitrile and maleic anhydride is twice as large as the k_H value.

The measured values listed in Table 1 show that the statistically corrected rate constant k_H increases by a factor of 730 on going from styrene to maleic anhydride, while in the series of α-methylated alkenes the addition constant k_{CH_3} increases by a factor of only 145.

The raising of the energy of the LUMO by a vinylic methyl group has almost no effect in the case of the less reactive competing pair styrene/α-methylstyrene ($k_H/k_{CH_3} = 1.1$). In contrast the rate constant of the more reactive maleic anhydride is decreased by a factor of 5.0 by introduction of a methyl group (Table 1). Thus, the more reactive the reaction partners, the greater the influence of the substituents.

Together with the gradation in selectivity and reactivity of the primary, secondary and tertiary radicals[1b, 5] this substituent effect clearly demonstrates that the free-radical addition to alkenes can be satisfactorily explained in terms of the frontier orbital theory. If steric effects play a subordinate role[6] the selectivity increases with increasing reactivity of the radicals and alkenes. This finding is of great importance in radical polymerization.

Received: November 17, 1978 [Z 142 IE]
supplemented: December 11, 1978
German version: Angew. Chem. *91*, 167 (1979)

CAS Registry numbers:
Compounds listed in Table 1, from top to bottom: 100-42-5; 98-83-9;

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0154 $ 01.00/0*

96-33-3; 80-62-6; 107-13-1; 126-98-7; 764-42-1; 37580-44-2; 108-31-6; 616-02-4; cyclohexyl, 3170-58-9

[1] a) *B. Giese, J. Meister*, Angew. Chem. *89*, 178 (1977); Angew. Chem. Int. Ed. Engl. *16*, 178 (1977); b) *T. Caronna, A. Citterio, M. Ghirardini, F. Minisci*, Tetrahedron *33*, 793 (1977).

[2] *F. Minisci*, Top. Curr. Chem. *62*, 1 (1976); *A. Citterio, F. Minisci, O. Porta, G. Sesana*, J. Am. Chem. Soc. *99*, 7960 (1977).

[3] Review in *I. Fleming*: Frontier Orbitals and Organic Chemical Reactions. Wiley, New York 1976.

[4] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).

[5] *B. Giese, J. Meister*, Chem. Ber. *110*, 2588 (1977); *B. Giese, W. Zwick*, Angew. Chem. *90*, 62 (1978); Angew. Chem. Int. Ed. Engl. *17*, 66 (1978). Only in the case of α-methylstyrene are the products of disproportion and O_2-capture formed along with the H-capture product *(3)* from the adduct-radical *(2)*. This has been taken into account in the calculation of the relative reactivities.

[6] The k_K/k_{CH_3} value of 1.1 for the competing system styrene/α-methylstyrene shows that steric shielding by a methyl substituent on the neighboring vinylic C-atom has little influence on the addition of cyclohexyl radicals. In contrast the steric effect of a methyl group is of great importance for the regioselectivity of radical additions. *B. Giese, J. Meixner*, Tetrahedron Lett. *1977*, 2779. Table 1 contains alkenes from fumaronitrile which bear a CN or C(O)O group on the carbon atom which is attacked; although the steric effect of these groups is extremely small, without such shielding the reactivities ought to be somewhat greater.

A New Cationic Binuclear Trihydrido Complex Containing One Four- and One Five-Coordinate Platinum Atom[**]

By *Gustav Bracher, David M. Grove, Paul S. Pregosin*, and *Luigi M. Venanzi*[*]

As part of our programme concerned with the chemistry of platinum hydrides we have characterized several derivatives containing a monohydrido bridge, *e.g. (1)*[1]. In an extension of this work we have prepared, and now report, the unusual binuclear platinum trihydrido complex *(2a)* which contains both a dihydrido bridge and a terminal hydride ligand. This is the first example of a class of binuclear platinum hydrides containing one four- and one five-coordinate metal center. The recently reported dimeric complex $[Pt_2(\mu H)_2(SiEt_3)_2(PCy_3)_2]$[2] (Cy = cyclohexyl) also contains a dihydrido bridge, but here both metal centers are equivalent and four-coordinate.

The synthetic route to *(2a)* is shown below:

$$[Pt(cod)_2] + 2Ph_3P + H_2 \rightarrow \text{"hydride intermediate"}, \quad (3)$$

$$(3) + trans\text{-}[PtH(MeCOMe)(Ph_3P)_2][BF_4] \rightarrow (2a) \quad (4)$$

(cod = 1,5-cyclooctadiene)

The reaction of $[Pt(cod)_2]$ with two moles of phosphane and subsequent treatment with gaseous hydrogen is known to afford bisphosphanedihydridoplatinum complexes[3,4].

In our case intermediate *(3)* was directly reacted with *(4)* to give the trihydrido complex *(2a)*, which was isolated from the reaction mixture as a pale-yellow air-stable solid. Its microanalytical data are consistent with the molecular formula shown and its infrared spectrum shows a weak band at 2205 cm^{-1}, which we assign to the terminal $Pt_B—H_B$ stretching vibration.

[*] Prof. L. M. Venanzi, G. Bracher, Dr. D. M. Grove and Dr. P. S. Pregosin
Laboratorium für Anorganische Chemie, ETH-Zentrum
Universitätstrasse 6, CH-8092 Zürich (Switzerland)

[**] This work was supported by the Swiss National Science Foundation.

The molecular structure of complex *(2a)* was deduced from the ^1H-, ^{31}P- and ^{195}Pt-NMR spectroscopic data.

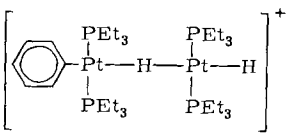
The ^1H-NMR spectrum [$(CD_3)_2CO$, 360 MHz] has, in addition to the resonances due to the aromatic protons of the PPh_3 ligands, a complex set of resonances in the region to high field of TMS. The appearance of these hydride resonances is indicative of a system containing strongly coupled spins and the spectral data were analyzed by computer simulation and iteration[5].

For the purposes of discussion the resonances are conveniently divided as follows:

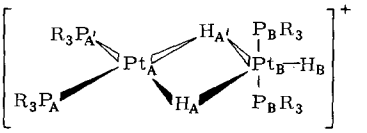
1. A terminal hydride resonance [$\delta H_B = -4.75$], of relative intensity one, which is coupled to two distinct platinum atoms [$^1J(H_BPt_B) = 1197$ Hz, $^3J(H_BPt_A) = 226$ Hz], two bridging hydride atoms [$^2J(H_AH_B) = 14$ Hz] and two equivalent phosphorus atoms [$^2J(H_BP_B = 25$ Hz].

2. A bridging hydride resonance, H_A, of relative intensity two, which is centred at $\delta = -3.20$ and coupled to two distinct platinum atoms [$^1J(H_APt) = 601$ and 397 Hz], four phosphorus atoms and the terminal hydride ligand. The division of this resonance into two well-separated multiplets arises from the large value of $\{^2J(H_AP_A) + {}^2J(H_AP_{A'})\}$ which is 110 Hz. This results from the fact that the values of $^2J(PH)$ for platinum complexes are large (> 100 Hz) for *trans*- and small (< 25 Hz) for *cis*-geometries[6].

A $^{195}Pt\{^1H\}$-NMR study showed resonances attributable to two distinct metal centers [CD_2Cl_2: $\delta Pt_A = -5104$, $\delta Pt_B = -4756$][7] each of which was coupled to two equivalent directly bound phosphorus atoms. The magnitude of the observed platinum-platinum coupling [$^2J(Pt_APt_B) = 325$ Hz] is comparable to that found for *(1)* (366 Hz) and is in accord with values found for other dimeric complexes containing bridging ligands[8].



BPh_4^- *(1)*



BF_4^-

(2a), R = C_6H_5
(2b), R = C_2H_5
(2c), R = $c\text{-}C_6H_{11}$

The $^{31}P\{^1H\}$-NMR spectrum of *(2a)* shows the expected resonances for the two types of phosphorus atoms with appropriate couplings to platinum [CD_2Cl_2: $\delta P_A = 31.9$, $^1J(P_APt_A) = 3008$ Hz, $^3J(P_APt_B) = 42$ Hz; $\delta P_B = 26.6$, $^1J(P_BPt_B) = 2803$ Hz, $^3J(P_BPt_A) = 18$ Hz][7]. An "off-resonance" ^1H-decoupling experiment resulted in a large residual splitting of the signals attributable to P_A confirming our proposal of a *trans* phosphorus-hydride arrangement about Pt_A.

Experimental

To a stirred toluene solution of PPh_3 (525 mg, 2 mmol) under a N_2 atmosphere at 0°C was added $[Pt(cod)_2]$ (411 mg, 1 mmol) to produce a clear orange solution. A separate solution of *trans*-$[PtH(MeCOMe)(PPh_3)_2]^+BF_4^-$ (865 mg, 1 mmol) was prepared at 0°C and saturated with H_2. The two solutions were mixed together at 0°C and then stirred under a H_2 atmosphere for ½ h. After removal of solvent *in vacuo* the mass was washed with methanol and the brown-yellow solid collected and dried. An acetone extract of this solid was treated

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*

0570-0833/79 0202-0155 $ 01.00/0

with active charcoal, filtered and concentrated *in vacuo*. Addition of methanol to this yellow solution precipitated *(2a)*, which was filtered off and dried (Yield 625 mg, 41%).—*(2b)* and *(2c)* can be obtained in the same way.

Received: November 30, 1978 [Z 149 IE]
German version: Angew. Chem. *91*, 169 (1979)

CAS Registry numbers:
(2a), 69277-93-6; *(2b)*, 69277-95-8; *(2c)*, 69277-97-0; *(4)*, 37036-05-8; $Pt(cod)_2$, 12130-66-4

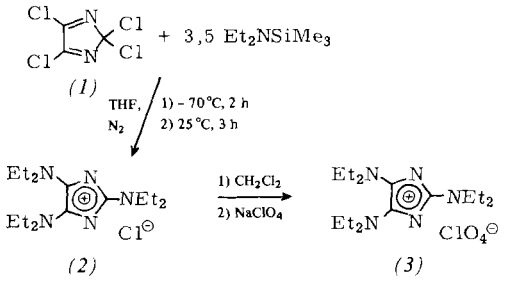
[1] *G. Bracher, D. M. Grove, L. M. Venanzi, F. Bachechi, P. Mura, L. Zambonelli*, Angew. Chem. *90*, 826 (1978); Angew. Chem. Int. Ed. Engl. *17*, 778 (1978).
[2] *M. Ciriano, M. Green, J. A. K. Howard, J. Proud, J. L. Spencer, F. G. A. Stone, C. A. Tsipis*, J. Chem. Soc. Dalton Trans. *1978*, 801.
[3] *J. Fornies, M. Green, J. L. Spencer, F. G. A. Stone*, J. Chem. Soc. Dalton Trans. *1977*, 1006.
[4] *G. K. Barker, M. Green, T. P. Onak, F. G. A. Stone, C. B. Ungermann, A. J. Welch*, J. Chem. Soc. Chem. Commun. *1978*, 169.
[5] LAME (Laocoon with Magnetic Equivalence, *C. W. Haigh*, University College, Swansea).
[6] *J. P. Jesson* in *E. Muetterties*: Transition Metal Hydrides. Marcel Dekker, New York 1971, Chapter IV.
[7] ^{195}Pt and ^{31}P chemical shifts in ppm relative to external Na_2PtCl_6 and H_3PO_4, respectively. For ^{195}Pt a negative sign indicates a shift to higher field.
[8] *N. M. Boag, J. Browning, C. Crocker, P. L. Goggin, R. J. Goodfellow, M. Murray, J. L. Spencer*, J. Chem. Res. (M) *1978*, 2962.

Stable Aza- and Diazacyclopentadienylium Salts[1]

By *Rudolf Gompper* and *Klaus Bichlmayer*[*]

Consistent with expectations from aromaticity criteria it has already been demonstrated experimentally that cyclopentadienyl cations are antiaromatic (resonance destabilized)[2]. From investigations on azacyclobutadienes[3, 4] it may be concluded—with supporting evidence from MO calculations[5]—that the antiaromatic character of aza- and 1,3-diazacyclopentadienyl cations is weaker than that of cyclopentadienyl cations. Moreover, donor groups, especially dialkylamino groups, also ought to have a stabilizing effect in all cyclopentadienyl cations.

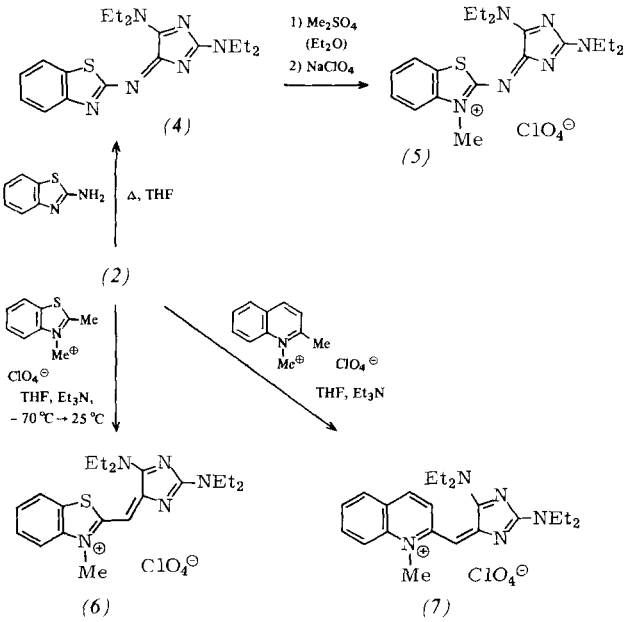
Treatment of tetrachloro-2*H*-imidazole *(1)*[6] in tetrahydrofuran with an excess of diethyl(trimethylsilyl)amine, first at



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

−70°C and then at room temperature, leads to separation of fine, bright-yellow needles whose composition, according to analytical and spectroscopic data and chemical behavior, has been established as 2,4,5-tris(diethylamino)-1,3-diazacyclopentadienylium chloride *(2)* (Table 1). The salt-like character of *(2)* is confirmed, *inter alia*, by the fact that it can be converted into the, likewise yellow, perchlorate *(3)* without any noticeable change in properties (Table 1).

Hydrolysis of *(2)* with aqueous hydrochloric acid affords, as expected, parabanic acid. Of preparative interest are the reactions of *(2)* with 2-aminobenzothiazole, 2,3-dimethylbenzothiazolium perchlorate, and 1,2-dimethylquinolinium perchlorate, which, respectively afford the orange merocyanine *(4)*, the red cyanine dye *(6)*, and the red quinolinium salt *(7)*. *(4)* reacts with dimethyl sulfate to give the orange azacyanine dye *(5)* (Table 1).



(4) *(5)* *(2)* *(6)* *(7)*

Table 1. Compounds prepared.

(2), yield 74%, m.p. 63–67°C (from THF); IR (KBr): 2940, 1660 (weak), 1610, 1575 cm^{-1}

(3), yield 61%, m.p. 83–84°C (from CH_2Cl_2/Et_2O); UV ($CHCl_3$): λ_{max} ($lg\varepsilon$) = 330 nm (4.30); IR (KBr): 2985, 2970, 2940, 1660 (weak), 1610, 1570, 1090 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.28 (mc; 18H), 3.61 (q; 8H), 3.72 (q; 4H); ^{13}C-NMR ($CDCl_3$): δ = 12.44, 13.90, 44.82, 47.15, 168.99 (C-4/5), 173.07 (C-2)

(4), yield 44%, m.p. 146°C (from Et_2O); UV/VIS ($CHCl_3$): λ_{max} ($lg\varepsilon$) = 480 (4.01), 445 (4.30), 425 (4.27), 260 nm (3.88)

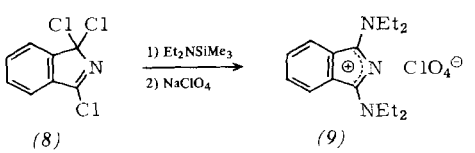
(5), yield 75%, bright-orange needles, m.p. 310°C (dec.); UV/VIS ($CHCl_3$): λ_{max} ($lg\varepsilon$) = 480 (4.18), 450 (4.40), 405 (4.24), 385 (4.26), 370 (4.19)

(6), yield 51%, red needles (from *i*PrOH/MeOH), m.p. 260—263°C (dec.); UV/VIS ($CHCl_3$): λ_{max} ($lg\varepsilon$) = 575 (4.55), 500 (4.51), 410 (3.87), 390 (4.03), 375 nm (4.02)

(7), yield 75%, deep-red lustrous needles (from iPrOH), m.p. 265—266°C (dec.); UV/VIS (EtOH): λ_{max} ($lg\varepsilon$) = 550 (4.55), 520 (4.48), 390 (3.94), 260 (4.21), 230 (4.26)

(9), yield 66%; bright-yellow rhombs (from CH_2Cl_2/Et_2O), m.p. 133—135°C; UV ($CHCl_3$): λ_{max} ($lg\varepsilon$) = 375 (3.84), 295 nm (4.20); IR (KBr): 2980, 2940, 1650, 1600, 1580, 1480, 1090 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.43 (t; 6H), 1.53 (t; 6H), 4.05 (q; 4H), 4.18 (q; 4H), 7.75–8.2 (m; 4H)

Stable derivatives of azacyclopentadienyl cations can also be prepared. The yellow 1,3-bis(diethylamino)-2-azaindenyl-



(8) *(9)*

ium perchlorate *(9)* can be obtained from trichloro-1*H*-isoindole *(8)*[7] in a manner resembling the formation of *(2)* from *(1)* (Table 1).

Received: December 12, 1978 [Z 138 IE]
German version: Angew. Chem. *91*, 170 (1979)

[*] Prof. Dr. R. Gompper, Dipl.-Chem. K. Bichlmayer
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79 0202-0156 S 01.00/0*

CAS Registry numbers:
(1), 59206-89-2; *(2)*, 69277-73-2; *(3)*, 69277-75-4; *(4)*, 69277-76-5; *(5)*, 69277-78-7; *(6)*, 69277-80-1; *(7)*, 69277-82-3; *(8)*, 21021-41-0; *(9)*, 69277-84-5; diethyl(trimethylsilyl)amine, 996-50-9; 2-aminobenzothiazole, 136-95-8; 2,3-dimethylbenzothiazolium perchlorate, 706-67-2; 1,2-dimethylquinolinium perchlorate, 20729-86-6

[1] Donor/Acceptor Substituted Aromatic Systems, Part 5. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 4: *R. Gompper, K. Schönafinger*, Chem. Ber., in press.

[2] a) *R. Breslow, J. M. Hoffman*, J. Am. Chem. Soc. *94*, 2110 (1972); b) *F. P. Lossing, J. C. Traeger, ibid. 97*, 1579 (1975).

[3] *B. M. Adger, C. W. Rees, R. C. Storr*, J. Chem. Soc. Perkin Trans. 1 *1975*, 45.

[4] *G. Seybold, U. Jersak, R. Gompper*, Angew. Chem. *85*, 918 (1973); Angew. Chem. Int. Ed. Engl. *12*, 847 (1973).

[5] *H.-U. Wagner*, private communication.

[6] *K. H. Büchel, H. Erdmann*, Chem. Ber. *109*, 1625 (1976).

[7] Br. Pat. 704595 (1954), Bayer AG; Chem. Abstr. *49*, 7001d (1955); *H. Vollmann, F. Baumann, B. Bienert*, US-Pat. 2701252 (1955), Bayer AG; Chem. Abstr. *49*, P10374b (1955).

An Example of the Equilibrium Ethylenehydridometal ⇌ Ethylmetal Complex[1]

By *Helmut Werner* and *Rainer Feser*[*]

It is generally assumed that both the insertion of C_2H_4 in a M—H bond as well as the reverse of this reaction proceed *via* an intermediate of the type *(1)*.

$$L_nMH + C_2H_4 \rightleftarrows \underset{(1)}{L_nMH(C_2H_4)} \rightleftarrows L_nM(C_2H_5)$$

Very few examples of stable isolable ethylenehydridometal complexes have previously been reported in the literature[2].

After having prepared $C_5H_5Rh(PMe_3)_2$ *(2)*[3] we have now also synthesized its monocarbonyl- *(3)* and ethylene-derivative *(4)* and investigated their behavior as Lewis bases.

$$\underset{(2)}{C_5H_5Rh(PMe_3)_2} + CO \rightarrow \underset{(3)}{C_5H_5Rh(CO)PMe_3} + PMe_3$$

$$[(C_2H_4)(PMe_3)RhCl]_2 + 2TlC_5H_5 \rightarrow \underset{(4)}{2C_5H_5Rh(C_2H_4)PMe_3} + 2TlCl$$

While *(2)* even reacts with NH_4PF_6 to give the complex $[C_5H_5RhH(PMe_3)_2]PF_6$, the stronger acid HBF_4 (in propionic anhydride) is necessary for the protonation of *(3)* and *(4)*; this is one case where the influence of the ligand—PMe_3 is a much better donor than CO or C_2H_4—on the basicity of the metal atom is more marked.

$$\underset{(3),(4)}{} + HBF_4 \rightarrow \underset{\substack{(5),\ L=CO \\ (6),\ L=C_2H_4}}{[C_5H_5RhH(L)PMe_3]BF_4}$$

The products *(5)* and *(6)* form light-brown, extremely air-sensitive crystals which are readily soluble in polar organic solvents such as *e.g.* CH_3NO_2.

As shown by the ^{1}H-NMR spectrum (cf. Table 1) *(5)* also exists in solution as the carbonylhydrido complex; evidence for insertion of the CO ligand in the Rh—H bond is not observed. In contrast, however, the temperature-dependence of the spectrum of *(6)* indicates, in this case, that an equilibrium is set up between ethylenehydrido- (a) and ethyl complex (b), where the free coordination site in the latter could possibly be occupied by a solvent molecule.

$$\underset{(a)}{[C_5H_5RhH(C_2H_4)PMe_3]^+} \rightleftarrows \underset{(b)}{[C_5H_5Rh(C_2H_5)PMe_3]^+}$$

In CD_3NO_2-solutions of *(6)* at room temperature only the signals of the C_5H_5- and PMe_3-protons are sharp, while those of the hydridic H atom ($\delta \approx -10.5$) and of the C_2H_4-protons ($\delta \approx 3.3$) appear as broad humps. At $+10$°C the signal at $\delta \approx 3.3$ splits into two less broader signals, which on further cooling to -20°C give two multiplets at $\delta = 3.0$ and 3.52. As expected, at -20°C a doublet of doublets (Table 1) is observed for the RhH signal. The signals of the C_5H_5- and PMe_3-protons remain unchanged on lowering the temperature[4].

Table 1. ^{1}H-NMR data for *(3)*—*(11)* (δ values, TMS int.; J in Hz; solvent for neutral complex: C_6H_6, for ionic compounds: CD_3NO_2).

Complex	C_5H_5	PMe_3	L [a]	Rh—R
(3)	5.29 d × d $J_{RhH}=0.7$, $J_{PH}=0.4$	1.15 d × d $J_{RhH}=1.4$, $J_{PH}=10$		
(4)	5.18 "t" $J_{RhH}=J_{PH}=0.7$	0.85 d × d $J_{RhH}=1.0$, $J_{PH}=9$	1.48 "t" br 2.78 "d" br	
(5)	5.97 d × d $J_{RhH}=1.0$, $J_{PH}=0.4$	1.90 d × d $J_{RhH}=1.2$, $J_{PH}=12.3$		−10.7 "t" $J_{RhH}=J_{PH}=21$
(6)	5.88 d × d $J_{RhH}=1.0$, $J_{PH}=0.4$	1.63 d × d $J_{RhH}=1.0$, $J_{PH}=11.8$	3.33 br (see text)	−10.5 d × d [−20°C] $J_{RhH}=18$, $J_{PH}=28$
(7)	5.70 m,	1.67 d × d $J_{RhH}=1.0$, $J_{PH}=10.8$	2.23 m [C*H*(CH$_3$)$_2$] 1.35 "d × d" [CH(C*H*$_3$)$_2$] [b] 1.32 "d × d" [CH(C*H*$_3$)$_2$]	−12.8 d × d × d $J_{RhH}=18$, $J_{PH}=25$; 32
(8)	5.70 d × d $J_{RhH}=1.0$, $J_{PH}=0.6$	1.60 d × d $J_{RhH}=0.9$, $J_{PH}=10.9$	3.47 m	[c]
(9)	4.88 d × d $J_{RhH}=1.4$, $J_{PH}=0.4$	1.15 d × d $J_{RhH}=0.9$, $J_{PH}=10.8$		1.62 "t" [d]
(10)	4.90 d × d $J_{RhH}=1.4$, $J_{PH}=0.4$	1.15 d × d $J_{RhH}=0.8$, $J_{PH}=10.8$		1.62 "t" [d]
(11)	4.92 d × d $J_{RhH}=1.5$, $J_{PH}=0.6$	1.22 d × d $J_{RhH}=0.8$, $J_{PH}=10.5$		1.59 "t" [d]

[a] L = C_2H_4 for *(4)*, *(6)* and *(8)*, L = P(*i*-C_3H_7)$_3$ for *(7)*; [b] because of the chirality center at rhodium the methyl groups of P(*i*-C_3H_7)$_3$ are diastereotropic; [c] signal for the ethyl group bound to the rhodium is partly covered by the PMe_3 signal and is thus not clearly locatable; [d] only the triplet-like A_3-part of the A_3B_2 spectrum is given; the signal for the methylene protons disappear because of numerous couplings in the base line noise.

The existence of the equilibrium (a)⇌(b) is confirmed by deuteration experiments. On addition of D_2O (excess) to the CD_3NO_2 solution of *(6)* at -20°C the previously observed

[*] Prof. Dr. H. Werner, Dipl.-Chem. R. Feser
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*

0570-0833/79/0202-0157 $ 01.00/0

^{1}H-NMR signals for the RhH and C_2H_4 protons disappear. If the solution of *(6)* in D_2O is treated with KOH and the resulting product extracted with benzene, the ^{1}H-NMR spectrum of the benzene extract is identical—except for the signals for complex-bound ethylene—with that of *(4)*. The mass spectrum of the product remaining after removal of solvent shows the line of highest intensity in the range $m/e = 270$—280 at $m/e = 276$, which corresponds to an ion of composition $C_5H_5Rh(C_2D_4)PMe_3^+$; the occurrence of weak lines at $m/e = 277$ to 281 indicate that reaction of D_2O with *(6)* can lead to deuteration not only of the ethylene but also, at least partially, to deuteration of the cyclopentadienyl ligand (the relatively low intensity of the C_5H_5-signal in the ^{1}H-NMR spectrum supports this assumption; cf. also [5]).

The equilibrium between ethylenehydrido- and ethyl-complex is also reflected in the reactivity of *(6)*: the ethylene of the complex can be replaced by CO or by P(*i*-Pr)$_3$. Reaction with C_2H_4 leads to formation of *(8)*, from which *(6)* can be regenerated, both in the solid state as well as in solution with elimination of C_2H_4; the formation of *(8)* could be formulated as involving an addition of ethylene to the free coordination site of the cation $[C_5H_5Rh(C_2H_5)PMe_3]^+$.

$$(6) + L \rightarrow [C_5H_5RhH(L)PMe_3]BF_4 + C_2H_4$$
$$(5),\ L = CO$$
$$(7),\ L = P(iPr)_3$$

$$(6) + C_2H_4 \rightleftharpoons [C_5H_5Rh(C_2H_5)(C_2H_4)PMe_3]BF_4$$
$$(8)$$

Analogously as with ethylene, *(6)* also reacts with NaCl, NaBr or NaI to give neutral complexes *(9)*—*(11)*, which have been characterized by elemental analysis, ^{1}H-NMR data and mass spectra. In the reaction of *(6)* with NaF (in water or nitromethane) a deprotonation of the ethylenehydrido-metal cation takes place and *(4)* is obtained.

$$(6) + NaX \rightarrow [C_5H_5Rh(C_2H_5)(PMe_3)X] + NaBF_4$$
$$(9),\ X = Cl$$
$$(10),\ X = Br$$
$$(11),\ X = I$$

$$(6) + NaF \rightarrow C_5H_5Rh(C_2H_4)PMe_3 + HF + NaBF_4$$
$$(4)$$

To our knowledge these findings provide the first evidence that an ethylenehydridometal complex can exist in equilibrium with an ethylmetal complex under normal conditions in solution. This finding is of general importance for an understanding of the insertion of olefins in M—H bonds.

Received: November 29, 1978 [Z 143a IE]
German version: Angew. Chem. *91*, 171 (1979)

CAS Registry numbers:
$(TBA)_2[Re_2Cl_8]$, 14023-10-0; $(TBA)_2[Re_2Br_8]$, 14049-60-6; $(TBA)_2[Re_2I_8]$, 67815-33-2

[1] Basic Metals, Part 15. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by donations of chemicals from Bayer AG, Leverkusen, and Degussa, Hanau. We thank *B. Klingert* for experimental assistance.—Part 14: *K. Dey, H. Werner*, J. Organomet. Chem., in press.

[2] *F. N. Tebbe, G. W. Parshall*, J. Am. Chem. Soc. *93*, 3793 (1971); *A. J. Deeming, B. F. G. Johnson, J. Lewis*, J. Chem. Soc. Dalton Trans. *1973*, 1848; *F. W. S. Benfield, M. L. H. Green, ibid. 1974*, 1324.

[3] *H. Werner, R. Feser, W. Buchner*, Chem. Ber., in press.

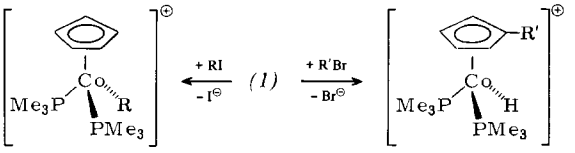
[4] On warming to +60 °C the shape of the two broad signals at $\delta \approx -10.5$ and 3.3 remains almost the same. Owing to the large difference in the chemical shift the coalescence point is probably first reached at much higher temperatures.

[5] *B. F. G. Johnson, J. Lewis, D. J. Yarrow*, J. Chem. Soc. Dalton Trans. *1972*, 2084.

Stepwise Addition of a Lewis Acid and a Lewis Base to a Metal-Metal Bond[1]

By *Helmut Werner* and *Werner Hofmann*[*]

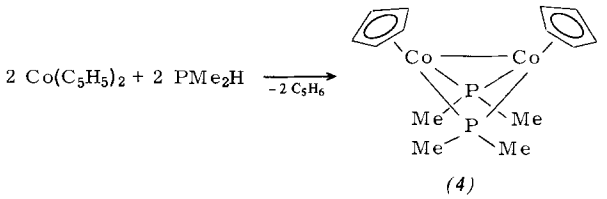
$C_5H_5Co(PMe_3)_2$ *(1)* reacts with methyl iodide and ethyl iodide to give ionic compounds of the type *(2)*[2a], and, surprisingly with isopropyl bromide and *tert*-butyl bromide to give compounds of type *(3)*[2b].



(2), R = Me, Et *(3)*, R' = *i*Pr, *t*Bu

If it is correct that steric factors are responsible for the different reaction course, it could be possible for a complex $C_5H_5CoL_2$—or even $C_5H_5Co(PMe_3)L$—containing a ligand L which is *smaller* than PMe_3 to react with *i*PrBr or *t*BuBr to give a cation with a stable Co—R' bond. We therefore attempted the preparation of $C_5H_5Co(PMe_2H)_2$ and/or $C_5H_5Co(PMe_3)(PMe_2H)$.

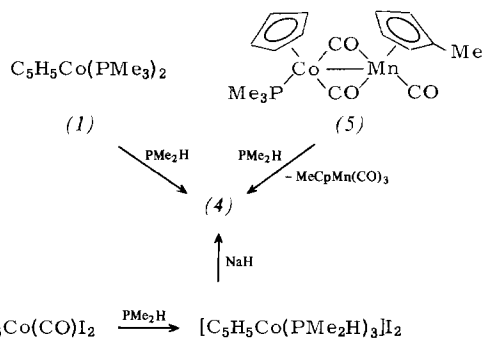
The bis(phosphite) complexes $C_5H_5Co[P(OR)_3]_2$ (R = Me, Et, Ph)[3a] as well as *(1)*[3b] are accessible from cobaltocene. Dimethylphosphane also reacts cleanly with $Co(C_5H_5)_2$, giving quantitatively the binuclear complex *(4)*; the half-sandwich complex $C_5H_5Co(PMe_2H)_2$ expected as intermediate has so far not been detected.



(4)

The bis(μ-*diphenyl*phosphido) complex analogous to *(4)* is accessible by reaction of $C_5H_5Co(CO)_2$ with P_2Ph_4[4]. Attempts to prepare *(4)* in this way have proved unsuccessful; reaction of $C_5H_5Co(CO)_2$ with P_2Me_4 afforded the μ-diphosphane complex $C_5H_5(CO)Co(PMe_2PMe_2)Co(CO)C_5H_5$[4].

Our attempts to synthesize $C_5H_5Co(PMe_3)(PMe_2H)$ also led to *(4)*. Its formation from *(5)* is noteworthy insofar as the (*Co—Mn*)-binuclear complex *always* reacts with other Lewis bases L (PPh_3, $P(OMe)_3$, $P(OPh)_3$, alkenes, alkynes *etc.*) to give $C_5H_5Co(PMe_3)L$ and $MeC_5H_4Mn(CO)_3$[5].

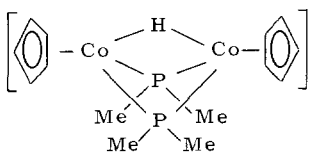


[*] Prof. Dr. H. Werner, Dipl.-Chem. W. Hofmann
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979
0570-0833/79/0202-0158 $ 01.00/0

(4) is also formed on reduction of the dication $[(C_5H_5Co(PMe_2H)_3]^{2+}$, which—similarly to $[C_5H_5Co(PMe_3)_3]^{2+}$[1,2a]—is obtainable in good yield by reaction of $C_5H_5Co(CO)I_2$ with PMe_2H in methanol.

According to MO calculations[6] for $[(CO)_nM(\mu\text{-}PPh_2)]_2$ the σ-electron pair of the metal-metal bond occupies the HOMO of this molecule. Should this also be the case for *(4)* its Co—Co bond ought to have nucleophilic character and react with electrophiles. It does not react with MeI at room temperature. On the other hand, *(4)* reacts rapidly and quantitatively with trifluoroacetic acid to give a cationic μ-hydridocobalt complex, which on precipitation with NH_4PF_6 affords the corresponding hexafluorophosphate *(6)* as dark-brown, air-stable crystals[7].

(4) $\xrightarrow[(NH_4PF_6)]{CF_3COOH}$  PF_6

(6)

We assume that the cation of *(6)* has a triple-decker-like structure[8]. According to *Hoffmann* et al.[9], binuclear complexes of this type ought to be stable when the two metal atoms possess 30 or 34 valence electrons; in the case of *(6)* the 34-electron rule applies. Consistent with the suggested bridged structure the NMR signal of the CoHCo proton is observed at much higher field ($\delta = -21$!) than that of the CoH proton of $[C_5H_5Co(PMe_3)_2H]^+$[2a]. The marked broadening of the signal is due to the fact that the bridge H-atom is bound to *two* Co nuclei (which have a quadrupole moment).

Like the 34-electron complex $[Ni_2(C_5H_5)_3]^+$[8], *(6)* also reacts with Lewis bases: reactions with PMe_3 and $P(OMe)_3$ afford the compounds *(7)* and *(8)*, respectively, in very good yields (>80%). The red crystals of *(7)* and *(8)* are readily soluble in acetone or nitromethane and are only slightly sensitive to air.

(6) + L ⟶ $[C_5H_5(L)Co(\mu\text{-}PMe_2)_2Co(H)C_5H_5]PF_6$

(7), L = PMe_3

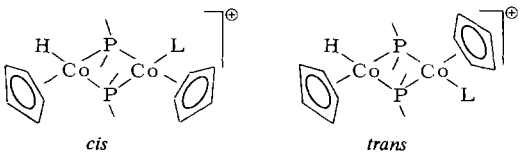
(8), L = $P(OMe)_3$

The opening of the CoHCo bridge during the formation of *(7)* and *(8)* is confirmed by the ^{1}H-NMR spectra (Table 1). For example, the hydride signal in the spectrum of *(7)* is shifted 7.7 ppm *downfield* compared to the same signal in the spectrum of *(6)* and appears in a similar region as for $[C_5H_5Co(PMe_3)_2H]^+$. While the reaction of *(6)* with PMe_3 gives essentially only one product, the NMR spectrum of *(8)* indicates the presence of two isomers—probably *cis/trans* isomers.

Table 1. ^{1}H-NMR data of the complexes *(4)*, *(6)*, *(7)* and *(8)* (δ values, TMS int.; *J* in Hz).

Complex	Solvent	C_5H_5	μ-PMe_2	Co—H	L
(4)	C_6H_6	4.60 t	1.7 vt		
		[J_{PH} = 0.8]	1.2 vt		
(6)	[D_6]-DMSO	5.23 t	1.73 vt	−21.0 t	
		[J_{PH} = 0.4]	1.54 vt	[J_{PH} = 60]	
(7)	CD_3NO_2	4.96 s	2.06 vt	−13.3 t	1.73 d
		4.80 s	1.47 vt	[J_{PH} = 66]	[J_{PH} = 10]
(8) [a]	CD_3NO_2	5.07 s	2.19—	−12.7 t (br)	4.09 d
		5.02 s	1.45 [b]		[J_{PH} = 4.2]
		4.83 s			3.92 d
		4.77 s			[J_{PH} = 4.0]

[a] Mixture of two isomers (see text); [b] overlapping of four virtual triplets.



cis *trans*

Trimethylphosphane is bulkier than trimethyl phosphite[10] and can therefore attack a cobalt atom of *(6)* only from the more sterically favorable side. The NMR data of *(7)* give no indication in this case whether the *cis*- or corresponding *trans*-isomer is present.

No addition takes place on reaction of *(6)* with anionic Lewis-bases such as H^- or Me^-: The reactions with NaH (in tetrahydrofuran) or with $LiCH_3$ (in ether) lead quantitatively to the neutral complex *(4)*.

Our observation that the *stepwise* addition of a Lewis acid and a Lewis base to a metal-metal bond is possible, *without disturbing the binuclear structure*, could be of general importance. Thus, the increased reactivity of carbonylmetal clusters (*e.g.* $Ir_4(CO)_{12}$) in the presence of Lewis acids such as $AlCl_3$[11] could be due to the initial opening of an M—M bond and the subsequent reaction of the intermediate with a Lewis base such as *e.g.* CO. *Vahrenkamp*[12] has recently pointed out the possibility that ligand substitution in binuclear complexes or clusters is initiated by cleavage of an M—M bond.

Received: December 12, 1978 [Z 143b IE]
German version: Angew. Chem. *91*, 172 (1978)

CAS Registry numbers:
(4), 69277-85-6; *(6)*, 69277-87-8; *(7)*, 69277-89-0; *cis-(8)*, 69292-12-2; *trans-(8)*, 69277-91-4; $Co(C_5H_5)_2$, 1277-43-6

[1] Basic Metals, Part 17. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and by donations of chemicals from BASF, Ludwigshafen, and Bayer AG, Leverkusen. We wish to thank *J. Wolf* for experimental assistance.—Part 16: *A. Spencer, H. Werner*, J. Organomet. Chem., in press.

[2] a) *H. Werner, W. Hofmann*, Chem. Ber. *110*, 3481 (1977); b) Angew. Chem. *89*, 835 (1977); Angew. Chem. Int. Ed. Engl. *16*, 794 (1977).

[3] a) *H. Neukomm, H. Werner*, Helv. Chim. Acta *57*, 1065 (1974); b) *H. Werner, B. Juthani*, unpublished.

[4] *R. G. Hayter, L. F. Williams*, J. Inorg. Nucl. Chem. *26*, 1977 (1964).

[5] *K. Leonhard, H. Werner*, Angew. Chem. *89*, 656 (1977); Angew. Chem. Int. Ed. Engl. *16*, 649 (1977); *K. Leonhard, B. Juthani, H. Werner*, unpublished.

[6] *B. K. Teo, M. B. Hall, R. F. Fenske, L. F. Dahl*, Inorg. Chem. *14*, 3103 (1975).

[7] On the protonation of binuclear complexes and the isolation of stable PF_6 salts cf. *K. Fauvel, R. Mathieu, R. Poilblanc*, Inorg. Chem. *15*, 976 (1976).

[8] *H. Werner*, Angew. Chem. *89*, 1 (1977); Angew. Chem. Int. Ed. Engl. *16*, 1 (1977).

[9] *J. W. Lauher, M. Elian, R. H. Summerville, R. Hoffmann*, J. Am. Chem. Soc. *98*, 3219 (1976).

[10] *C. A. Tolman*, Chem. Rev. *77*, 313 (1977).

[11] *G. C. Demitras, E. L. Muetterties*, J. Am. Chem. Soc. *99*, 2796 (1977).

[12] *H. Vahrenkamp*, Angew. Chem. *90*, 403 (1978); Angew. Chem. Int. Ed. Engl. *17*, 379 (1978).

Hindered Rotation at the Triple Bond

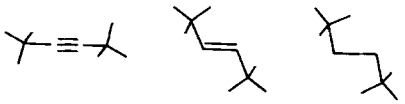
By *Philippe Koo Tze Mew* and *Fritz Vögtle*[*]

While rotation about the C—C single bond in ethanes is hindered even by small substituents[1a,1b], it is foreseeable that bulkier substituents are necessary to bring about such

[*] Prof. Dr. F. Vögtle, Dipl.-Chem. P. Koo Tze Mew
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn (Germany)

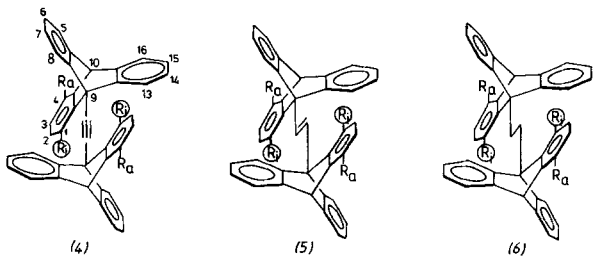
© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0159 $ 01.00/0*

hindrance in the case of the extended triple-bond system *(1)*[1c]. We have found that suitably substituted triptycene groups hinder rotation not only in butynes *(1)* but also in butenes *(2)* and butanes *(3)*.



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

DNMR spectroscopic investigation of the *un*substituted ditriptycenyl-ethyne *(4a)*, -ethene *(5a)*[2], and -ethane *(6a)* (see Table 1) revealed detectable steric interactions only for the ethane system at low temperature.

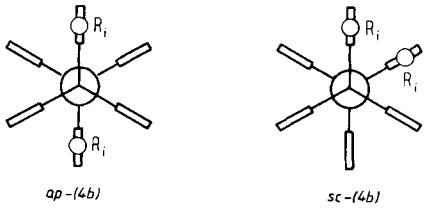


(4) *(5)* *(6)*

(a): $R_i = R_a = H$

(b): $R_i = R_a = CH_3$

Hindrance to rotation could, however, be achieved also in the ethyne system *(4)* by incorporation of internal substituents R_i[3]: for the internal methyl groups $(CH_3)_i$ of *(4b)* a broadened absorption is already observed at room temperature[4]; at higher temperatures it converts into a sharp singlet ($\delta = 2.80$ at 70°C, in $C_2D_2Cl_4$), and on cooling it splits into two singlets ($\delta = 2.66$, 3.16, in CD_2Cl_2) (coalescence temperature $T_c = +10$°C), the intensity ratio of which is temperature dependent. We interpret this behavior as indicative of the presence of two conformers at lower temperature, and their interconversion at higher temperature. We assign the more intense singlet to the antiperiplanar conformation (*ap-4b*), the less intense singlet to the synclinal conformation (*sc-4b*). On cooling, the population of the more stable *ap*- compared to the *sc*-conformer increases from 2.7:1 (0°C) to 7.6:1 (−80°C). Taking into account the difference in population of the conformers the threshold of the rotation is approximately[5]: $\Delta G_c^{\ddagger} = 63.1$ kJ/mol (15.1 kcal/mol) for the *sc*→*ap* conversion and 65.2 kJ/mol (15.6 kcal/mol) for the *ap*→*sc* conversion.

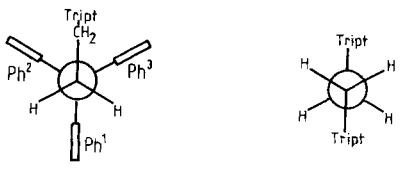


ap-(4b) *sc-(4b)*

Thus, in *(4b)* we have an obvious case of steric hindrance of the "nonbonded interaction" type by (methyl) substituents, which touch each other face-to-face without substantial steric contributions from neighboring groups[6, 7].

While the methyltriptycene-substituted ethene *(5b)* and the analogous ethane *(6b)* do not show temperature-dependent ^{1}H-NMR spectra, in the case of *un*substituted ditriptycenylethane *(6a)* a sharpening of the multiplets of the arene protons and singlet of the methylene protons compared to the singlet of the bridgehead protons is observed on increasing the temperature. Cooling to −20°C leads to increased broadening of the multiplets of the arene protons, especially of the multiplet of H-1, H-8 and H-13. At −40°C H-1, H-4 and H-2, H-3 split at $\delta = 7.42$ and 7.00 in the intensity ratio 1:1. These findings are consistent with free rotation of the triptycenyl groups about the C-9—CH_2 bond in *(6a)* at room temperature and the freezing out of rotation at lower temperature, for Ph^1 in the conformation *(6aA)* differs from the equivalent phenylene groups Ph^2 and Ph^3[8]. At −30°C the free energy of activation is $\Delta G^{\ddagger} = 58.5$ kJ/mol (14 kcal/mol)[9].

The sharp singlet of the four *methylene* protons in *(6a)* at room temperature indicates time-averaged predominance of the sterically more favorable antiperiplanar conformation *(6aB)* with equivalent methylene protons. The increased broadening with decreasing temperature (down to −80°C) indicates a slowing-down of the to-and-fro rotation of the triptycenylmethylene groups about the central CH_2—CH_2 bond. In the process *sc*-conformers can be formed, but the *sp* barrier is not crossed.



(6aA) *(6aB)*

Consistent with these explanations is the temperature-independence of the proton resonances of *(5b)* and *(6b)* which

Table 1. Yields, melting points and ^{1}H-NMR data (room temperature) of the synthesized triptycenes of type *(4)*—*(6)*.

Cpd.	Yield [%]	M. p. [°C] [a] (solvent)	^{1}H-NMR ($CDCl_3$/TMS int., δ values, 90 MHz) CH(phenylene)	CH(bridgehead)	—CH=CH— —CH_2—CH_2—	$(CH_3)_i$	$(CH_3)_a$
(4a)	10	450 [b] (Nitrobenzene)	7.08 (m, 12H), 7.48 (m, 6H) 8.01 (m, 6H)	5.54 (s, 2H)			
(4b)	16	423 (dec.) (Nitrobenzene)	6.71 (q, 4H, $J_{AB} = 7$ Hz), 7.09 (m, 8H) 7.46 (m, 4H), 8.22 (m, 4H)	5.73 (s, 2H)		2.78 (s, 6H)	2.53 (s, 6H)
(5a)	14	480 [c] (Nitrobenzene)	7.07 (m, 12H), 7.51 (m, 6H) 7.86 (m, 6H)	5.54 (s, 2H)	7.53 (s, 2H)		
(5b)	12	435 (dec.) (Nitrobenzene)	6.65 (q, 4H, $J_{AB} = 7$ Hz), 7.10 (m, 8H) 7.51 (m, 4H), 8.20 (m, 4H)	5.75 (s, 2H)	8.02 (s, 2H)	2.53 (s, 6H)	2.34 (s, 6H)
(6a)	51	475 (dec.) (Toluene)	7.06 (m, 12H), 7.46 (m, 6H) 7.89 (m, 6H)	5.44 (s, 2H)	4.11 (s, 4H)		
(6b)	47	443 (dec.) (Toluene)	6.57 (q, 4H, $J_{AB} = 7$ Hz), 7.13 (m, 8H) 7.50 (m, 4H), 8.33 (m, 4H)	5.68 (s, 2H)	4.33 (s, 4H)	2.49 (s, 6H)	2.31 (s, 6H)

[a] All melting points (uncorrected) were determined under nitrogen in sealed tubes. [b] Temperature at which decomposition commences; no melting is observed up to 500°C. [c] Partial decomposition above 389°C.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979
0570-0833/79/0202-0160 $ 01.00/0

have predominantly *ap* conformations and whose rotational barriers should even be higher.

Received: November 14, 1978 [Z 135 IE]
German version: Angew. Chem. 91, 163 (1979)

CAS Registry numbers:
(4a), 69224-93-7; *(4b)*, 69224-94-8; *(5a)*, 69224-95-9; *(5b)*, 69224-96-0; *(6a)*, 69224-97-1; *(6b)*, 69224-98-2

[1] a) *G. Binsch*, Top. Stereochem. *3*, 97 (1968); b) *F. Vögtle, H. Förster*, Angew. Chem. *89*, 443 (1977); Angew. Chem. Int. Ed. Engl. *16*, 429 (1977); c) *S. Patai*: The Chemistry of the Carbon-Carbon Triple Bond. Interscience, London 1978.

[2] *(5a)* appears to have been prepared from 9-formyltriptycenetosylhydrazone: *I. I. Brunovlenskaya, T. A. Gudasheva, V. R. Skvarchenko*, Zh. Org. Khim. *10*, 1495 (1974); but the melting point (388 °C) and ^{1}H-NMR data [δ = 7.4 (m, 12H), 7.0 (m, 14H), 5.4 (s, 2H), in thionyl chloride], are not in agreement with those found by us (Table 1, $CDCl_3$), nor those recorded in thionyl chloride for comparison.

[3] We synthesized *(4)*—*(6)* by reaction of the corresponding anthracenes with benzyne and 3,6-dimethylbenzyne respectively. Elemental analyses and spectroscopic data are consistent with the given structures.

[4] The outer CH_3 groups appear as a sharp singlet; the absorption of H-8, 11-13, however, is likewise broadened at room temperature; cooling leads to a sharp multiplet.

[5] *H. Shanan-Atidi, K. H. Bar-Eli*, J. Phys. Chem. *74*, 961 (1970).

[6] According to Stuart-Briegleb space-filling models such marked steric interactions are not to be expected, while CPK models suggest a very rigid structure. Present-day space-filling models are thus of limited use for predicting such steric interactions in large molecules.

[7] For the spatial requirements of methyl groups cf. [1b] and *Ch. Rüchardt, H.-D. Beckhaus, G. Hellmann, S. Weiner, R. Winiker*, Angew. Chem. *89*, 913 (1977); Angew. Chem. Int. Ed. Engl. *16*, 875 (1977); and references cited therein.

[8] Cf. *e.g.* a) *Yu. K. Grishin, N. M. Sergeyev, O. A. Subbotin, Yu. A. Ustynyuk*, Mol. Phys. *25*, 297 (1973); b) *F. Vögtle, P. Koo Tze Mew*, Angew. Chem. *90*, 58 (1978); Angew. Chem. Int. Ed. Engl. *17*, 60 (1978).

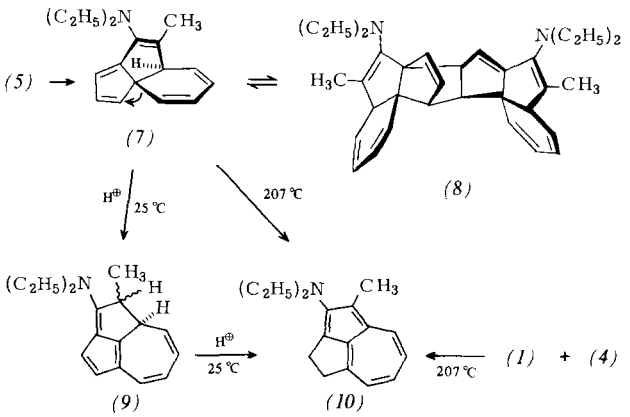
[9] "Temperature of stereochemical rigidity"; *N. M. Sergeyev, K. F. Abdulla, V. R. Skvarchenko*, J. Chem. Soc. Chem. Commun. *1972*, 368.

Surprising Transformation of Azulene by Cycloaddition with 1-(Diethylamino)propyne[**]

By *Klaus Hafner, Hans Jörg Lindner*, and *Werner Ude*[*]

Azulene *(1)* reacts as the prototype of nonbenzenoid "aromatic" hydrocarbons[1] with electrophiles and nucleophiles *via* substitution at positions 1(≡3) and 4(≡8), respectively, or 6. With electron-poor alkynes such as dimethyl acetylenedicarboxylate, *(1)* can undergo not only additive substitution[2a] but—like electron-rich alkenes[2b] also thermally induced dipolar cycloaddition at the five-membered ring; subsequent valence isomerization of the primary adduct *(2)* yields the next-higher homologue of *(1)*, *viz.* the heptalene derivative *(3)*[2c]. We have now attempted reaction of *(1)* with electron-rich alkynes such as 1-(diethylamino)propyne *(4)* in order to obtain the adduct *(5)* *via* (presumably also dipolar) cycloaddition to the seven-membered ring. Valence isomerization of *(5)* could lead to the hitherto unknown cyclopentacyclononene system *(6)*[3].

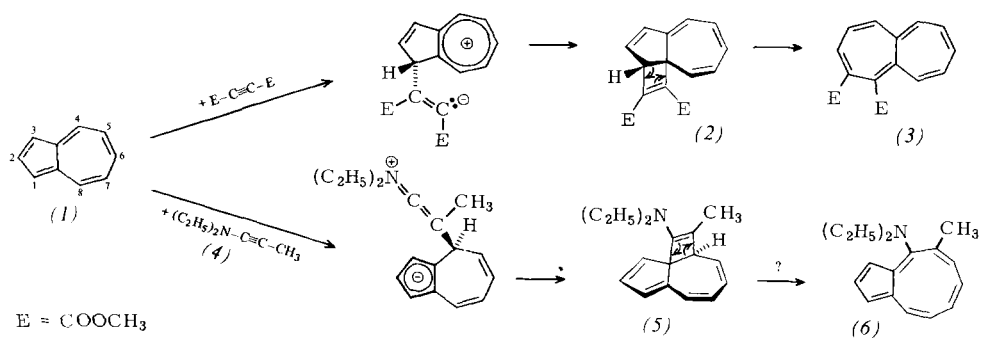
Surprisingly, *(1)* and *(4)* give a colorless crystalline 1:1 adduct *(7)*, m.p. 76 °C, even at room temperature. Compound *(7)* was isolated after 20 d in 83 % yield (based on reacted azulene)[4]. The constitution of the bridged spiro[4.5]decatetraene *(7)* has been confirmed by X-ray structure analysis[5] and ^{1}H- and ^{13}C-NMR spectra (Table 1). Thus *(7)* exists in the crystal as a dimer *(8)* formed by [4+2] cycloaddition of its cyclopentadiene moiety whereas a rapid retro-Diels-



Alder raction to give *(7)* occurs in solution (benzene, trichloromethane). This indicates only low activation energy for dimerization of *(7)* and for the cycloreversion of *(8)* (E_a < 25 kcal/mol)[6].

Formation of *(7)* probably involves the primary adduct *(5)* containing the structural unit of a spiro[3.4]octa-1,5,7-triene, which has been shown by *R. D. Miller et al.*[7] to resist isolation at −10 °C, partly due to a presumably 1,5 sigmatropic ring expansion to form a dihydropentalene. Analogous rearrangement of the 1,3-diene-bridged derivative *(5)* should lead to *(7)*.

In the presence of catalytic amounts of glacial acetic acid at room temperature, *(7)* undergoes fast isomerization in solution (CH_3OH)—possibly by renewed 1,5 sigmatropic alkyl shift—to give 20 % of the 1,8a-dihydrocyclopent[*c,d*]azulene derivative *(9)* (lemon yellow needles, m.p. 87 °C; see Table 1), which is transformed under the same reaction conditions



within *ca.* 3 h to give 2-(diethylamino)-1-methyl-3,4-dihydrocyclopent[*cd*]azulene *(10)* (brown platelets, m.p. 52 °C, yield 80 %; see Table 1). In boiling tetralin, on the other hand, *(7)* gives *(10)* directly in 30 % yield. The same tricyclic com-

[*] Prof. Dr. K. Hafner, Prof. Dr. H. J. Lindner, Dipl.-Ing. W. Ude
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

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

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*
0570-0833/79/0202-0161 $ 01.00/0

pound also results from reaction of *(1)* with *(4)* in boiling tetralin (yield 17%), probably also *via (7)* as intermediate.

In contrast to *(1)*, 4,6,8-trimethylazulene *(11)* reacts with *(4)* only in boiling tetralin; cycloaddition is hindered by the alkyl groups in positions 4 and 8.

The major product isolated was found to be 15% of the dihydrocyclopentaindene derivative *(14)* (yellow platelets,

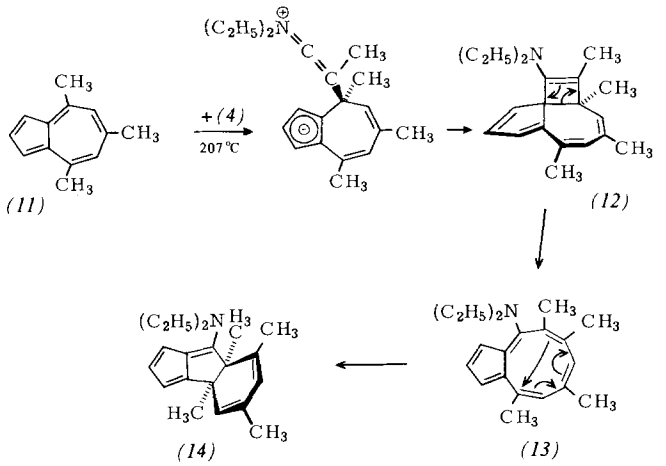


Table 1. Spectroscopic data of *(7)*, *(9)*, *(10)*, and *(14)*.

Cpd.	100 MHz-^{1}H-NMR (δ, J) in $CDCl_3$	UV, λ_{max} [nm] (log ε) in *n*-hexane
(7) [a]	6.37 (dd, $J_1=4.5$ Hz, $J_2=2$ Hz; 1H), 6.2–5.6 (m, 5H) 4.9–4.7 (m, 1H), 3.2–2.8 (m, 1H), 2.97, 2.93 (q, $J=7$ Hz; 4H, CH_2—CH_3), 1.70 (d, $J=2$ Hz; 3H, CH_3), 0.98 (t, $J=7$ Hz; 6H, CH_2—CH_3)	328 (3.09) sh, 259 (3.89)
(9)	6.8–6.5 (m, 1H), 6.65, 6.25 (d, $J=4.5$ Hz; 2H), 6.0–5.6 (m, 2H), 5.5–5.4 (m, 1H), 4.9–4.0 (m, 6H), 1.48 (d, $J=7$ Hz; 3H, CH_3), 1.30 (t, $J=7$ Hz; 6H, CH_2—CH_3)	400 (3.62), 336 (4.25), 319 (4.13) sh, 273 (4.08), 267 (4.04) sh, 252 (3.89) sh, 213 (4.16)
(10)	7.61 (d, $J=10$ Hz; 1H), 7.2–6.4 (m, 3H), 3.7–3.2 (m, 4H, CH_2—CH_2), 3.46 (q, $J=7$ Hz; 4H, CH_2—CH_3), 2.52 (s, 3H, CH_3), 1.16 (t, $J=7$ Hz; 6H, CH_2—CH_3)	530 (2.51), 436 (4.06), 429 (3.89) sh, 410 (3.88), 403 (3.75) sh, 392 (3.59) sh, 363 (3.61) sh, 337 (3.83) sh, 316 (4.75), 306 (4.58) sh, 295 (4.26) sh, 256 (4.17), 224 (4.10) sh
(14)	6.55 (dd, $J_1=4$ Hz, $J_2=2.5$ Hz; 1H), 6.16 (dd, $J_1=4$ Hz, $J_2=1$ Hz; 1H), 5.80 (dd, $J_1=2.5$ Hz, $J_2=1$ Hz; 1H), 5.60, 5.44 (mc, 2H), 3.9–3.3 (m, 4H, CH_2—CH_3), 1.93, 1.65 (d, $J=1.5$ Hz; 6H, CH_3), 1.34, 1.16 (s, 6H, CH_3), 1.28 (t, $J=7$ Hz; 6H, CH_2—CH_3)	333 (4.24), 266 (3.84), 217 (3.98) sh

[a] 25.2 MHz-^{13}C-NMR (δ) in $CDCl_3$: 165.8 (quart. C), 140.7 (2 quart. C), 135.3, 135.1, 130.5, 124.3 (1 C—H each), 122.8(2 C—H), 115.6 (C—H), 69.1 (quart. C), 47.4 (2 CH_2—CH_3), 44.2 (C—H), 13.8 (2 CH_2—CH_3), 13.2 (CH_3).

m.p. 123—124 °C; see Table 1)[8], containing a resonance-stabilized aminofulvene moiety whose structure was established by spectroscopy and X-ray studies[9]. This thermally induced reaction should also involve initial formation of the primary adduct *(12)* analogous to *(5)*, which for steric reasons related to its substituents is no longer capable of 1,5 sigmatropic ring expansion but instead undergoes valence isomerization to the likewise unstable cyclopentacyclononene system *(13)*. Valence isomerization in a manner characteristic of cyclononatetraene derivatives[10] ultimately gives the thermally stable systems *(14)*.

Received: November 21, 1978 [Z 147a IE]
German version: Angew. Chem. 91, 173 (1979)

CAS Registry numbers:
(1), 275-51-4; *(4)*, 4231-35-0; *(5)*, 69258-21-5; *(6)*, 69278-32-6; *(7)*, 69258-22-6; *(8)*, 69258-23-7; *(9)*, 69258-24-8; *(10)*, 69278-31-5; *(11)*, 941-81-1; *(12)*, 69258-25-9; *(14)*, 69258-26-0

[1] *E. Heilbronner* in *D. Ginsburg*: Non-Benzenoid Aromatic Compounds. Wiley-Interscience, New York 1959, pp. 171 ff.; *A. Streitwieser*: Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961, p. 297.

[2] a) *W. Treibs*, Naturwissenschaften *52*, 452 (1965); b) *R. Huisgen*, Acc. Chem. Res. *10*, 117 (1977), and references cited therein; c) *K. Hafner, H. Diehl, H. U. Süss*, Angew. Chem. *88*, 121 (1976); Angew. Chem. Int. Ed. Engl. *15*, 104 (1976).

[3] We have observed a corresponding reaction sequence on treatment of the aceheptylene system with the ynamine *(4)*: *K. Hafner, H. Diehl, W. Richarz*, Angew. Chem. *88*, 125 (1976); Angew. Chem. Int. Ed. Engl. *15*, 108 (1976); *K. Hafner, H. D. Diesel, W. Richarz, ibid. 90*, 812 (1978) and *17*, 763 (1978).

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

[5] Triclinic needles $P\bar{1}$. $a=1773(1)$, $b=1231(1)$, $c=680.7(5)$ pm, $\alpha=101.00(5)$, $\beta=85.94(5)$, $\gamma=106.63(5)°$, $Z=2$; 2148 observed reflections with $|F|>2\sigma_F$ (STOE two circle diffractometer, $Cu_{K\alpha}$ radiation $\lambda=154.18$ pm); refined to $R=0.108$ [11].

[6] Dimerization of 1,3-di-*tert*-butylpentalene-5-carbaldehyde, -5-carbonitrile, and -5-carboxylic methyl ester, as well as cycloreversion of the dimers have similarly low activation energies (*M. Suda, K. Hafner*, Tetrahedron Lett. *1977*, 2449).

[7] *R. D. Miller, M. Schneider*, Tetrahedron Lett. *1975*, 1557; cf. also: *R. D. Miller, D. Kaufmann, J. Mayerle*, J. Am. Chem. Soc. *99*, 8511 (1977); *A. de Meijere, L. U. Meyer*, Chem. Ber. *110*, 2561 (1977).

[8] In addition, 9% of an isomer (colorless leaflets, m.p. 86 °C) of *(14)* is isolated, which is probably a diethylamino(tetramethyl)dihydro-*s*-indacene.

[9] Orthorhombic platelets, $P2_12_12_1$, $a=1675(1)$, $b=1331(1)$, $c=754.6(5)$ pm, $Z=4$; 764 observed reflections with $|F|>2\sigma_F$ (STOE two circle diffractometer, $Cu_{K\alpha}$ radiation $\lambda=154.18$ pm); refined to $R=0.070$ [11].

[10] *G. Boche, H. Böhme, D. Martens*, Angew. Chem. *81*, 565 (1969); Angew. Chem. Int. Ed. Engl. *8*, 594 (1969); *G. Boche, H. Weber, D. Martens, A. Bieberbach*, Chem. Ber. *111*, 2480 (1978), and references cited therein.

[11] *G. M. Sheldrick*, SHELX-76, unpublished.

Facile Ring Enlargement of Azulene to Give the Cyclopentacyclononene System by Dipolar Cycloaddition[**]

By *Klaus Hafner, Hans Jörg Lindner*, and *Werner Ude*[*]

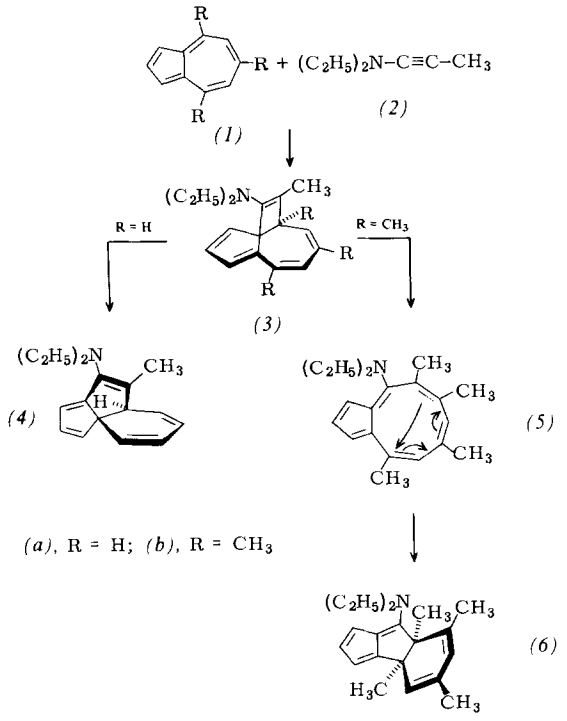
Azulene *(1a)* and 4,6,8-trimethylazulene *(1b)* react with 1-(diethylamino)propyne *(2)* to form 1,3-diene-bridged spiro-[3.4]octa-1,5,7-triene derivatives *(3)*, which undergo stabilization by 1,5 sigmatropic ring enlargement to bridged spiro-[4.5]decatetraene *(4)* or by valence isomerization *via* the cyclopentacyclononene *(5)* to give the dihydrocyclopentaindene derivative *(6)*[1a]. Owing to the valence isomerization characteristic of cyclononatetraenes[1b], the azulene-homologous cyclopentacyclononene system could not yet be isolated. This result prompted a study of cycloadditions of *(2)* with azulenes bearing substituents which hinder or rule out valence isomerization of the nine-membered ring in *(5)*. Inspection of models suggested that the readily accessible 1,2-dihydrocyclopent[*cd*]azulene *(7)*[2] should be particularly suitable for this purpose.

The bridged azulene *(7)* reacts like azulene with *(2)* at room temperature to give a brownish red crystalline 1:1

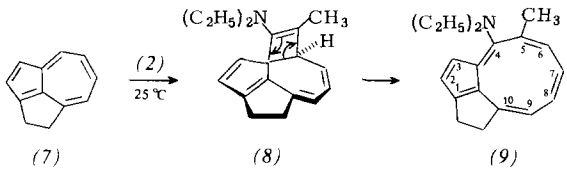
[*] Prof. Dr. K. Hafner, Prof. Dr. H. J. Lindner, Dipl.-Ing. W. Ude
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Prof. Dr. *H. Kessler*, Frankfurt, for recording the 270-MHz ^{1}H-NMR spectrum.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0162 $ 01.00/0*



adduct[3] of m.p. 127—129 °C [43 % yield based on reacted *(7)*]. According to X-ray structure analysis (Fig. 1)[4] and spectroscopic results, the expected 1,10-ethano-bridged 4-(diethylamino)-5-methylcyclopentacyclononene *(9)* is indeed formed.



The five-membered ring of the "6-amino-1-vinylfulvene system" present in *(9)* is planar, with an exocyclic double bond twisted through about 30° and a 1-vinyl group twisted only slightly out of the plane of the ring. The bond lengths in this partial structure lie in the region characteristic of 6-aminofulvenes[5] and suggest extensive π-electron delocalization. The resulting weakening of the exocyclic double bond of the fulvene system is manifested in the relatively large twisting of this bond. The torsional angles of the other single bonds in the nine-membered ring (53, 83, 93°) are extremely large. The conformation of this ring resembles the tub form of cyclooctatetraene and thus corresponds to that of 1-(dimethylcarbamoyl)-azonine[6].

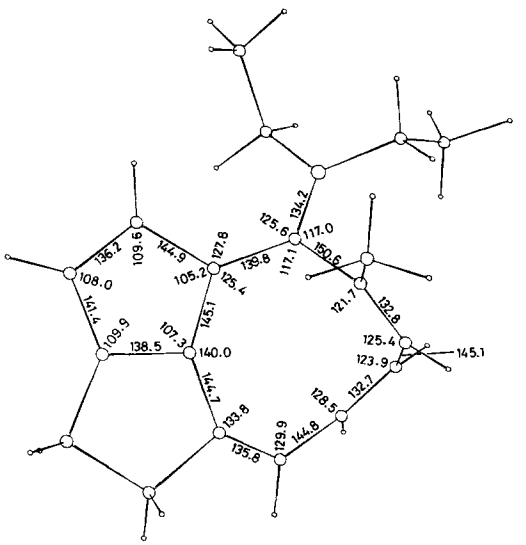


Fig. 1. Molecular structure of *(9)* with bond lengths [pm] and bond angles [°] of the cyclopentacyclononene system (standard deviations $\sigma_r = 0.4$ pm; $\sigma_\alpha = 0.4°$).

UV/VIS and NMR spectra of *(9)* are in accord with this structure[7]. The UV spectrum corresponds to that of 6-(dimethylamino)-1-(2-methoxyvinyl)fulvene[8].

The novel ring system *(9)*, presumably resulting by valence isomerization of the primary adduct *(8)*, is the first cyclononatetraene derivative which is thermally stable and inert towards atmospheric oxygen, and is not stabilized by benzo-annelation[9]. No isomerization of *(9)* takes place in boiling toluene or in the presence of protic acids. Reversible protonation of *(9)*, presumably occurring at one of the ring C atoms, is possible in 2 N H_2SO_4 and conc. acetic acid.

Received: November 21, 1978 [Z 147b IE]
German version: Angew. Chem. *91*, 175 (1979)

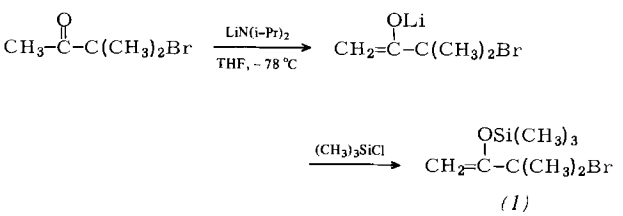
CAS Registry numbers:
(2), 4231-35-0; *(7)*, 14311-07-0; *(9)*, 69258-16-8

[1] a) *K. Hafner, H. J. Lindner, W. Ude*, Angew. Chem. *91*, 173 (1979); Angew. Chem. Int. Ed. Engl. *19*, 161 (1979); b) *G. Boche, H. Weber, D. Martens, A. Bieberbach*, Chem. Ber. *111*, 2480 (1978), and references cited therein.
[2] *K. Hafner, K.-P. Meinhardt, W. Richarz*, Angew. Chem. *86*, 235 (1974); Angew. Chem. Int. Ed. Engl. *13*, 204 (1974).
[3] Elemental analysis and mass spectrum gave correct values.
[4] Monoclinic prisms, $P2_1/a$, $a = 2088(1)$, $b = 866.7(5)$, $c = 899.1(5)$ pm, $\beta = 108.00(5)°$, $Z = 4$. 1608 observed reflections with $|F| > 2\sigma_F$ (STOE two circle diffractometer, $Cu_{K\alpha}$ radiation $\lambda = 154.18$ pm); solution of structure and refinement with SHELX-76 (*G. M. Sheldrick*, unpublished), refined to $R = 0.069$.
[5] *H. L. Ammon, G. L. Wheeler*, Chem. Commun. *1971*, 1032.
[6] *C. C. Chiang, I. C. Paul, A. G. Anastassiou, S. W. Eachus*, J. Am. Chem. Soc. *96*, 1636 (1974).
[7] UV (*n*-hexane): $\lambda_{max} = 378$ ($\log\varepsilon = 4.09$), 320 (4.06), 293 sh (3.96) nm; 270 MHz-^{1}H-NMR ($CDCl_3$): $\delta = 6.49$, 6.20 (d, $J = 4.2$ Hz, H-2, H-3), 5.85, 5.25 (mc, 3 H or 1 H, H-6, 7, 8, 9), 3.8 (mc, 4 H, CH_2—CH_3), 1.35 (t, 6 H, $J = 7$ Hz, CH_2—CH_3), 1.75 (3 H, CH_3), 3.15, 2.7 (mc, 1 H or 3 H, —CH_2—CH_2—); 25.2 MHz ^{13}C-NMR ($CDCl_3$): $\delta = 166.5$, 148.2, 145.2, 137.6, 135.3 (1 quart. C each), 133.0 (1 C—H), 124.7 (2 C—H), 124.1, 121.3, 113.7 (1 C—H each), 108.3 (1 quart. C), 108.2 (1 C—H), 44.1 (2 CH_2—CH_3), 41.2, 25.9 (—CH_2—CH_2—), 23.3 (CH_3), 12.8 (2 CH_2—CH_3).
[8] *P. Kluge*, Dissertation, Technische Hochschule Darmstadt 1975.
[9] *P. J. Garrat, K. A. Knapp*, Chem. Commun. *1970*, 1215; *J. Willner, M. Rabinovitz*, Tetrahedron Lett. *1976*, 3335.

3-Bromo-3-methyl-2-trimethylsiloxy-1-butene—A New Cycloaddition Reagent[1]

By *Hideki Sakurai, Akihiko Shirahata*, and *Akira Hosomi*[*]

We have found that 3-bromo-3-methyl-2-trimethylsiloxy-1-butene *(1)* can be obtained in good yield from 3-bromo-3-

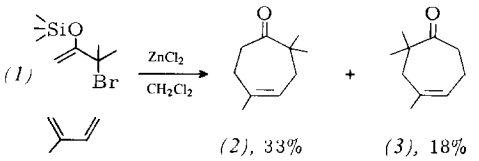


[*] Prof. Dr. H. Sakurai, Dipl.-Chem. A. Shirahata, Dr. A. Hosomi
Department of Chemistry, Faculty of Science, Tohoku University
Sendai 980 (Japan)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*
0570-0833/79/0202-0163 $ 01.00/0

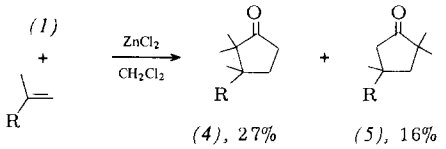
methyl-2-butanone, and is a useful reagent for synthesis of seven- and five-membered cyclic ketones from 1,3-dienes and olefins, respectively.

The reaction of *(1)* with 1,3-dienes in dichloromethane in the presence of zinc chloride gives cycloheptenones, *i.e.* [3+4] cycloadducts, in good to excellent yields (Table 1). With isoprene (experiment no. 4), karahanaenone *(2)*[2] was obtained in 33% yield with its regio isomer *(3)*.



With isoprene and 1,3-butadiene, [3+2] cycloadducts were also obtained in small amounts.

Styrene derivatives gave [3+2] cycloadducts as major products (Table 1). For example, 2-(*p*-methylphenyl)-1-propene (experiment no. 7) afforded the aromatic sesquiterpene (±)-α-cuparenone *(4)*[3] and its regio isomer *(5)*. Zinc chloride was again the most satisfactory catalyst examined.



R = *p*-CH_3–C_6H_4

[3+4] and [3+2] cycloadditions have been reported for α,α′-dibromoketones with zinc-copper couple[4] or carbonyl-iron compounds[5] as catalysts and using 2-methoxyallyl bromide with silver perchlorate as catalyst[6]. However, the new reagent *(1)* generally gives higher yields, and the reactions would appear to have important mechanistic implications.

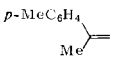
Procedure

To a solution of lithium diisopropylamide, prepared from diisopropylamine (12.1 g, 0.12 mol) in THF (100 ml) and 1.0 M *n*-butyllithium in *n*-hexane (120 ml, 0.12 mol) is added 3-bromo-3-methyl-2-butanone (16.5 g, 0.10 mol) dropwise at −78 °C. The mixture is stirred for 30 min at −78 °C and then chlorotrimethylsilane (13.0 g, 0.12 mol) is added to the mixture. The cooling bath is removed and the mixture is stirred for 6 h at room temperature. After the solvent has been stripped, *(1)* (16.5 g, 70% yield) is distilled at 63 °C/9 torr. ^{1}H-NMR (CCl_4): δ = 0.40 (9H, s), 1.95 (6H, s), 4.10 (1H, d, J = 2 Hz), 4.60 (1H, d, J = 2 Hz); IR (film): 1620 cm.

Received: November 20, 1978 [Z 146 IE]
German version: Angew. Chem. *91*, 178 (1979)

[1] Chemistry of Organosilicon Compounds. Part 121. – Part 120: *A. Hosomi, M. Saito, H. Sakurai*, Tetrahedron Lett., in press.
[2] a) *Y. Naya, M. Kotake*, Tetrahedron Lett. *1968*, 1645; b) *E. Demole, P. Enggist*, Helv. Chim. Acta *54*, 456 (1971); c) *S. Hashimoto, A. Itoh, Y. Kitagawa, H. Yamamoto, H. Nozaki*, J. Am. Chem. Soc. *99*, 4192 (1977); d) *H. M. R. Hoffmann, R. Chidgey*, Tetrahedron Lett. *1978*, 85; e) *R. Chidgey, H. M. R. Hoffmann, ibid. 1978*, 1001.
[3] a) *G. L. Chetty, S. Dev*, Tetrahedron Lett. *1964*, 73; b) *R. Noyori, Y. Baba, S. Makino, H. Takaya, ibid. 1978*, 993.
[4] *H. M. R. Hoffmann*, Angew. Chem. *85*, 877 (1973); Angew. Chem. Int. Ed. Engl. *12*, 819 (1973), and references cited therein.
[5] *H. Takaya, S. Makino, Y. Hayakawa, R. Noyori*, J. Am. Chem. Soc. *100*, 1765 (1978), and references cited therein.
[6] *A. E. Hill, G. Greenwood, H. M. R. Hoffmann*, J. Am. Chem. Soc. *95*, 1338 (1973).

Table 1. Cycloaddition of 3-bromo-3-methyl-2-trimethylsiloxy-1-butene *(1)* to 1,3-dienes and olefins in the presence of zinc chloride in dry dichloromethane. Correct elemental analyses and satisfactory NMR, IR, and mass spectra were obtained for all products.

No.	*(1)* (mmol)	Diene or olefin (mmol)	Reaction conditions RT = (room temp.)	Products yield [%] [a]
1	(5)	 (20)	−78° → RT, 1 h then RT, 30 min	 97
2	(5)	 (10)	−78° → RT, 1.5 h then RT, 20 min	 54
3	(5)	 (35)	−78° → RT, 1 h then RT, 1 h	 26 +  14
4	(5)	 (20)	−78°, 30 min then RT, 20 min	*(2)* 33 [b] + *(3)* 18 +  6
5	(5)	 (20)	−78° → RT, 1 h then RT, 1 h	 60
6	(1)	 (1.5)	−78° → RT, 30 min then RT, 30 min	 10 +  40
7	(1)	 (2)	−78° → RT, 1 h then RT, 1 h	*(5)* 16 + *(4)* 27

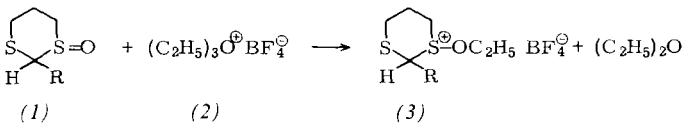
[a] Yields after isolation; not all optimized. [b] Relative yield of seven- and five-membered compounds was determined by GLC. Yields of *(2)* and *(3)* determined by NMR comparison with authentic samples.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0164 $ 01.00/0*

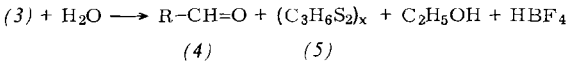
Facile Regeneration of Carbonyl Compounds from 1,3-Dithiane 1-Oxides *via* 1-Ethoxy-1,3-dithianium Salts[**]

By *Ingfried Stahl, Jürgen Apel, Rainer Manske*, and *Jürgen Gosselck*[*]

Carbonyl compounds can be protected as 1,3-dithiane 1-oxides *(1)*; they are usually released again in an acid medium[1]. We have found that *(1)* can be alkylated regioselectively at the O-atom with triethyloxonium tetrafluoroborate *(2)*, even at 0 °C (CH_2Cl_2, argon), to give the hitherto unknown 1-ethoxy-1,3-dithianium tetrafluoroborates *(3)*, which are isolable in high yields.



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



(4) *(5)*

The salts *(3)* rapidly cleave in aqueous neutral medium at 5 °C, giving the carbonyl compounds *(4)* and propylene disulfide *(5)* in high yields (over 60%). The observed separation of *(5)*, which was also isolated in the acid hydrolysis of *(1)*[2], confirms the postulated reaction mechanism *via* hydroxydithianium ions.

This hydrolytic variant for the cleavage of 1,3-dithiane 1-oxides *(1)* *via* *O*-ethyl derivatives *(3)* constitutes a novel and preparatively simple method.

As precursors for the preparation of *(3)* we used the *trans*-2-substituted sulfoxides *(1)* (Table 1) (content of *trans* isomer >90%), which we synthesized from the 1,3-dithianes[3] by monooxidation with $NaIO_4$[4].

Table 1. Some new 1,3-dithiane 1-oxides *(1)* [a].

	R	Yield [%]	*trans*/*cis*	M.p. [°C]	^{13}C-NMR, δ-values [b]
(1e)	C_6H_4-OCH_3-(*p*)	90	92:8	166	68.8, 29.2, 31.2, 54.4, 55.0 (OCH_3)
(1f)	C_6H_4-NO_2-(*p*)	83	91:9	176–177	68.6, 29.2, 31.0, 54.7
(1g)	C_6H_4-CH_3-(*p*)	94	92:8	165	68.8, 29.0, 30.8, 52.2, 20.7 (CH_3)

[a] *(1a)*, R = H; *(1b)*, R = CH_3; *(1c)*, R = $C(CH_3)_3$; *(1d)*, R = C_6H_5 are known. [b] ^{13}C-NMR of the *trans*-compounds (23 MHz, $CDCl_3$, TMS = 0); the signals are given in the sequence C-2, C-4, C-5, C-6 [5].

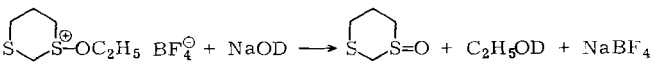
The tetrafluoroborates *(3)* were characterized as 2,4,6-trinitrobenzenesulfonates *(3')* (Table 2).

Table 2. Some 1-ethoxy-1,3-dithianium tetrafluoroborate salts *(3)* and -2,4,6-trinitrobenzenesulfonates *(3')*. All compounds gave correct C, H, N values. The rearrangement of *(1e)* into *(3e)*, R = C_6H_4-OCH_3-*p*, led to an insufficiently pure product.

	R	Yield [%]	M.p. [°C] (dec.)	^{1}H-NMR, δ-values [a]
(3a)	H	80	115	5.16, 4.96 d, $^2J = -12$ Hz; 4.64 q; $(CD_3)_2CO$
(3a')	H	75	145	4.90, 4.62 d, $^2J = -12$ Hz; 4.48 q; CD_3CN
(3b')	CH_3	67	103	4.90, 5.05 q; 4.49, 4.46 q; CD_3CN
(3c')	$C(CH_3)_3$	75	92	5.20, 5.05 s; 4.50; CD_2Cl_2
(3d)	C_6H_5	80	77–80	6.05 s; 3.87 q; CD_2Cl_2
(3d')	C_6H_5	75	101–104	5.97 s; 3.85 q; CD_3CN
(3f')	C_6H_4-NO_2-(*p*)	47	101	6.25 s; 3.90 q; $(CD_3)_2CO$
(3g')	C_6H_4-CH_3-(*p*)	52	75–78	6.00 s; 3.85 q; CD_3CN

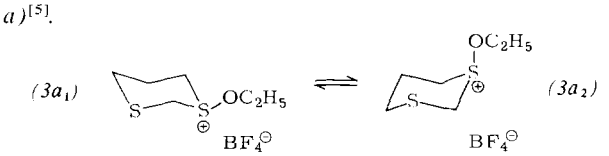
[a] The signals are given in the order S–CH_2–$S^{\oplus}$ or S–CH–$S^{\oplus}$; O–CH_2 [6].

Evidence for the regioselective ethylation at the *O*-atom of *(1)* is provided, *inter alia*, by the quantitative nucleophilic cleavage of the S–O bond of *(3a)* with NaOD in the NMR experiment. *S*-alkoxysulfonium salts behave analogously[7].



(3a) *(1a)*

We carried out a ^{13}C-NMR analysis on the parent compound *(3a)*. The signals of the ring-C-atoms were assigned on the basis of selective ^{1}H-^{13}C decoupling, those of the ethyl-C-atoms were locatable under off-resonance conditions [^{13}C-NMR (CD_3CN): δ = 75.1 (OCH_2); 46.7 (C-6); 45.8 (C-2); 29.0 (C-5); 27.2 (C-4); 15.5 (CH_3)]. The sequence of the ring-C-atom signals corresponds to that of the starting sulfoxide *(1a)*[5].

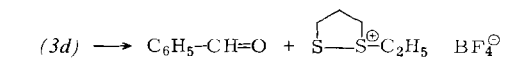


(3a$_1$) *(3a$_2$)*

A low-temperature ^{1}H-NMR experiment [in $(CD_3)_2CO$; *T* up to −106 °C] provided no evidence of a conformational process in the sense of the equilibration *(3a$_1$)* ⇌ *(3a$_2$)*. The splitting of the A-resonance of the AB doublet of the C-2 protons ($J_{2e6e} = 2.5$ Hz) at lower field strength, the size of the geminal coupling constant ($^2J_{AB} = 12$ Hz)[8], and the separation of H_{6e} and H_{6a} by *ca.* 0.4 ppm in the ^{1}H-NMR spectrum (100 MHz) indicate almost exclusive participation of the conformer *(3a$_1$)*.

Conformationally fixed forms are also present in the salts *(3b)*–*(3g)*; *(3b)* and *(3c)* contain small proportions of *cis* isomers.

A novel intramolecular decomposition has been observed in the case of *(3d)*. In anhydrous dichloromethane at room temperature it cleaves quantitatively within about 1 h into benzaldehyde *(4d)* and 1-ethyl-1,2-dithiolanium tetrafluoroborate *(6)*.



(3d) *(4d)* *(6)*

The salt *(6)* was isolated as the 2,4,6-trinitrobenzenesulfonate *(6')* (dec. pt. 153–154 °C) [^{1}H-NMR (CD_3CN) of *(6')*:

[*] Prof. Dr. J. Gosselck, Dr. I. Stahl [+], J. Apel, Dipl.-Chem. R. Manske
Bereich Organische Chemie der Universität/Gesamthochschule
Heinrich-Plett-Str. 40, D-3500 Kassel (Germany)

[+] Author to whom correspondence should be addressed.

[**] This work was supported by the Fonds der Chemischen Industrie. We thank Dr. *S. Berger* (Universität Marburg) for help with the experiments on the selective decoupling and low-temperature ^{1}H-NMR measurements and Prof. Dr. *H. Lackner* (Universität Göttingen) for recording the 100 MHz ^{1}H-NMR spectra. Thanks are also due to Prof. Dr. *H. Kessler* (Universität Frankfurt/Main) for valuable discussions regarding the temperature-dependent ^{1}H-NMR spectra.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*
0570-0833/79/0202-0165 $ 01.00/0

1.41 (t, 3H), 2.74 (t of t, 2H), 3.32 (q, 2H), 3.75 (t, 2H), 3.99 (t, 2H), assignment by proton decoupling]. The spectral pattern corresponds to that of 1,2-dithiolane 1,1-dioxide[9].

General Procedure

Synthesis of *(3)*: *(1)* (6 to 8 mmol) is dissolved in anhydrous CH_2Cl_2 in the absence of moisture and the solution treated with 2 g of molecular sieve (4 Å, MERCK). An equimolar amount of *(2)* in 10 ml of anhydrous CH_2Cl_2 is then added at 0 °C and the mixture stirred for up to 3 h under argon. The salt *(3)* is precipitated with anhydrous ether, the solution decanted off, and the crude product *(3)* dried over P_4O_{10} at 0.1 torr/25 °C. The salts *(3')* are first obtained by addition of a concentrated ethanolic solution of picrylsulfonic acid to the crude *(3)* and then reprecipitated from acetonitrile/ether or CH_2Cl_2/ether.

Regeneration of *(4)*: The dried crude tetrafluoroborate *(3)* is treated with water (5 °C). After a few minutes the precipitate of *(5)* is removed by filtration and the aldehyde worked-up or precipitated as the 2,4-dinitrophenylhydrazone derivative.

Received: November 13, 1978 [Z 148 IE]
German version: Angew. Chem. *91*, 179 (1979)

CAS Registry numbers:
(1a), 16487-10-8; *(1b)*, 60349-75-9; *(1c)*, 41893-04-3; *(1d)*, 60349-76-0; *(1e)*, 69278-13-3; *(1f)*, 69278-14-4: *(1g)*, 69278-15-5; *(2)*, 368-39-8; *(3a)*, 69278-17-7; *(3a')*, 69278-18-8; *(3b')*, 69278-20-2; *(3c')*, 69292-14-4; *(3d)*, 69278-22-4; *(3d')*, 69278-23-5; *(3f')*, 69278-25-7; *(3g')*, 69278-27-9; *(4d)*, 100-52-7; *(5)*, 42557-04-0; *(6)*, 69278-29-1; *(6')*, 69278-30-4

[1] Review of hydrolysis methods: *B.-T. Gröbel, D. Seebach*, Synthesis *1977*, 357.
[2] *R. Kuhn, F. A. Neugebauer*, Chem. Ber. *94*, 2629 (1961).
[3] Review: *D. Seebach*, Synthesis *1969*, 17.
[4] Review of oxidations with $NaIO_4$: *A. J. Fatiadi*, Synthesis *1974*, 229.
[5] *F. A. Carey, O. D. Dailey, Jr., W. C. Hutton*, J. Org. Chem. *43*, 96 (1978).
[6] *I. Stahl*, Dissertation, Universität Gießen 1973.
[7] Review: *J. P. Marino* in: Topics in Sulfur Chemistry. Vol. 1. Thieme, Stuttgart 1976, p. 68.
[8] *J. B. Lambert, S. I. Featherman*, Chem. Rev. *75*, 611 (1975).
[9] *L. Field, R. B. Barbee*, J. Org. Chem. *34*, 316 (1969).

Bond Switch with Participation of π-Bonded S^{IV} in Thiathiophthene-Analogous Systems[**]

By *Kin-ya Akiba, Shin-ichi Arai, Tohru Tsuchiya, Yohsuke Yamamoto*, and *Fujiko Iwasaki*[*]

In the thiathiophthenes, a class of stable π-hypervalent molecules, the S—S bonds are influenced by substitution or introduction of heteroatoms into the ring[1]. Both iminothiadiazolines[2a] and iminooxadiazolines[2b] react with activated acetylenes with cycloaddition-elimination; the elimination is probably due to the great difference in electronic nature of the two five-membered rings of the intermediate π-λ^4-sulfurane. In all these reactions, the original S-heteroatom bond is opened, while the newly formed five-membered ring remains intact, *i.e.* bond switch is observed at π-hypervalent sulfur.

We report here on a simple and typical example of bond switch. When 3,4-disubstituted 5-imino-Δ^2-1,2,4-thiadiazoline *(1)*[3] is heated with excess imidate at 60—80 °C without solvents, ethanol is eliminated and the 1:1 adduct *(3)* of *(1)* and the nitrile R^3—CN is obtained in good yields (in Table 1).

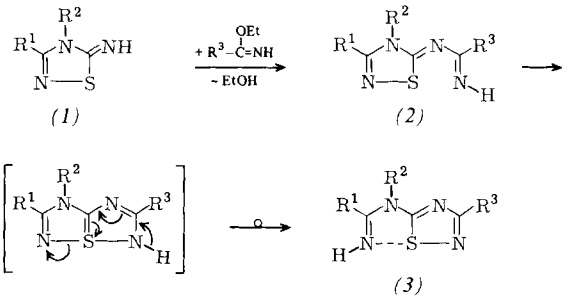


Table 1. Some 1,2,4-thiadiazole *(3)*. (^{1}H-NMR data: δ values, $CDCl_3$, Me_4Si int. [4]).

	R^1	R^2	R^3	M.p. [°C]	Yield [%]
a	Me 2.36 ± 0.03 [a]	Me 3.69 ± 0.13	Me 2.54 ± 0.03	139.2–140.2	66
b	Me	Me	Ph 7.2–7.6 (m, 3H) 8.0–8.4 (m, 2H)	182.2–183.7	80
c	Et	Me	Me	149.2–150.2	77
d	Ph 7.48 ± 0.02	Me	Me	174.1–175.1	48

[a] Coupling with NH (δ = 9.5, J = 1.5 Hz).

The structure of the adduct *(3)* was deduced by comparison of its NMR spectral data with those of related compounds[5]. The IR spectra contain characteristic absorptions at 3250 (ν = NH) and 1630—1640 cm^{-1} (νC=NH)[6a].

We also synthesized *(3a)*, *(3c)* and *(3d)* *via* an independent route by heating the nitriles R^1—CN with the thiadiazole *(4)*[5] to 80—100 °C in the presence of $AlCl_3$; the yield of *(3)* was about 20%[7].

Finally, the structure of *(3a)* was determined by an X-ray structure analysis on a single crystal. The molecule is almost planar (dihedral angle between the "rings": 174.7°); the N···S and N—S bond lengths are 2.500 and 1.668 Å, respectively, thus confirming intramolecular N···S interaction.

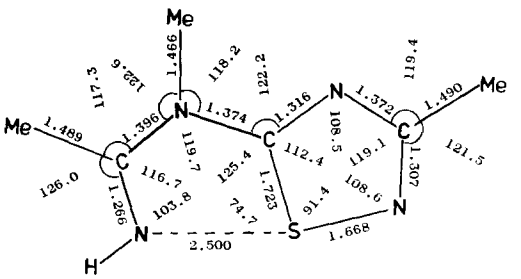


Fig. 1. Bond lengths [Å] and angles [°] in compound *(3a)* (Details: *F. Iwasaki, K. Akiba*, unpublished).

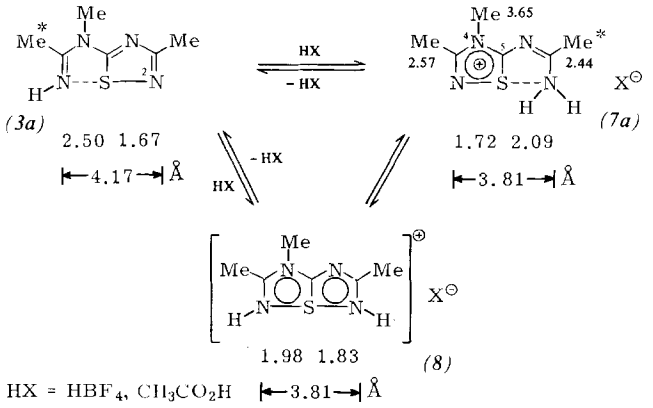
Surprisingly, the salt formation of the bases *(3)* proceeds *via* bond switching. Thus the tetrafluoroborates of *(3a)* and *(3c)* have the structures *(7a)* and *(7c)*, respectively, derived as shown below by long range coupling with the NH proton (the position is marked by an asterisk). This is supported by the finding that the protons of the three analogous methyl

[*] Prof. Dr. K. Akiba, Dipl.-Chem. S. Arai, Y. Yamamoto, Dr. T. Tsuchiya
Department of Chemistry, Faculty of Science, The University of Tokyo
Hongo, Tokyo 113 (Japan)
Prof. Dr. F. Iwasaki
Department of Materials Science, The University of Electro-Communications
Chofu-shi, Tokyo 182 (Japan)

[**] This work was supported in part by the Itoh Science Foundation.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979
0570-0833/79/0202-0166 $ 01.00/0

groups in the salts *(7a)*, *N*-methyl-*(7a)* and *N,N*-dimethyl-*(7a)*[8] give almost identical NMR signals (δ values, in [D_6]-dimethyl sulfoxide ([D_6]-DMSO), Me_4Si int.). On addition of excess trifluoroacetic acid (TFA) to *(3a)* and *N*-methyl-*(3a)* in $CDCl_3$ the same chemical shifts occur for the corresponding methyl protons as in *(7a)* and *N*-methyl-*(7a)* (both BF_4^- salts). The remarkable red shift and hyperchromism in the UV spectrum of *(7a)* compared to that of the base *(3a)* clearly demonstrates that *(7a)* is a salt with a conjugated thiadiazolium ion. *N*-Methyl-*(7a)* behaves similarly.



When about a half-molar amount of TFA was added to the base *(3a)* in $CDCl_3$/[D_6]-DMSO at 34 °C, only three methyl signals were observed between those of *(3a)* and *(7a)*. Under the same conditions *N*-methyl-*(3a)* is half converted into *N*-methyl-*(7a)* (eight methyl signals). This finding indicates the presence of a rapid equilibrium between *(3a)* and *(7a)*. The equilibrium was confirmed by the fact that a linear relationship was observed between the chemical shift of the Me* protons in *(3a)* and the amount of TFA added.

The bond switch is thus explained in terms of the protonation of *(3a)* at N-2[6b] and affords the 6aλ^4-thia-1,3,4,6-tetraazapentalenium tetrafluoroborate *(8)*, which is converted by prototropy into the thermodynamically more stable compound *(7a)*. Rapid equilibrium is effected by deprotonation with the residual free base *(3a)* and/or X^-.

Finally, let us consider the bond lengths. In *(3a)* (see Fig. 1) and *N,N*-dimethyl-*(8)*[9] they have been determined by X-ray crystallography. The N—S bond length in *(7a)* can be estimated on the basis of the data for an isothiazolium salt of analogous structure to be 1.72 Å[10]. The S···N bond length in *(7a)* then becomes 2.09 Å, if it is assumed that the NSN distances in the singly positively charged compounds *(7a)* and *(8)* are the same. It can then be visualized that the central sulfur atom moves back and forth rapidly along the N—S···N bond in the range between 0.78 Å [maximum: 4.17 − (1.72 + 1.67)] and 0.26 Å [minimum: 3.81 − (1.72 + 1.83)], most probably *ca.* 0.40 Å.

Received: September 15, 1978;
in shortened form: January 30, 1979 [Z 132 IE]
German version: Angew. Chem. *91*, 176 (1979)

CAS Registry numbers:
(1a), 59027-00-8; *(1c)*, 69225-17-8; *(1d)*, 69225-18-9; *(3a)*, 69225-19-0; *N*-methyl-*(3a)*, 69225-20-3; *(3b)*, 69225-21-4; *(3c)*, 69225-22-5; *(3d)*, 69225-23-6; *(4)*, 35550-13-1; *(7a)*, 69225-25-8; *N*-methyl-*(7a)*, 69225-27-0; *N,N*-dimethyl-*(7a)*, 69225-29-2; *(7b)*, 69225-31-6; *(7c)*, 69225-33-8; *(8)*, 69225-35-0; *N,N*-dimethyl-*(8)*, 69225-37-2; acetonitrile, 75-05-8; benzonitrile, 100-47-0; propanenitrile, 107-12-0

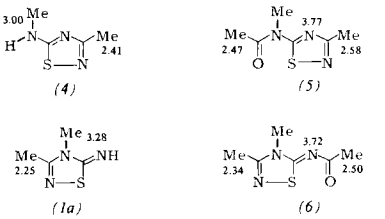
[1] a) *N. Lozac'h*, Adv. Heterocycl. Chem. *13*, 161 (1971); *E. Klingsberg*, Q. Rev. Chem. Soc. *23*, 537 (1969); b) *A. Hordvik*, *L. J. Saethre*, Isr. J. Chem. *10*, 239 (1972); *J. E. Oliver*, *R. T. Brown*, J. Org. Chem. *39*, 2228 (1974).

[2] a) *K. Akiba*, *M. Ochiumi*, *T. Tsuchiya*, *N. Inamoto*, Tetrahedron Lett. *1975*, 459; *K. Akiba*, *T. Tsuchiya*, *N. Inamoto*, *ibid. 1976*, 1877; *K. Akiba*, *T. Tsuchiya*, *M. Ochiumi*, *N. Inamoto*, *ibid. 1975*, 455; b) *M. Baudy*, *A. Robert*, J. Chem. Soc. Chem. Commun. *1976*, 912.

[3] *J. Goerdeler*, Chem. Ber. *87*, 57 (1954); *J. Goerdeler*, *W. Roth*, *ibid. 96*, 534 (1963).

[4] *L. A. Lee*, *J. W. Wheeler*, J. Org. Chem. *37*, 348 (1972); *R. N. Butler*, Can. J. Chem. *51*, 2315 (1972).

[5] ^{1}H-NMR-Data of the standards *(4)*, *(1a)*, *(5)* and *(6)* (δ values, $CDCl_3$, Me_4Si int.):



[6] a) *K. Akiba*, *T. Tsuchiya*, *N. Inamoto*, *K. Onuma*, *N. Nagashima*, *A. Nakamura*, Chem. Lett. *1976*, 723; b) *K. Akiba*, *T. Tsuchiya*, *N. Inamoto*, *K. Yamada*, *H. Tanaka*, *H. Kawazura*, Tetrahedron Lett. *1976*, 3819.

[7] *P. Oxley*, *M. W. Partridge*, *W. F. Short*, J. Chem. Soc. *1947*, 1110.

[8] *(7a)*, m.p. 144.5—146.0 °C; *N*-methyl-*(7a)*: m.p. 116.5—118.0 °C, *N*-Me: $\delta = 3.07$ (d, $J = 4.2$ Hz); *N,N*-dimethyl-*(7a)*: m.p. 133.0—134.0 °C, *N*-Me: $\delta = 3.38$.

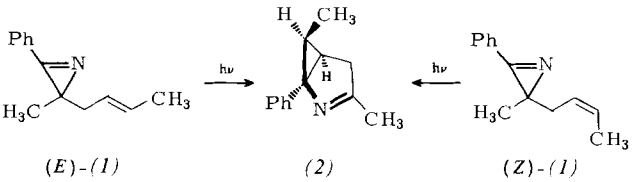
[9] *K. Akiba*, *S. Arai*, *F. Iwasaki*, Tetrahedron Lett. *1978*, 4117.

[10] *A. Hordvik*, *K. Julsham*, Acta Chem. Scand. *26*, 343 (1972).

Synchronous Mechanism of the 1,1-Cycloaddition of Nitrile Ylides to C=C Double Bonds[1]

By *Janos Fischer* and *Wolfgang Steglich*[*]

On irradiation of both (*E*)- and (*Z*)-2-(2-butenyl)-2-methyl-3-phenyl-2*H*-azirine [(*E*)-*(1)* and (*Z*)-*(1)*, respectively], *Padwa* and *Carlsen*[2] obtained *endo*-3,6-dimethyl-1-phenyl-2-azabicyclo[3.1.0]hex-2-ene *(2)* by intramolecular 1,1-cycloaddition of the intermediary nitrile ylide. The lack of stereospecificity and formation of mixtures of isomeric azabicyclohexenes in



closely related cases led the authors to postulate a stepwise addition of the 1,3-dipole to the double bond, with generation of a trimethylene intermediate ("six-membered ring dipole") [cf. *(8)*]. Since this mechanism is in direct contrast to the well-documented synchronous mechanism of 1,3-dipolar cycloadditions[3] and singlet-carbene additions[4], and since photochemical effects cannot be ruled out, we have reinvestigated the stereochemistry of 1,1-cycloaddition with thermally generated nitrile ylides.

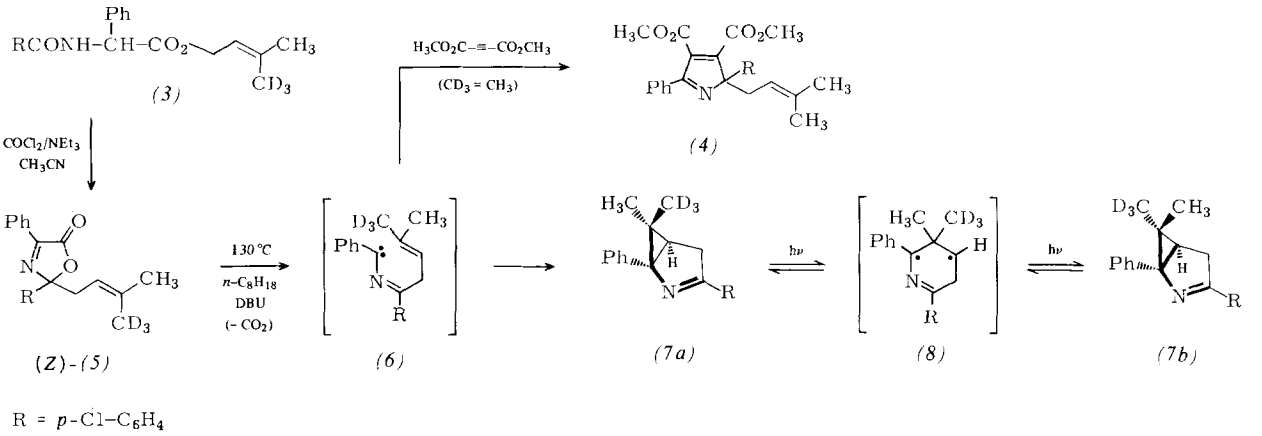
A suitable model for this purpose is the trideuteriated 3-oxazolinone *(5)*; the thermolysis of the unlabeled compound to 2-azabicyclo[3.1.0]hex-2-ene *(7)* (CH_3 instead of CD_3) has already been described[11]. *(5)* was prepared by cyclization

[*] Prof. Dr. W. Steglich
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn (Germany)
Dr. J. Fischer
Egyt Pharmacochemical Works
Box 100, H-1475 Budapest (Hungary)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*

0570-0833/79/0202-0167 $ 01.00/0

of (*Z*)-*N*-(*p*-chlorobenzoyl)-2-phenylglycine 3-trideuteriomethyl-2-butenyl ester *(3)*[5] with phosgene/triethylamine in acetonitrile[6]. According to the ^{1}H-NMR spectrum ($CDCl_3$) a 9:1 mixture of the (*Z*/*E*) isomers was formed [(*Z*)-*(5)*: $\delta_{CH_3}=1.61$; (*E*)-*(5)*: $\delta_{CH_3}=1.53$].



R = *p*-Cl–C_6H_4

When a mixture of (*Z*)-*(5)* in *n*-octane and some added diazabicycloundecene (DBU) was heated under reflux for 2 h, a 9:1 mixture of the *endo*- and *exo*-CD_3 isomers of the 2-azabicyclo[3.1.0]hex-2-ene [*(7a)*: $\delta_{CH_3}=0.94$; *(7b)*: $\delta_{CH_3}=0.89$] was formed in good yield. The ratio of epimers remained unchanged even after chromatography of the crude product and recrystallization from methanol (m.p. 85—87 °C). The configuration at C-6 follows from the ^{13}C-NMR spectrum ($CDCl_3$)[8]: the intense signal at $\delta=23.4$ is assigned to the *exo*-CH_3 group of *(7a)*, the weak signal at $\delta=13.4$ to the *endo*-CH_3 group of *(7b)*, whose resonance is shifted to higher field owing to the γ effect[9].

The result of the thermolysis experiment shows, within the accuracy of measurement, that the 1,1-cycloaddition of the thermally generated nitrile ylide *(6)* proceeds with retention of configuration. This provides evidence against the stepwise addition and in support of a synchronous mechanism.

On irradiation with an immersion lamp (Philips HPK 125, Vigor filter) in benzene the 9:1 ratio of *(7a)* to *(7b)* changes within 4 min to 7:3. Hence the epimerizations and isomerizations of the 2-azabicyclo[3.1.0]hex-2-enes *(7)* observed in the photolysis of azirines could be due to photochemical secondary reactions, probably involving a trimethylene intermediate [*e.g. (8)*][2]. That the nitrile ylide *(6)* is in fact generated in the thermolysis of *(5)* is demonstrated by trapping with dimethyl acetylenedicarboxylate (toluene, 6 h reflux), whereupon the oily 2*H*-pyrrole derivative *(4)* is obtained *via* 1,3-dipolar cycloaddition[3] [^{1}H-NMR (CCl_4): $\delta=1.37$, 1.48 (each br. s, 6H); 3.13 (m, 2H); 3.62, 3.66 (each s, 6H); 4.45 (br. t, 1H) 7.2—7.5 (m, 3H); 7.8—8.1 (m, 2H); 7.40, 8.03 (AA'BB' system, 4H)].

Received: October 4, 1978 [Z 126 IE]
German version: Angew. Chem. *91*, 168 (1979)

[1] Thermolysis of Oxazolin-5-ones, Part 9.– Part 8: *N. Engel, J. Fischer, W. Steglich*, J. Chem. Res. (S) *1977*, 162. *J. F.* thanks the Alexander-von-Humboldt Stiftung for a fellowship grant. Thanks are also due to Prof. Dr. *R. Huisgen* for valuable and stimulating discussions.

[2] *A. Padwa, P. H. J. Carlsen*, J. Am. Chem. Soc. *98*, 2006 (1976); *99*, 1514 (1977); cf. also *ibid. 97*, 3862 (1975); *A. Padwa, A. Ku, A. Mazzu, S. I. Wetmore, Jr., ibid. 98*, 1048 (1976); *A. Padwa, P. H. J. Carlsen, A. Ku, ibid. 100*, 3494 (1978); review: *A. Padwa*, Angew. Chem. *88*, 131 (1976); Angew. Chem. Int. Ed. Engl. *15*, 123 (1976).

[3] Cf. *e.g. R. Huisgen*, Angew. Chem. *75*, 604, 742 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565, 633 (1963); J. Org. Chem. *33*, 2291 (1968); *41*, 403 (1976).

[4] Cf. *e.g. P. S. Skell, A. Y. Garner*, J. Am. Chem. Soc. *78*, 5430 (1956); *R. C. Woodworth, P. S. Skell, ibid. 81*, 3383 (1959); review: *D. Bethell* in *S. P. McManus*: Organic Reactive Intermediates. Academic Press, New York 1973, p. 101 ff.

[5] Prepared by base-catalyzed transesterification of *N*-(*p*-chlorobenzoyl)-2-phenylglycine methyl ester with (*Z*)-3-trideuteriomethyl-2-buten-1-ol in the presence of 4 Å molecular sieve[6]. The deuteriated alcohol was prepared according to the method of *Corey et al.* by reduction of 2-butyn-1-ol with $LiAlH_4/2\,NaOCH_3$ (tetrahydrofuran, 3 h, reflux), decomposition of the vinylaluminum compound with an excess of I_2 (2 h, –60 °C; after gentle warming 12 h, 20 °C) [7a], and subsequent reaction of the (*Z*)-3-iodo-2-buten-1-ol obtained with lithium bis(trideuteriomethyl)-cuprate (Et_2O, 46 h, 0 °C) [7b].

[6] *N. Engel, B. Kübel, W. Steglich*, Angew. Chem. *89*, 408 (1977); Angew. Chem. Int. Ed. Engl. *16*, 394 (1977).

[7] a) *E. J. Corey, J. A. Katzenellenbogen, G. H. Posner*, J. Am. Chem. Soc. *89*, 4245 (1967); b) *E. J. Corey, G. H. Posner, ibid. 89*, 3911 (1967); *90*, 5615 (1968).

[8] $\delta=13.4$ (*endo*-CH_3); 23.4 (*exo*-CH_3); 28.7 (C-6); 29.6 (C-5); 37.2 (C-4); 73.5 (C-1); 128.2, 128.7, 129.0, 129.5, 132.6, 136.4, 139.0, (arom.-C); 170.3 (C-3). According to *F. Bohlmann, R. Zeisberg, E. Klein*, Org. Magn. Reson. *7*, 426 (1975), the *endo*- and *exo*-methyl signals of 3-carene appear at $\delta=13.2$ and 28.4, respectively.

[9] Cf. *e.g. J. B. Stothers*: Carbon-13 NMR Spectroscopy. Academic Press, New York 1972, p. 57 ff.

S_2^{2-} as Simultaneous End-on and Side-on Bonded Ligand in the Novel Transition-Metal Complex $[Mo_4(NO)_4S_{13}]^{4-}$

By *Achim Müller, Werner Eltzner*, and *Nageswaran Mohan*[*]

Interesting coordination compounds (*e.g.* with metal-metal bonds, unusual coordination numbers, or polynuclear metal-sulfur bonding systems)[1] can be synthesized by reaction of H_2S or S_n^{2-}[2] with solutions of oxometalates of the transition metals in the presence of other ligands. In the case of molybdenum mainly polynuclear sulfur complexes are formed.

Reaction of molybdate ions with ammonium polysulfide in aqueous solution in the presence of hydroxylamine led to the formation of the orange-red crystalline compound $(NH_4)_4[Mo_4(NO)_4S_{13}]\cdot 2H_2O$ *(1)*, which was characterized by elemental analysis, DTA, TG, and magnetic measurements, as well as by ESCA and IR spectra and a single-crystal X-ray structural analysis[3]. *(1)* is diamagnetic, soluble in H_2O, and shows principal IR absorptions (cm^{-1}) of the anion at *ca.* 1520 (br, s) [ν(NO)], 615/600 (m) [δ(NO), ν(MoN)], 548 (w), 533 (w) [ν(SS)], 342 (w), 327 (w) [ν(MoS)].

The most important structural features (cf. Fig. 1) of the new compound are two equilateral triangular arrays of Mo

[*] Prof. Dr. A. Müller, Dipl.-Chem. W. Eltzner, Dr. N. Mohan
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld 1 (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0168 $ 01.00/0*

atoms (Mo—Mo 3.375(2) Å) "joined" by a common edge (angle between triangular arrays 127.59°) with two triply bonded sulfur atoms normal to each Mo-triangle (Mo—S 2.501(5) Å) and one further sulfur atom bonded to each of the four Mo atoms (Mo—S 2.616(5) Å) and situated on the other side of the triangular arrays. Four of the total of five S_2^{2-} ligands each function as unsymmetrical bridges between two Mo atoms, one S atom being bound to only one Mo center (Mo—S 2.465(5) Å), and the other to both Mo centers (Mo—S 2.492(5) Å). The distances in the S_2^{2-} ligands are almost equal (S—S 2.048(7) Å). In the functional group {MoNO} the N—O and Mo—N distances are 1.219(22) Å and 1.742(16) Å, respectively.

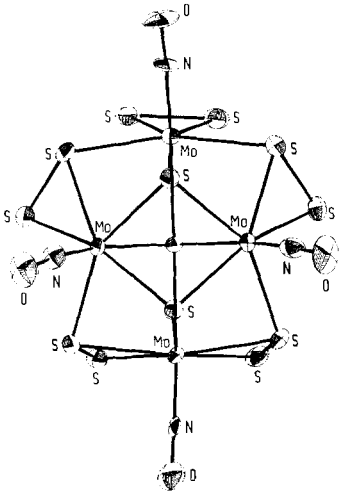


Fig. 1. Structure of the complex anion $[Mo_4(NO)_4S_{13}]^{4-}$.

(1) contains sulfur in *five different bonding states* and thus provides an example of the significance of S_2^{2-} ligands for the stabilization of unusual coordination compounds of the transition metals[4]. Particularly noteworthy here are the four S_2^{2-} ligands, each of which is coordinated *both end-on* (to one Mo atom) *as well as side-on* (to another Mo atom).

Procedure

An aqueous solution (10 ml) of $NH_2OH \cdot HCl$ (2.1 g) is added with stirring to a solution of 2.5 g of $(NH_4)_6Mo_7O_{24} \cdot 4H_2O$ and 15 g of $(NH_4)SCN$ in 40 ml of water. The yellow suspension is warmed to 80°C for 1 h, then, after addition of an equal volume of ammonium polysulfide solution, allowed to stand for *ca.* 10 h at 60°C in a closed vessel (any black precipitate that is formed is removed by filtration). On slow cooling, orange-red crystals of *(1)* precipitate out. These are washed with methanol, carbon disulfide, ether, and then dried over P_4O_{10} (yield 0.5 g).

Received: September 1, 1978 [Z 131 IE]
revised: November 17, 1978
German version: Angew. Chem. 91, 158 (1979)

[1] Cf. a detailed discussion of results of systematic investigations: *A. Müller, W. Eltzner, P. J. Aymonino, W. Jaegermann.* to be published.

[2] H_2S effects formation of thioanions (as reactive intermediates), reduction, and, in certain cases, generation of S^{2-} as ligand (true in the case of Mo, but not in general; cf. *e.g.* the preparation of $[V(NO)(CN)_6]^{4-}$, the first cyanonitrosyl complex with C.N. = 7; *A. Müller, P. Werle, E. Diemann, P. J. Aymonino,* Chem. Ber. *105*, 2419 (1972); *M. G. B. Drew, C. F. Pygall,* Acta Crystallogr. *B 33*, 2838 (1977); *S. Jagner, E. Ljungström, ibid. B 34*, 653 (1978)).

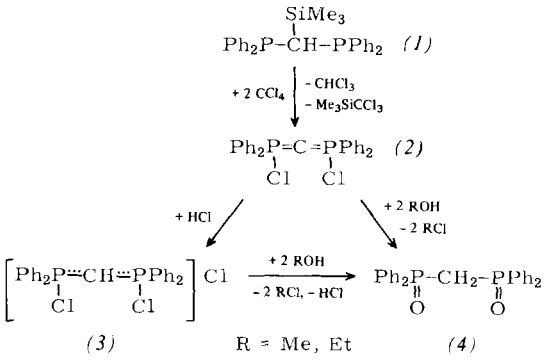
[3] *(1)* crystallizes with $a = 1604.0(2)$, $b = 1174.6(1)$, $c = 1565.7(2)$ pm, $\beta = 105.01(1)°$, in the monoclinic space group $P2_1/c$, $Z = 4$; 5374 independent reflections (Syntex $P2_1$ diffractometer, $2\theta_{max} = 54°$, MoKα); $R = 0.088$.

[4] Cf. *A. Müller, S. Sarkar, R. G. Bhattacharyya, S. Pohl, M. Dartmann,* Angew. Chem. *90*, 564 (1978); Angew. Chem. Int. Ed. Engl. *17*, 535 (1978).

Bis(chlorophenylphosphoranediyl)methane[1]

By *Rolf Appel* and *Karl Waid*[*]

"Carbodiphosphoranes" substituted at P by halogen are potential building blocks for the synthesis of theoretically interesting phosphorus-carbon ring systems[2]. Having previously prepared the partially halogenated compound (chlorodiphenylphosphoranediyl)(triphenylphosphoranediyl)-methane[3], we have now also been able to synthesize the symmetrical bis(chlorodiphenylphosphoranediyl)methane *(2)*. It is formed on reaction of tetrachloromethane with trimethylsilylmethylenebis(diphenylphosphane) *(1)* with elimination of (trichloromethyl)trimethylsilane and trichloromethane.



The yellow solid *(2)* undergoes smooth 1:1 addition with hydrogen chloride to give the salt *(3)*, which on reaction with alcohols undergoes a double Arbuzov rearrangement with cleavage of alkyl chloride to give the bis(diphenylphosphinoyl)methane *(4)*[4]. The dioxide *(4)* can also be obtained directly from *(2)* and alcohol.

Procedure

To a solution of *(1)*[5] (4.6 g, 10 mmol) in anhydrous dichloromethane (15 ml) is added CCl_4 (4.6 g, 30 mmol). The solution rapidly turns yellow and warms up. After 50 min the brown solution is evaporated down at reduced pressure, whereupon a yellow solid suddenly precipitates. Pentane (40 ml) is added, the mixture is filtered, washed with pentane (10 ml), and dried: yield 4.1 (90%) of $C_{25}H_{20}Cl_2P_2$ *(2)*, dec. pt. 150°C; M^+ at $m/e = 452$; $^{31}P\{H\}$-NMR (C_6H_6/C_6D_6, H_3PO_4 ext.): $\delta = +20.7$ (s); ^1H-NMR (CD_2Cl_2): $\delta = 7—8.5$ (m).

Received: November 14, 1978 [Z 141 IE]
German version: Angew. Chem. 91, 177 (1979)

CAS Registry numbers:
(1), 69258-10-2; *(2)*, 69258-11-3; *(3)*, (charged form) 69258-12-4; *(3)* (uncharged form), 69258-13-5; *(4)*, 2071-21-8

[*] Prof. Dr. R. Appel, Dipl.-Chem. K. Waid
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[1] Part 15 of Phosphorus-Carbon-Halogen Compounds.—Part 14: *R. Appel, G. Erbelding,* Tetrahedron Lett. *1978*, 2689.

[2] *R. Appel, F. Knoll, H. D. Wihler,* Angew. Chem. 89, 415 (1977); Angew. Chem. Int. Ed. Engl. *16*, 402 (1977).

[3] *R. Appel, H. D. Wihler,* Chem. Ber. *111*, 2054 (1978).

[4] *J. Richard, K. Burke, J. O'Laughlin, C. V. Banks,* J. Am. Chem. Soc. *83*, 1722 (1961).

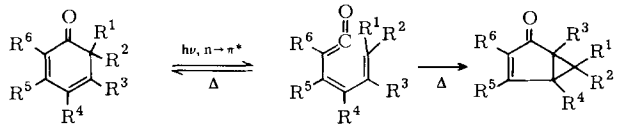
[5] *R. Appel, K. Geisler, H. F. Schoeler,* Chem. Ber., in press.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979
0570-0833/79/0202-0169 $ 01.00/0

Flash Vacuum Thermolysis of Doubly Unsaturated Acyl Halides to Give Phenols[**]

By *Eckehard V. Dehmlow* and *Marion Slopianka*[*]

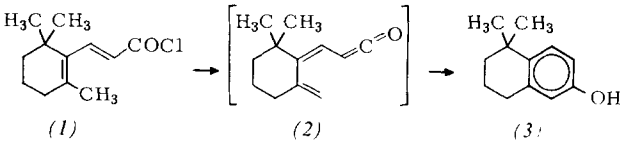
Dienylketenes have hitherto been observed and trapped only as products of $n \rightarrow \pi^*$ excitation of *ortho*-blocked cyclohexadienones at low temperatures[1]. In the absence of strong nucleophiles, recyclization occurs on warming to room temperature, yielding cyclohexadienones and in some cases bicyclo[3.1.0]hexenones[2] too.



It appeared interesting to know whether dienylketenes with R^1, $R^2 = H$ can be obtained from α,β,γ,δ-unsaturated acyl chlorides and whether their rearrangements to phenols can compete with possible polymerization.

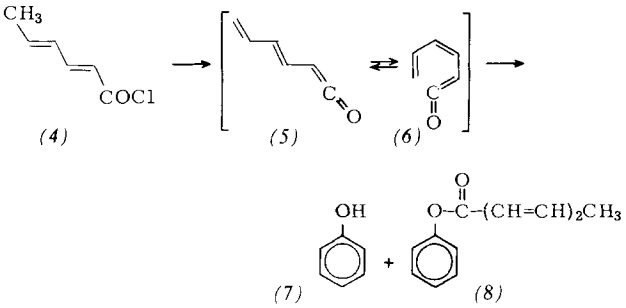
Treatment of doubly unsaturated acyl chlorides with triethylamine in dry ether always led to tars. *Schiess et al.*, however, showed that unsaturated ketenes with one conjugated and one nonconjugated double bond could be formed pyrolytically, *inter alia*, from acyl halides[3].

With the aim of preparing short-lived dienylketenes, we have performed flash vacuum thermolysis experiments in an apparatus of the kind developed by *Seybold*[4, 5]. *trans*-3-(2,6,6-Trimethyl-1-cyclohexenyl)propenoyl chloride *(1)* (*ca.* 5 mmol) was pyrolyzed at 660 °C/6×10^{-5} Torr. The pyrolyzate was condensed at −196 °C and then slowly warmed up to room temperature. The presumed intermediate ketene *(2)* contains two double bonds in an arrangement suitable for ring closure to give *(3)*. In fact, *(3)*[6] is the main product (yield 53 %) accompanied by traces of hydrocarbons and by unreacted *(1)*. Thermolysis of *(1)* at normal pressure gave mainly polymer besides *ca.* 10 % of *(3)*.



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

The expected primary pyrolysis product of sorboyl chloride *(4)* is the *trans*-dienylketene *(5)*. However, only isomer *(6)* is capable of ring closure. Experimentally, phenol *(7)* and phenyl sorbate *(8)* are obtained from *(4)* in 42 and 25 % yield, respectively, under the conditions defined above. Thus, the simplest possible dienylketene→phenol rearrangement has been accomplished.



(4) *(5)* *(6)* *(7)* *(8)*

Bicyclo[3.1.0]hexenones were not observed on flash thermolysis of *(1)* and *(4)* in spite of the fact that the bicyclic species possibly formed from *(1)* would not be readily transformed into *(3)*.

Received: November 8, 1978 [Z 145 IE]
German version: Angew. Chem. *91*, 163 (1979)

CAS Registry numbers:
(1), 69258-08-8; *(3)*, 51438-95-0; *(4)*, 67513-59-1; *(7)*, 108-95-2; *(8)*, 69258-09-9

[*] Prof. Dr. E. V. Dehmlow, M. Slopianka
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

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

[1] Reviews: *G. Quinkert*, Angew. Chem. *77*, 229 (1965); *84*, 1157 (1972); *87*, 851 (1975); Angew. Chem. Int. Ed. Engl. *4*, 211 (1965); *11*, 1072 (1972); *14*, 790 (1975).
[2] *J. Griffiths, H. Hart*, J. Am. Chem. Soc. *90*, 3297 (1968).
[3] *P. Schiess, P. Fünfschilling*, Helv. Chim. Acta *59*, 1745, 1756 (1976); *P. Schiess, P. Radimerski, ibid.* *57*, 2583 (1974); Angew. Chem. *84*, 345 (1972); Angew. Chem. Int. Ed. Engl. *11*, 288 (1972).
[4] *G. Seybold, U. Jersak*, Chem. Ber. *110*, 1239 (1977); *G. Seybold*, Angew. Chem. *89*, 377 (1977); Angew. Chem. Int. Ed. Engl. *16*, 365 (1977).
[5] Supplier: Otto Fritz GmbH (Normag), D-6238 Hofheim (Germany).
[6] M.p. 78 °C (from petroleum ether), MS: $M^+ = 176$; IR: OH band.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979*
0570-0833/79/0202-0170 $ 01.00/0

Koordinationschemische Katalyse organischer Reaktionen (Coordination-Chemical Catalysis of Organic Reactions). By *H. Pracejus*. Technische Fortschrittsberichte, Band 64 (Industrial Progress Reports, Vol. 64). Verlag Theodor Steinkopff, Dresden 1977. 287 pp., 174 figs., 12 tables, bound, *ca.* DM 50.00.

Pracejus has undertaken to set out in less than 300 A5 pages a summary, in the German language, of the whole field of coordination catalysis from the point of view of the organic chemist, and in this he has been successful. The mechanistic features are presented only as the principle for the arrangement of the text, and the kinetic investigations that form the basis for mechanistic representations are intentionally reported only in a secondary manner.

The book contains an introduction (21 pages), followed by chapters on hydrogenation and dehydrogenation (18), isomerization and disproportionation (12), oxidation (21), nonoxidative formation of C-heteroatom bonds (14), dimerization and oligomerization (44), polymerization (42), and syntheses by means of C_1 compounds (60); the last chapter concerns the relationships between homogeneous and heterogeneous catalysis by coordination catalysts (carrier-fixed complex compounds as catalysts (1), methods for carrier fixation (8), and special features of carrier-fixed complex catalysts (3)). Finally, the coordination-chemical phenomena observed in the catalysis by metals and metal oxides are described in 6 pages.

Facts are clearly presented, and what is still unclear is often plainly described as such. The main target of the book is to draw the still incomplete directions of research to the attention of advanced Students, post-graduate students, and interested specialist colleagues. Tables and clear diagrams facilitate orientation.

Admittedly, anyone wanting to know how polyethylene is in fact manufactured nowadays must search through the original and patent literature with the aid of the relatively complete citation of review articles, and there he will find "that the patent literature describes thousands of combinations of transition-metal compounds with maingroup metal alkyls, among which almost every transition metal is mentioned".

I failed to find any reference to the importance of Mg alkyls for Ziegler catalysts, to the system $TiCl_3 \cdot {}^1/_3 AlCl_3$, to the work of *B. Diedrich* [Appl. Polym. Symp. *26*, 1 (1975)] that leads to true high-yield catalysts, to the process review by *Weissermel et al.* [J. Polym. Sci. *C 51*, 187 (1975)], or to the book "Coordination Polymerisation" edited by *J. C. W. Chien*, Academic Press, New York 1975.

The setting is clean, structural formulas are cramped but clear, the quality of the paper still gives good legibility (slight transparency), and the binding permits frequent handling, which it is certain to receive.

Every interested person should obtain the book; several copies should be in every Institute's library.

Hansjörg Sinn [NB 437 IE]

Fundamentals of Chemical Relaxation (Monographs in Modern Chemistry 10). By *H. Strehlow* and *W. Knoche*. Verlag Chemie, Weinheim 1977, 1st edit., x, 133 pp., 41 figs., 12 tables, bound, DM 68.00.

Although relaxation methods (essentially based on *Eigen*'s work) as a tool for the measurement of the rates of fast reactions have greatly extended our knowledge of the kinetics and mechanisms of chemical reactions, they have only found passing mention in physical chemistry textbooks, even in those dealing with chemical kinetics. For this reason the authors' efforts to provide a comprehensive survey of relaxation methods are highly welcome.

The authors enter into the theory of the methods only insofar as it is necessary for understanding, without neglecting the necessary accuracy. For this reason the monograph can be readily understood even by the less advanced student.

The authors deal with the temperature, pressure, and field jump methods, and also with the "steady-state" methods based on ultrasonic absorption and dielectric loss. In each case not only the theory but also experimental details are described and exemplary calculations are given. Comparisons of the different relaxation methods with one another and with other methods for fast reactions indicate which method to choose for a given purpose. The following chapters, on the basis of theory and some selected practical examples, show what information can be obtained from relaxation methods under optimal experimental conditions.

A first-rate book, clear and precise despite its restricted presentation. The price, however, in no way appears appropriate.

Ulrich Schindewolf [NB 450 IE]

Collision Spectroscopy. Ed. by *R. G. Cooks*. Plenum Press, New York—London 1978, 1st edit., xiv, 458 pp., bound, $ 54.60.

Molecular beam experiments have long been known to physicists; more recently, in the variant form of ion beam processes, they have won a firm place in the repertoire of methods used by chemists and physical chemists. The information gained from such experiments relates to apparently differing aspects, *e.g.* the structure determination of gaseous ions, the analysis of reaction mechanisms, and the description of the dynamic relationships of ion/molecule reactions in the gas phase. A summary of the current state of the theoretical knowledge and a thoughtful discussion of the experimental probes available today were thus urgently needed, and the editor has filled this gap in no uncertain fashion with the aid of competent colleagues. The seven chapters not only reflect the most important literature published up to 1974 (altogether 650 references, which in part also cover the 1975/76 literature); the book also reflects the skill of its authors. It is very much more than a collection of seven mini-books (though each chapter can be read separately). In increasing order of complexity, the book deals first with ion beam experiments on atoms and on diatomic and polyatomic systems. A very wide range of interactions is discussed: electronic excitation, charge exchange, and dissociative excitation (collision-induced decomposition). There is a wealth of clear pictorial material, and mathematical symbolism is kept within limits.

In Chapter 1 (71 pages, 110 references), *Park* describes collision-induced excitation processes (experimental probes, theory) on simple systems (small atoms, diatomic molecules). In Chapter 2 (55 pages, 87 references) *Johnson* and *Böring* discuss in detail the theory of charge-transfer reactions. The advantages and the disadvantages of the currently available experimental methods are clearly outlined. In Chapter 3 (79 pages, 120 references), *Kessel*, *Pollack* and *Smith* present the latest experimental techniques, and also the consistent use of correlation diagrams for ion beam experiments on atoms. Multielectron transfers (with the possibility *e.g.* of a relatively precise determination of higher ionization potentials) are dis-

cussed by *Appell* (Chapter 4, 29 pages, 55 references). In Chapter 5 (31 pages, 24 references), *Kemp* and *Cooks* describe the various means by which ion/molecule reactions can be used to produce modified types of mass spectra, from which information on ionic structure may be obtained. In Chapter 6 (67 pages, 120 references), *Los* and *Gevers* demonstrate very convincingly the theoretical and methodological aspects of collision-induced decompositions of diatomic ions ($H_2^{+\bullet}$, $HHe^{+\bullet}$, $N_2^{+\bullet}$). These brilliantly written chapters are followed by an excellent discussion on the qualitative aspects of these processes with larger molecules (Chapter 7, 93 pages, 149 references). *Cooks* deals with topics as different as structure determination of thermochemical data, and isomerization of cations, without ever becoming superficial.

The book will prove useful to the expert, but it can also be unreservedly recommended to any scientist wishing to become acquainted with the wide-ranging field of gas-phase chemistry.

Helmut Schwarz [NB 451 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Fortschritte auf dem Gebiet der Kristallchemie der Silikate. By *F. Liebau*. Westdeutscher Verlag, Opladen 1978. 58 pp., paper, DM 12.00.—ISBN 3-531-08277-9

Applications of Polymer Spectroscopy. Edited by *E. G. Brame, Jr.* Academic Press, New York 1978. xiv, 289 pp., bound, $ 29.50.—ISBN 0-12-125450-X

Progress in Medicinal Chemistry, Vol. 15. Edited by *G. P. Ellis* and *G. B. West*. North-Holland, Amsterdam 1978. ix, 433 pp., bound, $ 69.00.—ISBN 0-7204-0655-2

Kirk-Othmer: Encyclopedia of Chemical Technology, Vol. 2. Alkoxides, Metal to Antibiotics, Peptides. John Wiley & Sons, London 1978. 3rd Edit. xxv, 1036 pp., bound, £ 50.00.—ISBN 0-471-02038-0

Energieversorgung. Ressourcen, Technologien, Perspektiven. By *M. Grathwohl*. Walter de Gruyter, Berlin 1978. 294 pp., bound, DM 68.00.—ISBN 3-11-007627-6

Oil Sand & Oil Shale Chemistry. Edited by *O. P. Strausz* and *E. M. Lown*. Verlag Chemie, New York 1978. xii, 384 pp., paper, DM 83.00.– ISBN 0-89573-102-9

Analysis with Ion-Selective Electrodes. By *J. Vesely, D. Weiss*, and *K. Stulik*. Ellis Horwood, Chichester 1978. 245 pp., bound, £ 16.00. —ISBN 0-85312-092-7

Chemisorption of Gases on Metals. By *F. C. Tompkins*. Academic Press, London 1978. xii, 370 pp., bound, £ 16.80.—ISBN 0-12-694650-7

Principles of Organic Synthesis. By *R. O. C. Norman*. Chapman & Hall, London 1978. 2nd Edit. xiii, 800 pp., paper, £ 9.95.–—ISBN 0-470-26317-2

IIC Studies. Studies in Industrial Property and Copyright Law. Vol. 2. Patents, Territorial Restrictions, and EEC Law. By *P. Demaret*. Verlag Chemie, Weinheim 1978. xx, 133 pp., paper, DM 45.00.–—ISBN 3-527-25696-2

Advances in Chemical Engineering, Vol. 10. Edited by *T. B. Drew, G. R. Cokelet, J. W. Hoopes, Jr.*, and *T. Vermeulen*. Academic Press, New York 1978. xiv, 336 pp., bound, $ 35.00.—ISBN 0-12-008510-0

Theoretical Chemistry, Vol. 3. Senior Reporters: *R. N. Dixon* and *C. Thomson*. The Chemical Society, London 1978. ix, 138 pp., bound, DM 70.00.—ISBN 0-85186-774-X.—A volume of the series "Specialist Periodical Reports"

Organophosphorus Chemistry, Vol. 9. Senior Reporter: *S. Tripett*. The Chemical Society, London 1978. xi, 288 pp., bound, DM 120.00. –ISBN 0-85186-086-9.—A volume of the series "Specialist Periodical Reports"

Space Groups for Solid State Scientists. By *G. Burns* and *A. M. Glazer*. Academic Press, New York 1978. xiii, 278 pp., bound, $ 14.50.—ISBN 0-12-145760-5

Physiologie der Mikroorganismen. By *I. W. Dawes* and *I. W. Sutherland*. "taschentext" 73. Verlag Chemie/Physik-Verlag, Weinheim 1978. 241 pp., paper, DM 24.00.—ISBN 3-527-21067-9 (Verlag Chemie); 3-87664-567-0 (Physik-Verlag)

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form by photoprint, microfilm, or any other means nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstraße 12, D-6940 Weinheim, Germany, Telephone (06201) 14036, Telex 465516 vchwh d.

Editor: *O. Smrekar* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*), Pappelallee 3, P.O. Box 1260/1280, D-6940 Weinheim, Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 3
March 1979
Pages 173–238

Anchimerically Accelerated Bond Homolyses

By Manfred T. Reetz[*]

Radical reactions of the type R^1—a—b—$R^2 \rightarrow {}^{\bullet}$a—b—$R^1 + {}^{\bullet}R^2$ are feasible if the new bond formed between b and R^1 is considerably stronger than the old bond between a and R^1. Furthermore, both the radical fragments formed must be resonance stabilized. An example of this reaction type is the thermolysis of benzyl trimethylsilylmethyl ethers, in which the trimethylsilyl group (with empty orbitals) migrates to the oxygen atom (with lone pairs). Assumption of a cyclic reactive intermediate with pentacoordinated silicon explains the observed intramolecular nature and the negative entropy of activation of such homolyses.

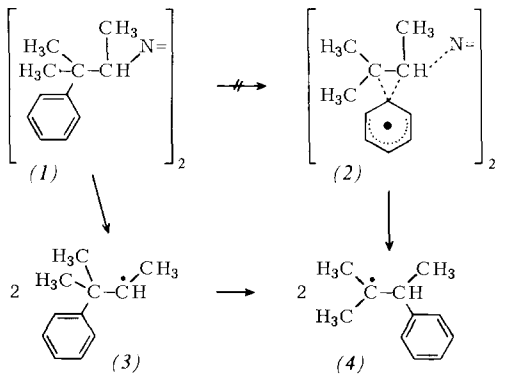
1. Introduction

In organic chemistry substituent effects are generally transmitted through bonds or through space. However, substituents can also influence reactions by bonding with the reaction center, thereby stabilizing transition states or intermediates[1]. This effect is called *neighboring group participation*, and may, but need not, result in rearranged products. If the neighboring group stabilizes the transition state in the rate determining step, one speaks of *anchimeric*[**] acceleration[2]. Once the phenomenon of anchimeric participation had been shown to be general in the field of carbocation chemistry, as evidenced by numerous examples, the search for analogous effects in *radical* processes began in the fifties. It turned out that a number of unimolecular[3] homolytic reactions failed to show anchimeric effects, in spite of the fact that the neighboring group in corresponding cationic systems exerts a pronounced accelerating effect.

[*] Doz. Dr. M. T. Reetz
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg (Germany)
Present address: Institut für Organische Chemie und Biochemie der Universität,
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

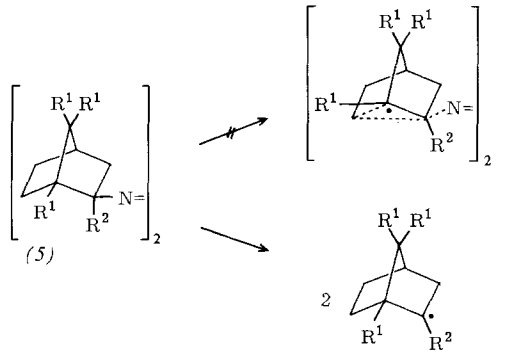
[**] The term "anchimeric" (Greek *anchi* near, *meros* part) was coined by *Winstein* [2].

For example, in his studies concerning the thermal decomposition of azo compounds *(1)*, *Overberger et al.*[4] excluded the participation of phenyl groups in the transition state of radical formation according to *(2)*. The generation of rearranged products was explained by a secondary phenyl group migration *(3)* → *(4)*.



Radical decomposition reactions of other azo compounds also show no appreciable anchimeric effects[5–7]. Among them are the thermolyses of bornyl and norbornyl derivatives *(5a)* and *(5b)*, respectively, studied by *Berson et al.*[5] and *Rüchardt et al.*[6].

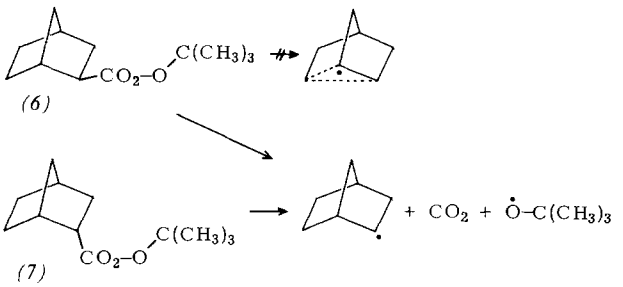
© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0202-0170 $ 01.00/0*



(5)

(a), $R^1 = CH_3$, $R^2 = H$; (b), $R^1 = H$, $R^2 = CH_3$

According to *Bartlett et al.*[8], thermal decomposition of the *tert*-butyl peroxynorbornanecarboxylates (6) and (7) proceeds at normal rates ($k_{exo}/k_{endo} = 4.1$). Again, the norbornyl framework induces no nonclassical effects. The search for anchimeric acceleration in the thermal decomposition of other peroxyesters as well as in other homolytic processes also remained fruitless[1, 9–13].



(6)

(7)

Why do carbenium ions and radicals behave differently? Apart from possible effects during the formation of carbenium ions and radicals, Wagner-Meerwein rearrangements proceed much more rapidly than analogous radical 1,2-sigmatropic shifts. The latter are in fact rare[14]. A simple explanation based on MO theory was published by *Zimmerman et al.*[15] in 1961 and later refined by *Jaffé* and *Orchin*[16]. The cyclic transition state is treated as a three-center bond with two, three, or four electrons, which gives rise to appreciable energy differences for carbenium ions, radicals and carbanions, respectively (see Fig. 1). Therefore, the participation of a neighboring group in a bonding manner during the formation of radicals will usually be of no energetic advantage.

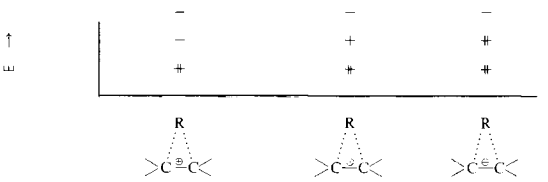
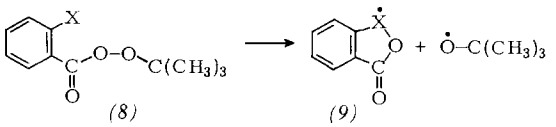


Fig. 1. MO scheme for 1,2-sigmatropic shifts in carbocations, radicals, and carbanions.

2. Thermolysis of *ortho*-Substituted *tert*-Butyl Peroxybenzoates

The above results suggest that appreciable anchimeric effects may at best be found in compounds that contain hetero atoms having low-lying empty orbitals and/or lone pairs. Such a system was described by *Leffler et al.*[17], and was generalized and mechanistically studied by *Martin*[18] in an impressive series of papers. It was observed that peresters of type (8) as well as corresponding dibenzoyl peroxides[13] undergo homolytic decomposition to (9) at different rates, depending upon the nature of the substituent X (Table 1).

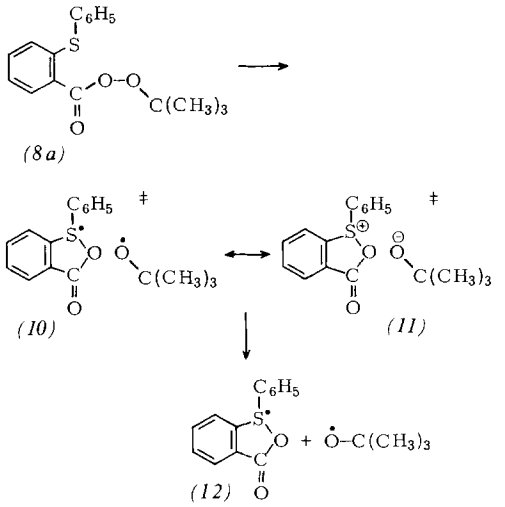


(8) (9)

Table 1. Kinetic data [18] of the radical fragmentation of *tert*-butyl perbenzoates (8). Chlorobenzene as solvent.

	X	k_{rel}	$\Delta H^{\neq}$ [kcal/mol]	$\Delta S^{\neq}$ [e.u.]
a	C_6H_5S	6.5×10^4	23.0	− 3.4
b	$CH{=}C(C_6H_5)_2$	150	26.3	− 5.0
c	I	80	28.0	− 0.8
d	$C(CH_3)_3$	2.4	34.4	+12.5
e	H	1.0	34.1	+10.0

In particular, sulfur gives rise to an enormous anchimeric effect (see Table 1). *Martin* postulates a transition state (10) for the rate determining step of the fragmentation of (8a) in which sulfur coordinates with oxygen, thereby weakening the O—O bond. Resonance forms (10) and (11) were proposed to describe the transition state. They explain the radical reaction path and the pronounced dependence of the fragmentation rate on solvent polarity. It is not quite clear whether (11) is also an *intermediate* on the way to (12)[19, 20]. However, there is no doubt that radicals are indeed generated, as shown by trapping experiments[18] and ESR studies[21].

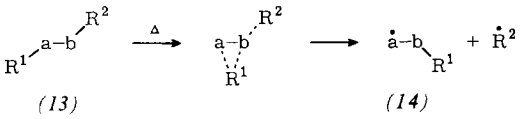


(8a) (10) (11) (12)

3. Thermolysis of Alkyl Silylmethyl Ethers

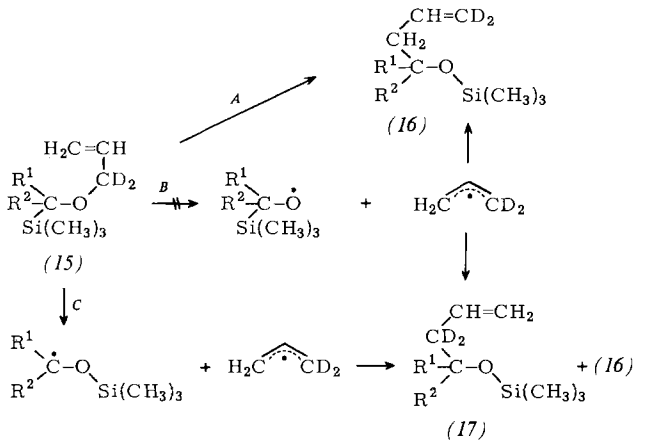
The reactions studied by *Martin* involve neither three-center transition states nor complete migration of the assisting group to the radical reaction center. In contrast, our own studies started from a completely different standpoint. We speculated that anchimerically accelerated homolyses of the type (13) → (14) may be possible if the new bond b—R^1 is consider-

ably stronger than the old bond a—R^1, and if the radicals generated are resonance stabilized.



(13) *(14)*

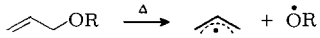
This working hypothesis evolved in 1974 from the observation that the dyotropic rearrangement[22] of allyl silylmethyl ethers *(15)* → *(16)* (Path *A*), which proceeds with allyl inversion, is accompanied by a radical reaction[23, 24]. Thermolysis (160—190 °C) affords 80% of *(16)* and 20% of the "wrong" isomer *(17)*. Formation of the latter can be explained by postulating the formation of allyl radicals. The overall yield of rearrangement product drops to 60% in the presence of a radical trapping agent. Importantly, it then contains 97% of *(16)*. Under these conditions the greater portion of the suspected allyl radicals are trapped.



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

$R^1 + R^2$ = 2,2'-Biphenylylene

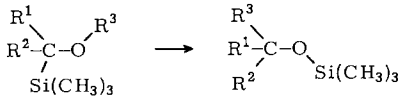
(15) and similar derivatives ($R^1 = R^2 = C_6H_5$; $R^1 = C_6H_5$, $R^2 = C_{10}H_8$) were found to rearrange with astonishingly low activation energies ($E_a \approx 33$ kcal/mol). Thus the hypothesis of allyl radical formation appeared rather dubious, since the homolysis of C—O bonds, generating resonance stabilized radicals usually requires *ca.* 50 kcal/mol[25]:



For these reasons, a simple radical cleavage of the C—O bond of *(15)* (Path *B*) was excluded[24]. In contrast, a mechanism was proposed in which the silyl group provides anchimeric assistance by migrating toward oxygen and initiating radical fragmentation (Path *C*). The formation of the very strong Si—O bond (110—130 kcal/mol)[26] as well as the generation of resonance stabilized radicals correspond to the general scheme *(13)* → *(14)*. In order to study these unusual and intruiging effects more closely, a number of alkyl silylmethyl ethers were synthesized which are *incapable* of allyl inversion (*e.g.* benzyl ethers)[27].

3.1. Structural Prerequisites for Radical Fragmentation[27, 28]

In order to ascertain the effect of R^1, R^2, and R^3 on the rate of decomposition of alkyl silylmethyl ethers, the kinetics of the rearrangement *(18)* → *(19)* were studied (Table 2). First order kinetics were found in all cases. The yield of rearrangement products is 85—98%.

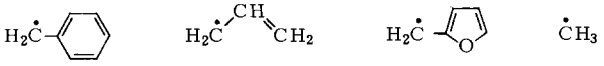


(18) *(19)*

Table 2. Kinetic data of radical fragmentation of alkyl silylmethyl ethers *(18)* to siloxy compounds *(19)* at 185 °C. Solvent: benzene.

	R^1	R^2	R^3	$k_{rel} \pm 0.05$
a	C_6H_5	C_6H_5	$C_6H_5CH_2$	0.3
b	C_6H_5	1-Naphthyl	$C_6H_5CH_2$	0.9
c	2,2'-Biphenylylene		$C_6H_5CH_2$	1.0
d	2,2'-Biphenylylene		p-CH_3—C_6H_5—CH_2	1.5
e	2,2'-Biphenylylene		p-CH_3O—$C_6H_5CH_2$	2.2
f	2,2'-Biphenylylene		p-NO_2—$C_6H_5CH_2$	0.2
g	2,2'-Biphenylylene		Furfuryl	0.3
h	2,2'-Biphenylylene		CH_3	—
i	H	C_6H_5	$C_6H_5CH_2$	$<10^{-4}$

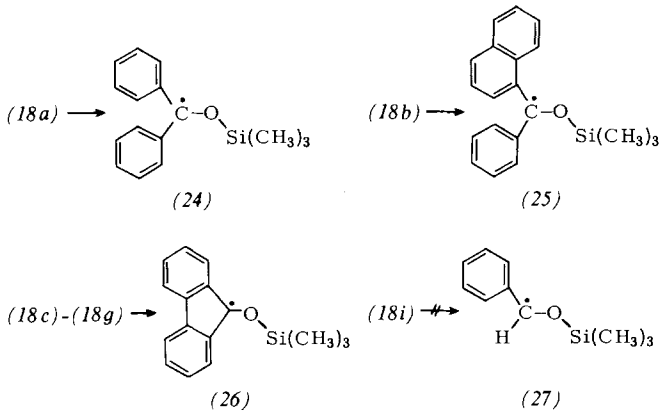
Within the fluorenyl series ($R^1 + R^2$ = 2,2'-biphenylylene) the benzyl and furfuryl ethers react with comparable rates, whereas the methyl ether *(18h)* is completely stable under the reaction conditions. This reflects the relative ability of the substituents R^3 to function as a radical leaving group. Whereas (substituted) benzyl[29], allyl[29] and furfuryl radicals[30] *(20)*, *(21)*, and *(22)*, respectively, are resonance stabilized, this fails to apply to the high energy methyl radical *(23)*[29].

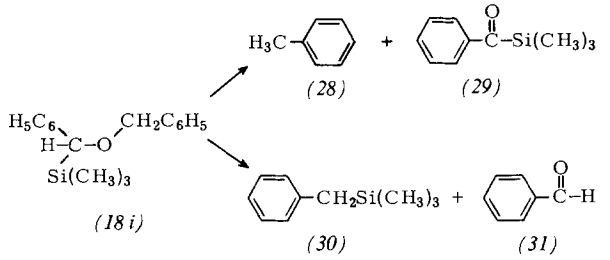


(20) *(21)* *(22)* *(23)*

The relative rates in relation to the nature of the substituent at the carbon atom (R^1 and R^2) are equally revealing. Di-aryl-substituted benzyl ethers *(18a)*—*(18g)* react at similar rates. However, if one of the arene groups is substituted by hydrogen, no rearrangement is observed; *(18i)* is stable between 150 and 195 °C. At 230 °C competing β-eliminations set in, so that only a lower limit of the theoretically possible radical fragmentation rate can be approximated: $k_{(18i)}/k_{(18c)} < 10^{-4}$. Assuming the intermediate formation of ketyl radicals (see ESR experiments, Section 3.4), a resonance effect can be invoked once more. Whereas *(24)*, *(25)*, and *(26)* are stabilized by two aromatic substituents, the potential radical *(27)* contains only one group capable of resonance. Therefore, competing β-eliminations leading to *(28)*, *(29)*, *(30)*, and *(31)* dominate.

Although the presence of bulky groups is known to significantly affect the rate of unimolecular homolyses[31, 32], steric acceleration could be ruled out as the dominating factor in the above cleavage. The *tert*-butyl derivative benzyl 9-*tert*-butyl-9-fluorenyl ether analogous to *(18c)* remains unchanged at 195 °C for several days. In sharp contrast, the half-life of the rearrangement *(18c)* → *(19c)* under identical conditions amounts to a mere 18 minutes. This underlines the dramatic influence of the trimethylsilyl group and is in line with the low activation energy of 32 kcal/mol and the negative





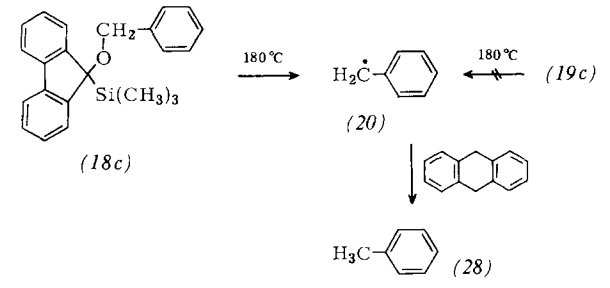
entropy of activation $\Delta S^{+} = -8.6$ e. u. for *(18c)*→*(19c)*. The entropy factor suggests a reduction in the number of degrees of freedom in the transition state.

3.2. Crossover Experiments[33]

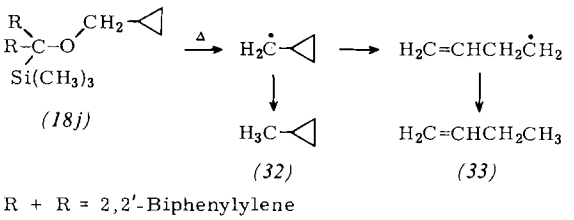
Crossover experiments using labeled compounds show that the silyl groups migrate 100% *intra*molecularly. On the other hand, the benzyl groups undergo *ca.* 25% *inter*molecular migration. These observations are also in accord with the postulated radical mechanism.

3.3. Radical Trapping Experiments[33]

If the thermolysis of *(18)* indeed leads to R^3 radicals, it should be possible to prove this by the use of appropriate trapping agents. The thermolysis of *(18c)* in the presence of an excess of 9,10-dihydroanthracene does in fact lead to toluene (59%) and anthracene. The thermolysis of independently synthesized rearrangement product *(19c)* does not generate benzyl radicals, *i.e.* no trace of toluene is observed under identical conditions.



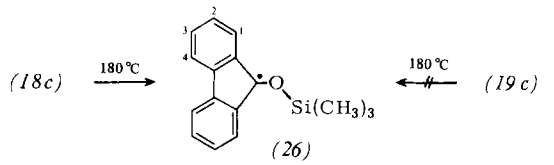
A similar experiment was performed with the cyclopropyl methyl ether *(18j)* which reacts considerably slower. If (cyclopropyl)methyl radicals are in fact formed, they should undergo rapid rearrangement to 4-butenyl radicals, as described by *Kochi*[34]. Thus, two different trapping products are to be expected. Indeed, methylcyclopropane *(32)* and 1-butene *(33)* were identified in a ratio of 1:74.



R + R = 2,2'-Biphenylylene

3.4. ESR Experiments[33]

The intermediate formation of ketyl radicals was proved directly by ESR spectroscopy. Heating *(18c)* to 180°C in an ESR spectrometer results in a well resolved spectrum with $a^{H} = 3.48$, 0.83, 3.78 and 0.83 G for the protons H-1, H-2, H-3, and H-4 of the fluorenyl ring in *(26)*. The values correspond to those of *Neumann et al.*[31], who prepared *(26)* by a different route. Under identical conditions the rearrangement product *(19c)* does not give rise to ESR signals. This control experiment again shows that the theoretically possible reverse reaction is *not* responsible for radical formation.



3.5. Solvent Effects[33]

In order to determine the influence of solvent polarity on the rate of decomposition, kinetic measurements were carried out in solvents having different E_T values (E_T values are empirical parameters of solvent polarity.) Utilizing *(18c)* at 185°C, the results point to a very small effect: k_{rel} (based on benzene) is 1.4 in *o*-dichlorobenzene and 2.2 in acetonitrile. The fact that the activation parameters of *(18c)* → *(19c)* do not change significantly in going from benzene to acetonitrile as solvent is mechanistically significant[23]. The intermediacy of ions or zwitterions is quite unlikely.

3.6. Influence of Substituents and Secondary Kinetic Isotope Effects in the Radical Leaving Group[27, 33, 35]

In order to examine possible electronic effects in the radical leaving group, a Hammett study utilizing (substituted) benzyl ethers *(18c)*—*(18f)* was undertaken. The k_{rel} values lie closely together (see Table 2). Whereas the application of σ constants leads to a good correlation ($\rho = -0.92$), no straight line results with σ^{+} values (Fig. 2). Thus, radical formation has not advanced to a significant degree in the transition state, *i.e.*, the C—O bond is not stretched much. The values can be explained on the basis of a small polar effect[27].

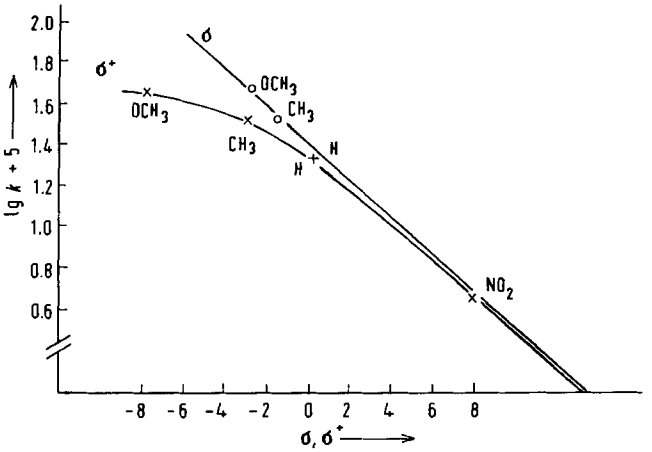
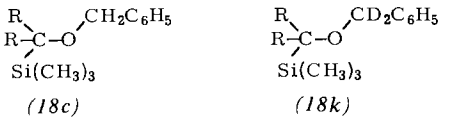


Fig. 2. Hammett plot for thermolysis of the (substituted) benzyl ethers *(18c)*—*(18f)* to *(19c)*—*(19f)* (see Table 2).

The above results are in line with the observation[35] that the secondary kinetic deuterium isotope effect at 150°C is rather small: $k_{(18c)}/k_{(18i)} = k_H/k_D = 1.04 \pm 0.03$.

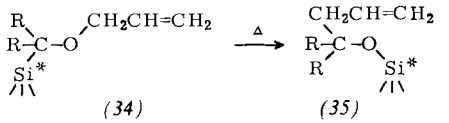


(18c) *(18k)*

R + R = 2,2'-Biphenylylene

3.7. Stereochemistry at the Migrating Silyl Group[24,36]

Although allyl ethers react only in part by a radical mechanism [cf. *e.g. (15)*], the stereochemistry at the silicon atom was investigated for the total rearrangement process. For this purpose a complete Walden cycle involving *(34)* and *(35)*, which contain an asymmetric silicon atom, was transversed. It turned out that the silyl group migrates from carbon to oxygen with >96% *retention* of configuration. This means that not only the concerted rearrangement, but also the radical rearrangement, proceeds stereospecifically.

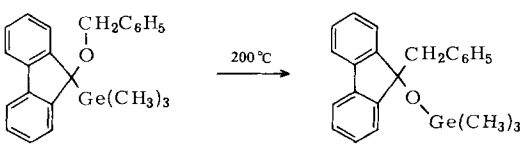


(34) *(35)*

$\overset{*}{\text{Si}}$ = Methyl(α-naphthyl)phenylsilyl

3.8. Replacement of Silicon by Germanium[37]

In order to study the role of the neighboring group more closely, the (germylmethyl) ether *(36)* analogous to *(18c)* was synthesized and thermally rearranged to *(37)*. *(36)* reacts much slower than the silicon analogue: $k_{(36)}/k_{(18c)} \approx 4 \times 10^{-5}$. At first glance this seems surprising, since in sigmatropic 1,5 rearrangements involving the cyclopentadienyl framework

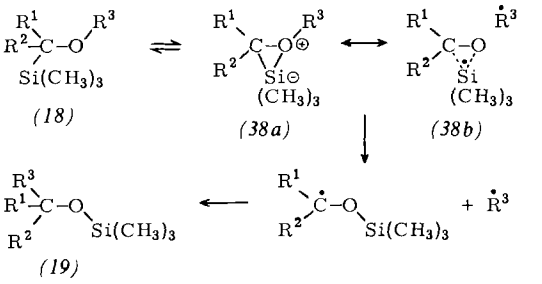


(36) *(37)*, 66%

germyl groups migrate *faster* than the analogous silyl moieties[38]. Apparently the strength of the new bond to oxygen plays an important role. The Ge—O bond (*ca.* 85 kcal/mol[39]) is weaker than the Si—O bond (110—130 kcal/mol)[26].

3.9. Mechanism of Radical Formation[33,40]

It is clear that the presence of the silyl group induces radical formation under mild conditions. But how does this neighboring group act? Rate-determining complexation between silicon and oxygen leading to the generation of a reactive intermediate[41] having cyclic three-membered structure *(38a)* in which the R^3—O bond is weakened [see resonance form *(38b)*], is in line with all presently known observations. This *may* involve d_π-p_π interaction. Rapid homolytic decomposition then leads to the complete formation of the strong Si—O bond and the generation of resonance stabilized radicals. If the potential radical is not sufficiently stabilized [for example in the case of the methyl ether *(18h)*], the complex merely reverts back to starting material, since an additional energy barrier would have to be overcome (see Fig. 3).



(18) *(38a)* *(38b)* *(19)*

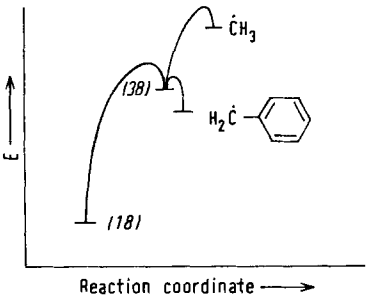
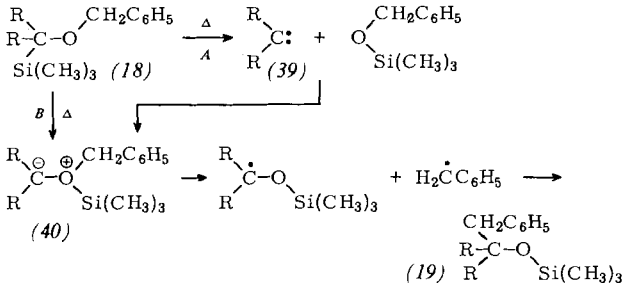


Fig. 3. Possible reaction profile for thermolysis of the ethers *(18c)* and *(18h)*.

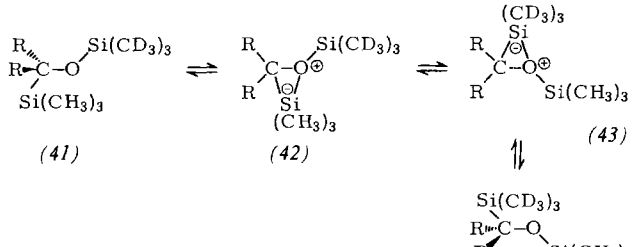
The formation of species *(38)* with pentacoordinated silicon is not only consistent with the intramolecularity and stereochemistry of silyl group migration, but also with the negative entropy of activation, the small kinetic deuterium isotope effect, and the results of the Hammett study. However, the existence of the reactive intermediate *(38)* cannot yet be proved beyond all doubt. Concerted fragmentation of *(18)* into radicals does not involve any local energy minimum along the reaction coordinate. The difference between the two-step and concerted mechanism is thus rather small. In both cases the motion of the neighboring group is far advanced compared to that of the leaving group. The pronounced affinity of silicon for oxygen is the driving force of the reaction and is responsible for the relatively low activation energy. The germanium analogue *(36)* rearranges slower, since the Ge—O bond is considerably weaker.

Since alternative mechanisms have been discussed in detail elsewhere[24, 33], only two of the most important possibilities are mentioned here. Path *A* involves rate-determining α-elimination affording carbene *(39)*. Related α-eliminations are known[42], but involve formation of stabilized nucleophilic carbenes. Path *A* appears unlikely because trapping experiments fail to afford carbene adducts[24].



It is more difficult to disprove the direct ylide mechanism (Path *B*), which represents anchimerically accelerated homolysis, just like the previously discussed mechanism involving *(38)*. The difference between the ylide *(40)* and the three-membered ring *(38)* has to do with the fact that in the former there is no bonding between silicon and carbon. Is it possible to detect this difference experimentally? Perhaps the formation of a genuine oxygen ylide would result in a larger solvent effect.

The main counterargument is more subtle. We observed that the dyotropic valence isomerism[43] of silyl methylsilyl ethers *(41a)*⇌*(44a)* occurs *without* radical formation[44, 45]. The silyl groups interchange their places strictly intramolecularly at 160—190°C with retention of configuration, whereby an equilibrium is reached. However, the activation parameters and solvent effects are almost identical to those of the radical fragmentation *(18)*→*(19)*. This suggests a similar transition state, namely rate-determining coordination between silicon and oxygen. It necessarily follows that the energy surface is characterized by a double minimum *(42)*⇌*(43)*. A mechanistically significant observation is that the benzhydryl derivative *(41b)* is completely stable under normal thermolysis conditions (160—190°C). Only at *ca.* 230°C does *slow* silyl-silyl exchange occur, along with considerable amounts of decomposition products.



(a), R + R = 2,2'-Biphenylylene
(b), R = Phenyl

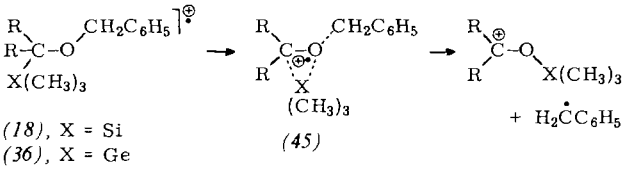
The dramatic difference between *(41a)* and *(41b)* ($k_{(41b)}/k_{(41a)} \approx 10^{-5}$) can only be explained by a steric model. The motion of the silyl group in *(41b)* from oxygen to the backside of the carbon atom in the reactive intermediates *(42)* and *(43)* is rapid only if the R-substituents do not give rise to steric inhibition, *e.g.*, as in flat fluorenyl derivatives and similar systems[44]. Such is not the case in the benzhydryl derivatives.

This effect was *not* found in radical reactions, where the benzhydryl and fluorenyl compounds [*e.g. (18a)* and *(18c)*] fragment at comparable rates. This is not surprising, since intermediate *(38)* has an "escape route", namely homolytic fragmentation which does not involve concerted backside attack. The strikingly different behavior of *(18)* and *(40)* in going from fluorenyl to benzhydryl derivatives *is not consistent with an ylide or a carbene mechanism.* However, it is in line with the formation of structurally related reactive intermediates *(38)* and *(42)*.

It remains to be explained why the rearrangement *(18)*→*(19)* proceeds with such surprisingly high yield, *i.e.*, without the formation of dimerization products such as bibenzyl. Relevant is the fact that preferred cross-dimerization is a common phenomenon in radical chemistry. In our case a somewhat enhanced concentration of ketyl radicals which trap just about all the benzyl radials could be the cause.

3.10. Comparison of Thermal, Electron-Impact Induced, and Photolytic Behavior

Surprisingly, silylmethyl- and germylmethyl ethers *(18)* and *(36)* as well as related compounds show very intense mass spectral peaks at $e/m = [M - CH_2C_6H_5]^+$[46]. Since electron-impact induced cleavages of C—O bonds with elimination of radicals and fixation of charge on the oxygen moiety are high energy processes which rarely afford intense fragment ions[47], a neighboring group effect was postulated. Migration of the metal from carbon to oxygen prevents charge localization.



(18), X = Si
(36), X = Ge

Indeed, further studies utilizing DADI spectra show that this new type of electron-impact induced ether cleavage occurs if the transition state *(45)* is stabilized by anchimeric participation of the silyl or germyl group[48]. Relevant and significant is the observation that in case of the *tert*-butyl analogue of *(18c)* (C in place of Si) the genesis of $[M - CH_2C_6H_5]^+$ does not come about, in spite of the fact that a stabilized benzyl radical could be generated. Thus, in this case there is a strict correspondence between thermal and electron-impact induced behavior.

These and other experiments confirm the decisive role of the silyl and germyl groups and also demonstrate that generation of ions by an alternative migration of the C^9—C^{10} σ-bond of the fluorenyl skeleton to the oxygen, which involves ring expansion, offers no competition. The observation that hydrogen scrambling processes—which are otherwise very evident in the low energy spectra of arenes—do not take place (deuterated allyl derivatives loose only $C_3H_3D^+$) also suggests a fast process facilitated by migration of the adjacent metal groups[48].

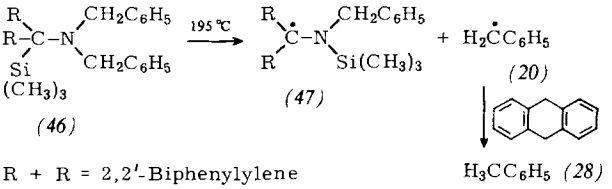
The differing rates of thermal fragmentation of *(18c)*, *(18h)*, and *(18i)* have no quantitative parallels in the mass spectrum.

The radical R^3 liberated on electron-impact induced decomposition is not necessarily resonance stabilized. Moreover, just *one* stabilizing group on the stationary C atom is sufficient [cf. *(18i)*]. The germyl compound shows effects of similar magnitude although it undergoes thermal fragmentation much slower than the silicon analogue.

It was of interest whether the above anchimerically accelerated ether cleavages can also be induced photochemically. Such a process would require specific photochemical excitation of the C—Si bond. The direct excitation of a certain σ-bond is generally difficult. *(18c)* was chosen as experimental substance[28] because the fluorenyl skeleton is a suitable chromophore in which the absorbed light energy can "flow" into the α-positioned σ-bond. Experiment (Hg high-pressure lamp, Pyrex filter) showed that the C—O bond, rather than the C—Si bond, reacts preferentially[28]: normal ether cleavage was detected. The experiments underline the fundamental difference between thermal and photolytic behavior.

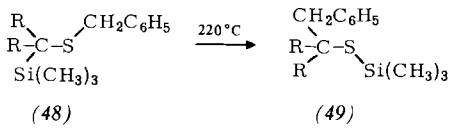
4. Thermolysis of Benzyl(silylmethyl)amines and Benzyl Silylmethyl Thioethers[49, 51]

If the hetero atom with a lone pair does in fact play a crucial role in the radical fragmentation of alkyl silylmethyl ethers, then the analogous amines should likewise undergo anchimerically assisted homolyses. Of course, the strength of the Si—N bond amounts to only *ca.* 85 kcal/mol[50]. The radical fragmentation of *(46)* does indeed proceed more slowly than that of the corresponding ether: $k_{(46)}/k_{(18c)} \approx 10^{-5}$. In the presence of 9,10-dihydroanthracene as a radical trapping agent, 76% of toluene is formed. A mechanism according to *(46)* → *(47)* + *(20)* is therefore likely[49]. In the absence of radical trapping agents a number of products are formed, among them bibenzyl (15%). In its mass spectrum *(46)* shows a low-intensity $[M-CH_2C_6H_5]^+$ peak[48], in contrast to the oxygen analogue *(18c)*. Hence there exists a parallel between thermolysis and electron impact.



These results underscore the central role of the heteroatom, with the strength of the new bond to silicon being of prime importance for the subsequent reactions. *Brook* has noted similar effects in the base-induced sigmatropic silyl migration in α-silyl alcohols and α-silylamines; the latter rearrange considerably slower[50].

The thioether *(48)* analogous to *(18c)* was also synthesized and thermolyzed in order to study possible anchimeric effects[51]. Although the mechanistic studies have not been completed, it is clear that the reaction *(48)* → *(49)* is much slower than *(18c)* → *(19c)*: $k_{(48)}/k_{(18c)} \approx 6 \times 10^{-6}$. Again, this observation supports the working hypothesis according to which the strength of the new bond to the neighboring group is decisive for the rate of radical fragmentation: $E_{Si-O} - E_{Si-S} \approx 30$ kcal/mol[52,53].



5. Summary

The rearrangements described in Sections 3 and 4 are the first known examples of anchimerically accelerated homolyses involving three-center bonds in the transition state as well as the migration of the neighboring group to the radical reaction center. The conjecture that such processes are possible if a strong new bond is made and if both radical fragments are resonance stabilized has been confirmed so far. Rate-determining complexation between the neighboring group having empty orbitals and a heteroatom having a lone pair is presently a useful working hypothesis. Some degree of correspondence is observed in many cases between thermal and electron-impact induced behavior. Further parallels are found in recent studies, *e.g.* on thermolysis and behavior of silyl methylacetates in the mass spectrometer[48, 54]. It remains to be seen whether groups other than SiR_3 (*e.g.*, phosphorus or boron) are also capable of anchimeric assistance.

This review was written by the author during his stay as guest professor at the Department of Chemistry, University of Wisconsin (Madison). I would like to thank the members of the department for their hospitality and for interesting discussions. Particular thanks are due to my co-workers Dr. M. Kliment, Dr. N. Greif, Dipl.-Chem. A. Maaroufi, and M. Plachky. Our work was generously supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Received: March 20, 1978 [A 258 IE]
German version: Angew. Chem. *91*, 185 (1979)

[1] *B. Capon, S. P. McManus:* Neighboring Group Participation. Vol. I. Plenum Press, New York 1976.
[2] *S. Winstein, C. R. Lindegren, H. Marshall, L. L. Ingraham*, J. Am. Chem. Soc. *75*, 147 (1953).
[3] Several examples of anchimerically accelerated bimolecular homolyses are known: *P. S. Skell, K. J. Shea* in *J. K. Kochi:* Free Radicals. Vol. II. Wiley, New York 1973, p. 809.
[4] *C. G. Overberger, J. Gainer*, J. Am. Chem. Soc. *80*, 4561 (1958).
[5] *J. A. Berson, C. J. Olsen, J. S. Walia*, J. Am. Chem. Soc. *84*, 3337 (1962).
[6] *J. Hinz, C. Rüchardt*, Tetrahedron Lett. *1970*, 3095.
[7] *S. Seltzer, S. Scheppele*, J. Am. Chem. Soc. *90*, 358 (1968).
[8] *P. D. Bartlett, J. M. McBride*, J. Am. Chem. Soc. *87*, 1727 (1965).
[9] *C. Rüchardt, R. Hecht*, Chem. Ber. *98*, 2460 (1965).
[10] *C. Rüchardt, R. Hecht*, Chem. Ber. *98*, 2471 (1965).
[11] *L. A. Singer* in *D. Swern:* Organic Peroxides. Vol. I, Wiley Interscience, New York 1970, p. 265.
[12] *C. Rüchardt, H. Trautwein*, Chem. Ber. *98*, 2478 (1965).
[13] *C. Rüchardt*, Fortschr. Chem. Forsch. *6*, 251 (1966).
[14] Review: *J. W. Wilt* in *J. K. Kochi:* Free Radicals. Vol. I, Wiley, New York 1973, p. 333.
[15] *H. E. Zimmerman, A. Zweig*, J. Am. Chem. Soc. *83*, 1196 (1961).
[16] *N. F. Phelan, H. H. Jaffé, M. Orchin*, J. Chem. Educ. *44*, 626 (1967).
[17] *J. E. Leffler, C. C. Petropoulos, R. D. Faulkner*, Chem. Ind. (London) *1956*, 1238.
[18] Review: *J. C. Martin* in *J. K. Kochi:* Free Radicals. Vol. II, Wiley, New York 1973, p. 493.
[19] *P. Livant, J. C. Martin*, J. Am. Chem. Soc. *98*, 7851 (1976).
[20] *W. A. Prior, H. W. Hendrickson*, J. Am. Chem. Soc. *97*, 1580 (1975).
[21] *J. C. Martin, P. Livant, M. M. Chau*, Abstr. Pap. 174th Nat. Meeting ACS, Chicago 1977, Orgn. 135.
[22] *M. T. Reetz*, Angew. Chem. *86*, 416 (1974); Angew. Chem. Int. Ed. Engl. *13*, 402 (1974).

[23] *M. T. Reetz*, Chem. Ber. *110*, 954 (1977).
[24] *M. T. Reetz*, Chem. Ber. *110*, 965 (1977).
[25] a) *K. Kwart, S. F. Sarner, J. Slutsky*, J. Am. Chem. Soc. *96*, 5234 (1973); b) *M. J. Mobra, E. Ariza*, An. R. Soc. Esp. Fis. Quim., Ser. B, *56*, 851 (1960).
[26] *A. G. Brook*, Acc. Chem. Res. *7*, 77 (1974).
[27] *M. T. Reetz, M. Kliment*, Tetrahedron Lett. *1975*, 797.
[28] *M. T. Reetz, M. Kliment, N. Greif*, Chem. Ber. *111*, 1083 (1978).
[29] *D. Griller, K. U. Ingold*, Acc. Chem. Res. *9*, 13 (1976).
[30] Furfuryl radicals have been generated by an alternative method: *L. D. Kispert, R. C. Quijano, C. U. Pittman*, J. Org. Chem. *24*, 3837 (1971).
[31] *W. P. Neumann, B. Schroeder, M. Ziebarth*, Justus Liebigs Ann. Chem. *1975*, 2279.
[32] *H.-D. Beckhaus, C. Rüchardt*, Chem. Ber. *110*, 878 (1977).
[33] *M. T. Reetz, N. Greif, M. Kliment*, Chem. Ber. *111*, 1095 (1978).
[34] *J. Kochi, P. J. Krusic, D. R. Eaton*, J. Am. Chem. Soc. *91*, 1877 (1969).
[35] *M. T. Reetz*, unpublished results 1977.
[36] *M. T. Reetz*, Tetrahedron Lett. *1976*, 817.
[37] *M. T. Reetz, N. Greif*, to be published.
[38] *A. V. Kisin, V. A. Korenevsky, N. M. Sergevev, Y. A. Ustynyuk*, J. Organomet. Chem. *34*, 93 (1972).
[39] *E. A. Ebsworth* in *A. G. MacDiarmid*: The Bond to Carbon. Vol. I, Part I, Marcel Dekker, New York 1968, p. 46.
[40] *N. Greif*, Dissertation, Universität Marburg 1977.
[41] In the thermal rearrangement of α-silyl ketones to vinyl silyl ethers the intermediacy of reactive pentacoordinated silicon species is likely: *H. Kwart, W. E. Barnette*, J. Am. Chem. Soc. *99*, 614 (1977).
[42] *A. G. Brook, P. J. Dillon*, Can. J. Chem. *47*, 4347 (1969).
[43] Definition: *M. T. Reetz*, Tetrahedron *29*, 2189 (1973); review: *M. T. Reetz*, Adv. Organomet. Chem. *16*, 33 (1977).
[44] *M. T. Reetz, M. Kliment, M. Plachky*, Chem. Ber. *109*, 2716 (1976).
[45] *M. T. Reetz, M. Kliment, M. Plachky*, Chem. Ber. *109*, 2728 (1976).
[46] *H. Schwarz, M. Kliment, M. T. Reetz, G. Holzmann*, Org. Mass. Spectrom. *11*, 989 (1976).
[47] *H. Schwarz, R. Wolfschütz*, Org. Mass. Spektrom. *11*, 773 (1976).
[48] *H. Schwarz, M. T. Reetz*, Angew. Chem. *88*, 726 (1976); Angew. Chem. Int. Ed. Engl. *15*, 705 (1976); *H. Schwarz, C. Wesdemiotis, M. T. Reetz*, J. Organomet. Chem. *161*, 153 (1978).
[49] *M. T. Reetz, A. Maaroufi*, to be published.
[50] *A. G. Brook, J. M. Duff*, J. Am. Chem. Soc. *96*, 4692 (1974).
[51] *M. T. Reetz, M. Kliment*, unpublished results 1979.
[52] *A. Haas*, Angew. Chem. *77*, 1066 (1965); Angew. Chem. Int. Ed. Engl. *4*, 1014 (1965).
[53] *M. T. Reetz, M. Kliment*, Tetrahedron Lett. *1975*, 2909.
[54] *M. T. Reetz, N. Greif*, Angew. Chem. *89*, 765 (1977); Angew. Chem. Int. Ed. Engl. *16*, 712 (1977); cf. *A. R. Bassindale, A. G. Brook, P. F. Jones, J. M. Lennon*, Can. J. Chem. *53*, 332 (1975).

New analytical methods (15)

Liquid Column Chromatography with Chemical Derivatizations after Separation

By Georg Schwedt[*]

Modern liquid column chromatography (high-pressure liquid chromatography, HPLC) has evolved in the last few years into a highly efficient and versatile separation technique. The selectivity of an analytical process that depends upon a previous separation step can in many cases be increased considerably by chemical derivatizations after the separation. In addition, lower detection limits can be achieved in this way than in detection without derivatization. The physicochemical principles of these combined processes involving chromatographic separation and chemical derivatization prior to detection (coupling of HPLC and a reaction detector) are presented and discussed. The state of development is outlined, with a survey of the more important applications so far described in the literature.

1. Introduction

The essential problems of modern analytical chemistry are to increase the sensitivity and selectivity and to improve the detection limits of analytical processes used to detect and determine trace elements and low contents of organic substances in complex mixtures. During the last two decades progress in this direction has been made possible mainly with the help of physics and physical methods of measurement, namely by novel analytical applications of physical effects and by improvements in the available apparatus.

While the development of analytical chemistry up to about 1960 was mainly characterized by the analytical application of chemical reactions and the discovery of new reagents for the classical gravimetric, volumetric, colorimetric, and photometric methods, it seems that the most significant part in further development is nowadays played by physical methods of measurement, for example spectroscopic methods.

In chromatography too, improvements in the equipment, above all in the fields of gas and liquid chromatography, have been responsible for a decisive improvement in separation performances and hence in selectivity. Technological advances in the manufacture of column packings with particle diameters below 10 μm, and improvements in pumping techniques that enable a constant pulsation-free delivery of the mobile phase against high pressures, have in the last ten years transformed classical liquid chromatography into the incomparably more efficient high-pressure liquid chromatography (HPLC). However, compared to the analytical side of HPLC, the detection stage has, as yet, not reached the same high level of sophistication as far as sensitivity, detection limits, and selectivity are concerned. Nevertheless, developments are appearing that

[*] Prof. Dr. G. Schwedt
Analytische Chemie, Fachbereich 8 der Gesamthochschule
Adolf-Reichwein-Strasse 2, D-5900 Siegen 21 (Germany)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0202-0170 $ 01.00/0

once more endow the chemical side, *i.e.* chemical reactions and reagents, with greater significance.

2. Reaction Detectors

2.1. Principles and Designs of the Analytical System

UV and fluorescence detectors with flow-through cells are at present the most usual, and from the point of view of instrumentation the best-developed detectors used with HPLC[1]. To improve the sensitivity and in particular the detection limits it is often recommended that the substances to be determined should be modified chemically to give compounds with higher molar extinction coefficients for UV detection, or compounds that can be detected fluorimetrically down to lower detection limits than can be attained by UV detection. Such derivatization can be performed either before or after the chromatographic separation[2].

Derivatization prior to a chromatographic analysis, with the aim of achieving more selective separations, and in particular lower detection limits than is possible with the original compounds, has been successfully applied in chromatography for some time[2, 3]. For this purpose the chemical derivatizations should be as quantitative as possible, and should lead to one definite product. In contrast, if the substances are to be derivatized after the separation step, reactions that do not proceed to completion may suffice, even if they yield several products, provided only that the signals to be measured are strong and reproducible. Moreover, in this case there is no longer any need for the sample preparation required with derivative formation before the separation, which is often laborious, time-consuming, and associated with losses of material.

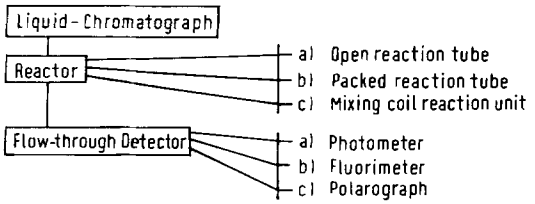


Fig. 1. System for liquid chromatographic analyses with chemical reactions after the separation step. The combination of a reactor and flow-through detector is called a reaction detector.

The analytical systems for liquid chromatography with chemical reactions after the separation consist of a liquid chromatograph, a reactor, and a flow-through detector (Fig. 1, cf. also [4]). The chemical reaction and the detection of the separated substances take place in on-line coupling after the chromatographic separation. In conformance with current practice, in what follows we shall refer to the reactor and the flow-through detector as the (chemical) reaction detector[5]. The reactor can consist of an open reaction tube (a capillary tube), a packed reaction tube (a tube of greater diameter than a capillary, packed with small particles such as glass beads), or a mixing coil reaction unit such as those used in equipment for automatic wet chemical analyses (AutoAnalyzers®). In this reaction unit a peristaltic pump is used for pumping the solutions through manifold tubes into the mixing coils. The liquid stream is divided into segments with air bubbles (see Fig. 2).

2.2. Diffusion Effects in the Reactors

In all reactors the chromatographically separated substances exhibit "band broadening" caused by diffusion effects, which can be described quantitatively.

The band broadening of a signal recorded in the detector in the form of a Gaussian distribution curve can be described in terms of the standard deviation σ or the variance σ^2. The variances of individual parts of the analytical system are additive (cf. Table 1):

$$\sigma_t^2 = \sigma_{tc}^2 + \sigma_{tv}^2 + \sigma_{td,g}^2 \text{ [s]} \tag{1}$$

(c: column, v: connections, td,g: total detection system, *i.e.* the reactor and flow-through detector).

2.2.1. Open Reaction Tube

In an open capillary tube connected to the outlet of the HPLC column *via* a T-piece, the variance as a function of the reaction time (according to [6, 7]) is given by:

$$\sigma_{td}^2 = \frac{d_t^2 t}{96 D_m} \tag{2}$$

Thus, for a given diffusion coefficient D_m the band broadening σ is proportional to the tube diameter d_t and to the square root of the reaction time t. Differences in band broadening between ideal and geometrically deformed tubes have been investigated by *Halász* and *Walkling*[6].

2.2.2. Packed Reaction Tube

Packed reaction tubes correspond to packed separation columns in chromatography, but they do not have any retaining action. The dependence of the variance upon the reaction time is here:

$$\sigma_{td}^2 = \left[\frac{\varepsilon \cdot D_m \pi^2 d_t^4}{8 F_l^2} + \frac{\pi d_t^2 \lambda_1 \cdot \lambda_2 d_p}{4 F_l [1 + \lambda_2 d_t (\pi D_m / d_p)^{1/2}]}\right] t \tag{3}$$

(The equation used in [8] has been rearranged.) The abbreviations are explained in Table 1. In this type of reactor the band broadening can be reduced by using finer particles, a higher flow-through rate, and a smaller tube diameter.

2.2.3. Mixing Coil Reaction Unit

In units of this kind the liquid stream is segmented by air bubbles (Fig. 2) and the band broadening resulting from diffusion effects in the longitudinal direction is thus reduced to a minimum[5, 9, 10].

The following equation, due to *Snyder*[5], gives the variance as a function of the reaction time:

$$\sigma_{td}^2 = \left[\frac{538 d_t^{2/3} (F_l + 0.92 d_t^3 n)^{5/3} \eta^{7/3}}{\gamma^{2/3} F_l D_{w,25}} + \frac{1}{n}\right] \times \left[\frac{2.35 (F_l + 0.92 d_t^3 n)^{5/3} \eta^{2/3}}{\gamma^{2/3} F_l d_t^{4/3}}\right] \cdot t \tag{4}$$

The optimal segmentation frequency n can in each case be determined as a function of the diameter of the mixing coil. The influences exerted by the flow rate F_l, viscosity

η of the reaction mixture, and surface tension γ have been investigated thoroughly by *Snyder*[5]. (For the abbreviations in eq. (4), see Table 1.)

Table 1. Explanation of the abbreviations used and some definitions.

c_{max}	Concentration of a substance at the band maximum [g·cm^{-3}]
c_0	Concentration of a substance in the sample solution [g·cm^{-3}]
d_f	Mean liquid-film thickness on the walls [cm]
d_i	Internal diameter of connectors or tubes
d_p	Particle diameter [cm]
d_t	Tube diameter [cm]
D_m	Molar diffusion coefficient [cm^2·s^{-1}]
$D_{w,25}$	Molar diffusion coefficient in water at 298 K [cm^2·s^{-1}]
F_l	Flow rate down the column, space velocity [cm^3·s^{-1}]
F_R	Flow rate of the reagent [cm^3·s^{-1}]
H	Height of a theoretical separation plate [mm]
k'	Capacity-, mass distribution ratio
l_s	Length of a liquid segment [cm]
L	Column length [cm]
m_s	Mass [g]
n	Segmentation frequency [s^{-1}]
N	Number of theoretical separation plates
p	Pressure [bar]
q	Free cross section of a separation column
r	Radius of mixing coil
R	Resolution of two bands
R_{max}	Maximum resolution
t	Reaction time [s]
t_R	Over-all retention time [s]
u	Linear flow velocity [cm·s^{-1}]
V_0	Sample volume [cm^3]
β	Ratio of liquid length/sum of liquid and gas lengths [*]
γ	Surface tension [dyne·cm^{-1}]
ε	Porosity: fraction of the free cross section available to the eluent
λ	Geometric constants for the packed reaction tube
η	Viscosity [dyne·s·cm^{-2}]
σ_t, σ_v	Band broadening [s] or [cm^3]
σ_{tc}	Band broadening in the column [s]
σ_{td}	Band broadening in the reactor [s]
$\sigma_{td,g}$	Band broadening in the whole detection system [s]
σ_{tv}	Band broadening in the connectors [s]

Sensitivity of a method: slope of calibration curve
Detection limit of a process: concentration for the measured quantity from blank value plus three times its standard deviation

[*] By "liquid length" and "gas length" are meant the lengths of the liquid and the gas segments, respectively.

Deelder and *Hendricks*[11] give the following relationship for the dependence of the variance on the mean thickness of the liquid film d_f on the walls and on the length l_s of a liquid segment (Fig. 2):

$$\sigma_{td}^2 = \frac{2\pi^2 d_f l_s L r^3}{F_l} \qquad (5)$$

According to *Hrdina*[12], the following relation exists for the value of 4σ:

$$4\sigma = 2\sqrt{n t d_f/(\beta d_t)} \qquad (6)$$

Here β represents the ratio of the liquid length to the sum of the liquid and gas lengths (see Table 1).

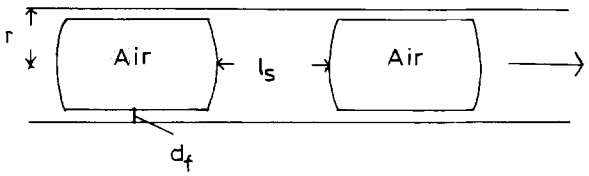


Fig. 2. Schematic representation of the segmentation of the liquid stream in a mixing spiral reaction unit. r: radius of the glass tube (of the mixing coil); d_f: mean liquid-film thickness on the walls; l_s: length of a liquid segment.

Eq. (4)[5] makes it possible to calculate the band broadening from directly measurable or known magnitudes of the reactor, while the application of the simpler relationships (5) and (6) requires knowledge of the mean thickness of liquid-film on the walls.

Further investigations concerning the dynamics of the analysis with continuously segmented flow have been performed *e.g.* by *Begg*[13], *Thiers et al.*[14], and *Walker et al.*[15], and on band broadening in columns by *Halász et al.*[16] and by *Huber* and *Hulsman*[17].

2.3. Comparison of the Reactors and General Relationships

If we compare the variances or the band broadening for several types of reactors in relation to the reaction time (Table 2), the mixing coil unit proves to be best. In practice, however, additional broadening occurs as a result of diffusion in the connections of the mixing coil to the chromatographic column, in the air separator, and in the connection to the detector (see, for example, [11]). Experimental values of σ for several reactors are shown in Table 3.

An open reaction tube is also suitable for very rapid reactions lasting a few seconds. Indeed, when mixing coil reaction units are used, greater band broadening than the calculated value is observed due to the connectors; nevertheless, this type of reactor is preferred to the two others for long reaction times, particularly when several reaction steps are involved.

Table 2. Parameters for the calculation of band broadening σ_t in several reactor types.

	Open reaction tube	Packed reaction tube	Mixing coil reactor
Internal tube diameter d_t [cm]	0.05	0.5	0.1
Diffusion coefficient D_m [cm^2·s^{-1}]	2×10^{-5}	2×10^{-5}	$D_{w,25}$: 3.5×10^{-5}
Flow rate F_l [cm^3·s^{-1}]	—	0.025	0.025
Viscosity η [dyne·s·cm^{-2}]	—	0.004	0.004
Surface tension γ [dyne·cm^{-1}]	—	—	25
Packing particle diameter d_p [cm]	—	1.6×10^{-3}	—
Segmentation frequency n [s^{-1}]	—	—	7.3
Constants λ_1	—	11	—
λ_2	—	18	—
Calculated variance as a function of reaction time [s^2]	σ_t^2 $1.30t$	$5.14\times10^{-2}t$	$4.97\times10^{-3}t$

Table 3. Examples of experimentally obtained band broadenings σ_t and σ_v in several types of reactor.

Open reaction tube (after [21])

Determination of thioridazine in blood. Chromatography: partition with ternary phases; reaction: oxidation with potassium permanganate; detector: fluorimeter.

	$\sigma_v \cdot 10^{-3}$ [cm^3]
System: Sample loop + flow-through cell	36
Sample loop + flow-through cell + open reaction tube	120

Conditions: $t=5$ [s], $F_1=2$ [cm^3 min^{-1}], $d_t=0.04$ [cm], $L=150$ [cm]

$\sigma_t=3.6$ [s] (calculated from σ_v)

Packed reaction tube (after [70])

Determination of isoenzymes. Chromatography: in a modified cellulose exchanger; reaction: transformation with lactate/NAD$^+$; detector: photometer or fluorimeter.

System: column packed with nonporous glass beads.

Conditions: $L=30$ [cm], $d_t=0.41$ [cm], $p=7$ [bar], $d_p=5\times10^{-5}$ [cm], $u=0.4$ [cm^{-1}], $t=75$ [s]

$\sigma_t=3.1$ [s] (calculated from Fig. 3 in [70] with $H=0.5$ [mm]) [*]

Mixing coil reaction unit (after [11])

Determination of cyclohexanone. Chromatography: partition with ternary phases; reaction: transformation with 2,4-dinitrophenylhydrazine; detector: photometer.

		σ_{td}^2 [s^2]
System: Mixing coil I: $L=2$ [m], $d_t=0.24$ [cm]		16
Mixing coil II: $L=1$ [m], $d_t=0.24$ [cm]		6
Connectors		11
	Total	33 ($\sigma_{td,g}^2$)

Conditions: $t=180$ [s], $u=0.15$ [cm·s^{-1}], $k'=0.3$ $R_{max}=3$ (without a reactor), $R=2.4$ (with a reactor): $\sigma_{tc}>7$ [s] decreases the resolution R by less than 20% [11].

$\sigma_t=5.7$ [s] (calculated from $\sigma_{td,g}^2$)

[*] σ_{td}^2 amounts to only one-third of the value when the same reaction is carried out in an open capillary tube 15.25 m long and with an internal diameter of 0.05 cm [70].

Only at high temperatures does the packed reaction tube seem to offer advantages[18], since no tubing or plastic connections such as in the mixing coil reaction unit are required. In more recent publications, *Frei et al.*[19, 20] have compared the various possibilities of post-column derivatization.

For the ratio of the resolution of two signals, recorded in the flow-through detector, and the resolution R_{max} attained by the chromatographic system with $\sigma_t=\sigma_{tc}$ and $\sigma=0$, we have (according to [8, 11]):

$$R/R_{max}=[1+\sigma_{td}^2/\sigma_{tc}^2]^{-1/2} \tag{7}$$

If a decrease of 5% in the resolution R_{max} is allowed for, then $\sigma_{td}=0.33\,\sigma_{tc}$. From this condition we obtain a minimum retention time of

$$t_{R2}=2\sigma_{td}\sqrt{N} \tag{8}$$

(Example: $\sigma_{td}=2$ [s], $N=10000$, $t_{R2}=400$ [s]) at a given resolution R for a pair of substances in dependence on the number of theoretical separation stages N.

The dilution effect in liquid chromatography can be expressed as the ratio of the concentration of a substance at the band maximum c_{max} to its concentration in the sample c_0 (after [11]):

$$\frac{c_{max}}{c_0}=\frac{V_0}{q(1+k')\sqrt{2\pi LH}} \tag{9}$$

The product $c_0 V_0$ corresponds to the quantity of the sample.

In the reactor the sample solution is further diluted by the addition of reagents and the band broadening[11]:

$$\frac{c_{max}}{c_0}=\frac{F_1}{F_1+F_R}\cdot\frac{\sigma_{tc}}{\sigma_t}\cdot\frac{V_0}{q(1+k')\sqrt{2\pi LH}} \tag{10}$$

With the assumption of a Gaussian distribution, we have for c_{max} (see [21]):

$$c_{max}=\frac{m_v}{\sqrt{2\pi}\sigma_v} \tag{11}$$

3. Examples of Application

Most of the so far described liquid chromatographic analyses involving a reaction detector are related to the fields of organic chemistry or biochemistry. The analysis of amino acids has already been carried out successfully for about 20 years, using a chromatographic separation (ion exchange) directly coupled to a chemical reaction stage before the detection, in automatic reaction systems (with mixing coil reaction units)[22]. Apart from the classical ninhydrin[18, 23], phthalaldehyde[29–32], fluorescamine[29, 37, 38] and pyridoxal[40] have been used for the photometric or fluorimetric determination of amino acids (see Table 4).

Peptide separations have also been combined with a reaction step using phthalaldehyde[34] or fluorescamine[39]. In part, these methods have been extended to the determination of amines[24–27, 30, 33]. In the analysis of biogenic amines such as catecholamines, special chemical reactions are carried out in mixing coil reaction units after the chromatographic separation: a) transformation with ethylenediamine[4, 41, 42] and b) oxidation to fluorimetrically detectable trihydroxyindoles[43–48]. Owing to the selective reaction to trihydroxyindoles, with the aid of reversed-phase HPLC it is even possible to determine the catecholamines in urine directly without preliminary separation ([48], see also [85]).

Other oxidizing agents such as potassium permanganate[21], Ce(IV) sulfate[49–54], chromic acid[56, 57], and periodate[56, 57] find application in the fluorimetric and absorption-spectrometric determination of various organic substances in combination with liquid chromatography (see Table 4). Oxidizing compounds such as hydroperoxides are transformed with sodium iodide; the iodine released is determined photometrically in the through-flow[8]. Redox indicators such as tetrazolium blue and neocuproine are suitable for the analysis of reducing sugars[58, 59].

Carboxylic acids can be detected using acid-base indicators after ion-exchange chromatographic separation[60–62].

Further reagents are listed in Table 4. For chromatographically separated and chemically modified substances one can also use electrochemical detection methods, such as the detection of citrals with semicarbazide[69].

Special reagents and reaction systems have been described for enzyme analysis[70, 71]. In environmental analysis, the enzymatic inhibition of cholinesterase is used as an indication

4. Outlook: Development Trends

Selective chemical reactions with a variable flow-through detector in combination with high-performance separation systems offer the possibility of direct and sensitive analyses of individual substances in complex mixtures such as urine or blood without sample preparation.

Table 4. Examples of (chemical) reaction detector applications.

Reagent	Substance or group of substances	Detection [a]
Ninhydrin	amino acids [18, 23], amines [24, 25], polyamines [26, 27], γ-aminobutyric acid [28]	F, A
Phthalaldehyde	amino acids [29—32], amines [30, 33], catecholamines [33], peptides [34], 5-hydroxyindoleacetic acid [35], *N*-methylcarbamate [36]	F
Fluorescamine	amino acids [29, 37, 38], peptides [39]	F
Pyridoxal	amino acids [40]	F
Ethylenediamine	catecholamines [4, 41, 42]	F
Oxidizing agents		
a) Potassium hexacyanoferrate(III)	catecholamines [43—48]	F
b) Potassium permanganate	thioridazine and metabolites [21]	F, A
c) Cerium(IV) sulfate	arenecarboxylic acids [49—51], carbohydrates [52, 53], phenols [54], 5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxanilide [55]	F, A
d) Chromic acid	hydroxycarboxylic acids [56, 57]	F, A
e) Periodate	hydroxycarboxylic acids [56, 57]	F, A
Sodium iodide	hydroperoxides [8]	A
Tetrazolium blue	sugar [58]	A
Neocuproine	reducing sugars [59]	A
Acid-base indicators	carboxylic acids [60—62]	A
Carbazole	hydroxycarboxylic acids [56, 57], uronic acids [63]	A
Phenol	carbohydrates [64]	A
Sulfanilic acid/*N*-(1-naphthyl)ethylenediamine	nitrosamide [65]	A
7-Chloro-4-nitrobenzofuran (NBD-chloride)	proline, hydroxyproline [66]	F
2,4-Dinitrophenylhydrazine	cyclohexanone [11]	A
Acids (hydrochloric, sulfuric, acetic)	glycosides [20], carbohydrates [67], estrogens [68]	F
Semicarbazide	citral [69]	E
6,6′-Dinitro-3,3′-dithiodibenzoic acid	enzymes [70]	A
p-Nitrophenyl-*p*-guanidinobenzoate	enzymes [70]	A
Lactate/NAD^+	enzymes [70, 71]	A, F
Cholinesterase	organophosphorus compounds, carbamates, insecticides [72, 73]	A
Molybdate	monofluorophosphate [74]	A
4-(2-Pyridylazo) resorcinol (PAR)	metal ions [75, 76]	A
Luminol	metal ions [77—79]	F
Zincon	zinc [80]	
Ce(IV) sulfate	polythionates [81]	

[a] A: absorption measurements; F: fluorescence measurements; E: electrochemical detection.

for organophosphorus compounds, carbamates, and insecticides[72,73].

In inorganic analysis too, reactions after ion-exchange chromatographic separations with molybdate, metal reagents, or even Ce(IV) sulfate find some application[74–81].

The examples set out in Table 4 are not differentiated in terms of classical or modern HPLC in columns. According to *Engelhardt*[82], the borderline between HPLC and classical liquid chromatography is defined by a packing particle diameter greater than 50 μm for the latter. *Snyder* and *Kirkland*[83] characterize modern column chromatography as high-speed or high-performance liquid chromatography with a high separation power and short separation times ranging from a few minutes up to an hour. Further examples of reactions in systems with continuous through-flow in combination with classical column chromatography are given in a monograph by *Foreman* and *Stockwell*[84].

Examples of such applications of reaction detectors have been described, among others, for carbohydrates in urine and serum[52], for free proline and hydroxyproline in serum[66], and for free epinephrine and norepinephrine in urine[48] (Fig. 3). Further examples are the direct determinations of dopamine and serotonin in brain homogenates by reversed-phase chromatographic separation and reaction with phthalaldehyde (Fig. 4) (see also [85]).

Such analytical processes, especially when they are used for the trace analysis of organic substances, are mainly effective in reducing problems connected with separation from the material and the stability of the substances or derivatives prepared for the liquid chromatography. Moreover, they shorten the analysis time compared to a process comprising separation, derivatization of the test substance, and chromatographic analysis. Another objective of such systems that combine HPLC and (chemical) reaction detectors is the separation

and determination of as many materials as possible in a single operation. Examples of this are provided mainly by the analysis of amino acids, of carbohydrates, and of metallic ions, which are derivatized by means of group reagents and thereby determined all together after a chromatographic separation (see Table 4). The precondition for the applicability of this process

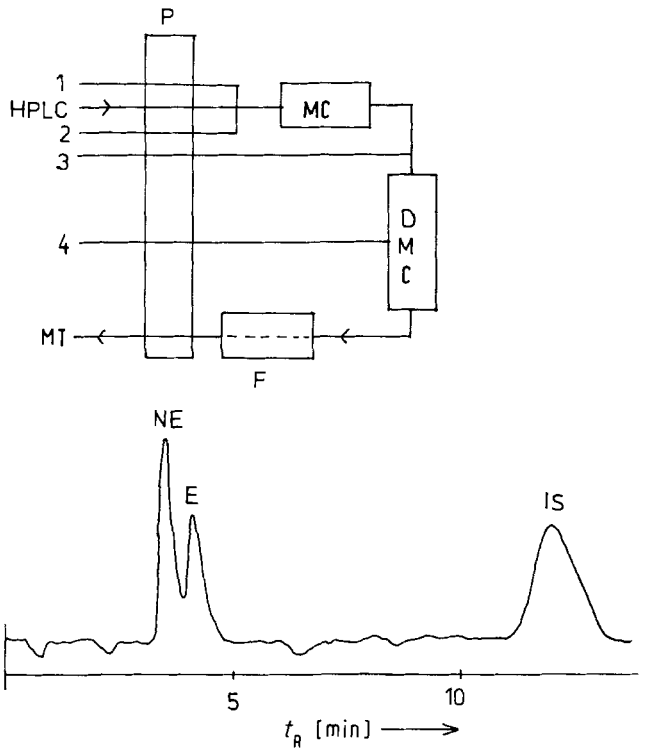


Fig. 3. Direct determination of epinephrine (E) and norepinephrine (NE) in 200 µl of urine by a combination of reversed-phase chromatography (column: LiChrosorb RP 18, mobile phase: 0.05 M phosphate buffer pH 3, flow rate: 1.5 ml·min^{-1}, pressure: 60 bar) with a (chemical) reaction detector. IS denotes internal standard.
Flow diagram: 1: Oxidizing solution: 0.3 M formate buffer pH 4/0.1 M boric acid/0.1 % potassium hexacyanoferrate(III)/2·10^{-3} % copper acetate (tube: d_i 0.76 mm); 2: Air (tube: d_i 1.42 mm); 3: Reducing solution: 5 % mercaptoethanol in water/20 % sodium sulfite in water/10 M caustic soda, proportions by volume 1:1:1 (tube: d_i 0.76 mm); 4: 4 M acetic acid/4 % boric acid (tube: d_i 1.14 mm); MT: Main tube d_i 1.85 mm; P: Peristaltic pump, F: Fluorimeter (excitation wavelength 405 nm, fluorescence-edge filter 450 nm, sensitivity 0.03 µA/full scale); MC: Mixing coil, DMC: Double mixing coil (d_i 2.4 mm). Urine sample: 14.5 ng epinephrine/ml and 59 ng norepinephrine/ml (corresponding to 2.9 ng epinephrine and 11.8 ng norepinephrine in the column).

is a selective chromatographic system with a high separating efficiency. Thanks to developments in modern liquid chromatography, the analysis time in the case of amino acids has been reduced from over 12 h[22] to less than 1 h[38].

Moreover, with the systems described, the accuracy of analytical results can be checked, as can be seen from the following example:

For the analysis of biogenic amines in biological material, interference-free analytical processes combining separation and enrichment processes (ion exchange, liquid-liquid partition) with selective chemical reactions have been developed. Considering the example of serotonin, HPLC and chemical reaction with fluorimetric measurement after the separation have shown that with urine samples the separation processes with *n*-butanol usually used for brain specimens give erroneous (high) values. In the chromatogram alongside the

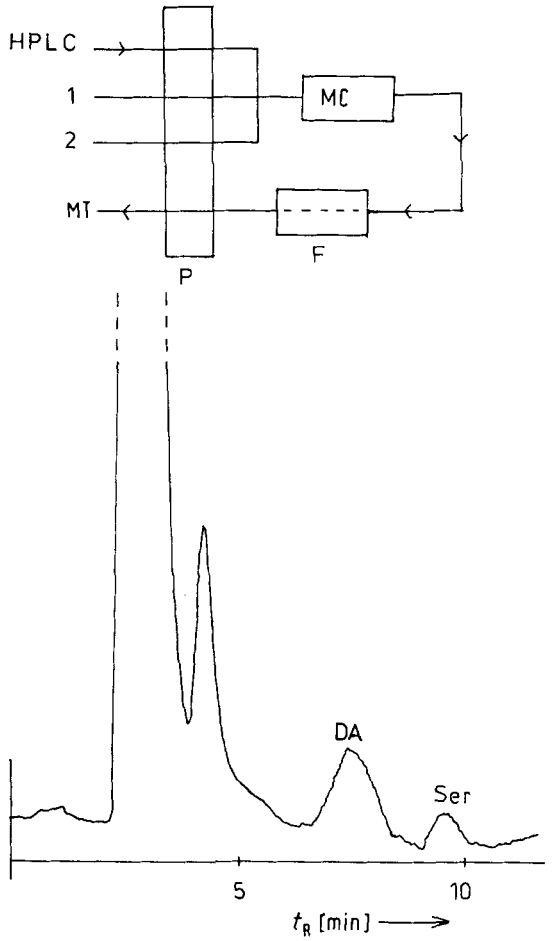


Fig. 4. Direct determination of dopamine (DA) and Serotonin (Ser) in 50 µl of brain homogenate (1.5 g of rat brain homogenized in 10 ml of 0.1 N hydrochloric acid) by a combination of reversed-phase chromatography (column: Li-Chrosorb RP 18, mobile phase: 20 % methanol in an aqueous solution of 0.4 M acetic acid/boric acid pH 3.2, flow rate 1.2 ml·min^{-1}, pressure: 80 bar) with a (chemical) reaction detector.
Flow diagram: 1: Reagent: phthalaldehyde, 0.02 wt-%/0.05 vol-% mercaptoethanol in 0.2 M borate buffer pH 9 (tube: d_i 0.76 mm); 2: Air (tube: d_i 0.76 mm); MT: Main tube (d_i 1.14 mm); P: Peristaltic pump; F: Fluorimeter (excitation wavelength 365 nm, fluorescence edge filter 450 nm, sensitivity: 0.3 µA/full scale); MC: mixing coil.

serotonin signal a further signal was recorded, which is measured as serotonin when no separation has been performed, in spite of the selective reaction (with phthalaldehyde in hydrochloric acid at 80 °C)[86].

Received: May 23, 1978 [A 261 IE]
German version: Angew. Chem. *91*, 192 (1979)
Translated by AD-EX (Translations) Ltd., London.

[1] *R. P. W. Scott:* Liquid Chromatography Detectors. Elsevier, Amsterdam 1977.
[2] *J. F. Lawrence, R. W. Frei:* Chemical Derivatization in Liquid Chromatography. Elsevier, Amsterdam 1976.
[3] *M. S. F. Ross*, J. Chromatogr. *141*, 107 (1977).
[4] *G. Schwedt*, Chromatographia *10*, 92 (1977).
[5] *L. R. Snyder*, J. Chromatogr. *125*, 287 (1976).
[6] *I. Halász, P. Walkling*, Ber. Bunsenges. Phys. Chem. *74*, 66 (1970).
[7] *R. P. W. Scott, P. Kucera*, J. Chromatogr. Sci. *9*, 641 (1971).
[8] *R. S. Deelder, M. G. F. Kroll, J. H. M. van den Berg*, J. Chromatogr. *125*, 307 (1976).
[9] *L. R. Snyder, H. J. Adler*, Anal. Chem. *48*, 1017 (1976).
[10] *L. R. Snyder, H. J. Adler*, Anal. Chem. *48*, 1022 (1976).
[11] *R. S. Deelder, P. J. H. Hendricks*, J. Chromatogr. *83*, 342 (1973).
[12] *J. Hrdina:* 6th Colloquium in Amino Acid Analysis. Technicon Monograph *3*, 87 (1968).

[13] R. D. Begg, Anal. Chem. 43, 854 (1971).
[14] R. E. Thiers, R. R. Cole, W. J. Kirsch, Clin. Chem. 13, 451 (1967).
[15] W. H. C. Walker, G. A. Pennock, G. K. McGowan, Anal. Chim. Acta 27, 421 (1970).
[16] I. Halász, H. D. Gerlach, A. Kroneisen, P. Walkling, Z. Anal. Chem. 234, 97 (1968).
[17] J. F. K. Huber, J. A. R. J. Hulsman, Anal. Chim. Acta 38, 305 (1967).
[18] K. M. Jonker, H. Poppe, J. F. K. Huber, Chromatographia 11, 123 (1978).
[19] R. W. Frei, L. Michel, W. Santi, J. Chromatogr. 142, 261 (1977).
[20] J. C. Gfeller, G. Frey, R. W. Frei, J. Chromatogr. 142, 271 (1977).
[21] R. G. Muusze, J. F. K. Huber, J. Chromatogr. Sci. 12, 779 (1974).
[22] D. H. Spackman, W. H. Stein, S. Moore, Anal. Chem. 30, 1190 (1958).
[23] G. Ertringshausen, H. J. Adler, A. S. Reichler, J. Chromatogr. 42, 355 (1969).
[24] H. Hatano, K. Sumizu, S. Rokushika, F. Murakami, Anal. Biochem. 35, 377 (1970).
[25] P. Vandkerckhove, H. K. Henderickx, J. Chromatogr. 82, 379 (1973).
[26] H. Adler, M. Margoshes, L. R. Snyder, C. Spitzer, J. Chromatogr. 143, 125 (1977).
[27] C. W. Gehrke, K. C. Kuo, R. L. Ellis, J. Chromatogr. 143, 345 (1977).
[28] C. E. Vandercook, R. L. Price, J. Assoc. Off. Anal. Chem. 57, 124 (1974).
[29] J. R. Benson, P. E. Hare, Proc. Nat. Acad. Sci. USA 72, 619 (1975).
[30] J. R. Cronin, P. E. Hare, Anal. Biochem. 81, 151 (1977).
[31] M. Roth, A. Hampai, J. Chromatogr. 83, 353 (1973).
[32] M. Roth, J. Clin. Chem. Clin. Biochem. 14, 361 (1976).
[33] G. Schwedt, Anal. Chim. Acta 92, 337 (1977).
[34] E. H. Creaser, G. J. Hughes, J. Chromatogr. 144, 69 (1977).
[35] H. H. Brown, M. C. Rhindress, R. E. Griswold, Clin. Chem. 17, 92 (1971).
[36] H. A. Moye, S. J. Scherer, Anal. Lett. 10, 1069 (1977).
[37] A. M. Felix, G. Terkelsen, Arch. Biochem. Biophys. 157, 177 (1973).
[38] K. Zech, W. Voelter, Chromatographia 8, 350 (1975).
[39] R. W. Frei, L. Michel, W. Santi, J. Chromatogr. 126, 665 (1976).
[40] M. Maeda, A. Tsuji, S. Ganno, Y. Onishi, J. Chromatogr. 77, 434 (1973).
[41] A. Kojima-Sudo, Ind. Health 12, 153 (1974).
[42] K. Mori, Jap. J. Ind. Health 17, 170 (1975).
[43] A. Kojima-Sudo, Ind. Health 11, 105 (1973).
[44] A. Kojima-Sudo, Ind. Health 13, 69 (1975).
[45] K. Mori, Jap. J. Ind. Health 17, 116 (1975).
[46] K. Mori, Ind. Health 12, 171 (1974).
[47] G. Schwedt, J. Chromatogr. 143, 463 (1977).
[48] G. Schwedt, Z. Anal. Chem. 293, 40 (1978).
[49] S. Katz, W. W. Pitt, Anal. Lett. 5, 177 (1972).
[50] S. Katz, W. W. Pitt, G. Jones, Clin. Chem. 19, 817 (1973).
[51] S. Katz, W. W. Pitt, J. E. Mrochek, J. Chromatogr. 104, 303 (1975).
[52] S. Katz, S. R. Dinsmore, W. W. Pitt, Clin. Chem. 17, 731 (1971).
[53] S. Katz, W. W. Pitt, J. E. Mrochek, S. Dinsmore, J. Chromatogr. 101, 193 (1974).
[54] A. W. Wolkoff, R. H. Larose, J. Chromatogr. 99, 731 (1974).
[55] A. W. Wolkoff, F. I. Onuska, M. E. Comba, R. H. Larose, Anal. Chem. 47, 754 (1975).
[56] B. Carlsson, T. Isaksson, O. Samuelson, Anal. Chim. Acta 43, 47 (1968).
[57] B. Carlsson, O. Samuelson, Anal. Chim. Acta 49, 247 (1970).
[58] K. Mopper, E. T. Degens, Anal. Biochem. 45, 147 (1972).
[59] M. H. Simatupang, H. H. Dietrich, Chromatographia 11, 89 (1978).
[60] L. Kesner, E. Muntwyler, Anal. Chem. 38, 1164 (1966).
[61] K. W. Stahl, G. Schäfer, W. Lamprecht, J. Chromatogr. Sci. 10, 95 (1972).
[62] R. H. Gaddy, R. S. Dorsett, Anal. Chem. 40, 429 (1968).
[63] S. Johnson, O. Samuelson, Anal. Chim. Acta 36, 1 (1966).
[64] R. L. Jolley, W. W. Pitt, C. D. Scott, Anal. Biochem. 28, 300 (1969).
[65] G. M. Singer, S. S. Singer, D. G. Schmidt, J. Chromatogr. 133, 59 (1977).
[66] M. Roth, Clin. Chim. Acta 83, 273 (1978).
[67] S. Katz, L. H. Thacker, J. Chromatogr. 64, 247 (1972).
[68] Sj. van der Wal, J. F. K. Huber, J. Chromatogr. 135, 305 (1977).
[69] B. Fleet, C. J. Little, J. Chromatogr. Sci. 12, 747 (1974).
[70] T. D. Schlabach, S. H. Chang, K. M. Goodning, F. E. Regnier, J. Chromatogr. 134, 91 (1977).
[71] R. R. Schröder, P. J. Kudirka, E. C. Toren, J. Chromatogr. 134, 83 (1977).
[72] K. A. Ramsteiner, W. D. Hörmann, J. Chromatogr. 104, 438 (1975).
[73] H. A. Moye, T. E. Wade, Anal. Lett. 9, 891 (1976).
[74] C. Benz, R. M. Kelley, Anal. Chim. Acta 46, 83 (1969).
[75] K. Kawazu, J. S. Fritz, J. Chromatogr. 77, 397 (1973).
[76] K. Kawazu, M. Shibata, H. Kakiyama, J. Chromatogr. 115, 543 (1975).
[77] A. Hartkopf, R. Delumyea, Anal. Lett. 7, 79 (1974).
[78] M. P. Neary, R. Seitz, D. M. Hercules, Anal. Lett. 7, 583 (1974).
[79] W. R. Seitz, W. W. Suydan, D. M. Hercules, Anal. Chem. 44, 957 (1972).
[80] H. Matsui, Anal. Chim. Acta 66, 143 (1973).
[81] A. W. Wolkoff, R. H. Larose, Anal. Chem. 47, 1003 (1975).
[82] H. Engelhardt: Hochdruck-Flüssigkeits-Chromatographie. 2. Edit. Springer, Berlin 1977.
[83] L. R. Snyder, J. J. Kirkland: Introduction to Modern Liquid Chromatography. Wiley-Interscience, New York 1974.
[84] J. K. F. Foreman, P. B. Stockwell: Automatic Chemical Analysis. Wiley, New York 1975.
[85] G. Schwedt, Instrument und Forschung, in press (1979).
[86] M. Angst, Part of Diplomarbeit, Gesamthochschule Siegen 1978.

Structural Chemistry of Fluorides and Oxide Fluorides of Nonmetals

By Konrad Seppelt[*]

The structural features of the nonmetal fluorides and oxide fluorides can now be explained and useful predictions can be made. The same applies in part to the chemistry of this class of compounds. Statements concerning structures can easily be made on the basis of the electron pair repulsion model (VSEPR theory). Some rules for the number of ligands provide structural predictions for larger units than isolated molecules or ions. This is important for the fluorides and oxide fluorides of the heavier elements. This class of compounds has its limits in the lighter noble gases which, even with fluorine, form only weak bonds or no bonds at all.

1. Introduction

The number of research papers on the fluorides and oxide fluorides of the nonmetals runs into thousands. A complete survey of the literature cannot be given in this article—for this the reader may be referred, for example, to specialist review periodicals[1–3]. Here we shall be considering common features in the structural chemistry of this class of compounds.

Simple rules are now known which help us to predict the structures of compounds. If we confine the discussion to the nonmetals, and permit only oxygen and fluorine as ligands, we are in a position to make almost complete structural

[*] Priv.-Doz. Dr. K. Seppelt
Anorganisch-Chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

predictions. These predictions can often be extended to the reactivity of the compounds. In the case of monomeric compounds of types AF_x or AO_xF_y the structure is obtained from the electron pair repulsion model (VSEPR theory; VSEPR = *V*alence *S*hell *E*lectron *P*air *R*epulsion). Although this model is not based on bonding theory considerations (which is actually its strength), all known structures can be explained with its aid and its predictions have been found to be correct. However, in the case of high coordination numbers and other ligands, such as chlorine, the VSEPR model encounters increasing difficulties (cf. Section 2). Nevertheless, cations and anions such as SF_3^+ or $IO_2F_2^-$ fit well into the scheme. With such species complications arise only because of the impossibility of distinguishing between molecular-ionic and bridged-polymeric structures, since the boundary between them is not rigid. Structures in which molecular fragments can no longer be recognized, *i.e.* salts, are of course rare in the class of substances under consideration.

For the first row of the periodic table the octet rule is obeyed. An analogous duodecet rule for the second and possibly even the third rows must, however, be taken with a pinch of salt. Here again modern MO theory best explains the bonding. Although the physical reality is questionable, it is visually attractive to include the d-orbitals in the consideration, particularly in the case of higher-valent fluorides and oxide fluorides[4, 5] (see Section 4).

It is known that only some of the nonmetal fluorides and oxide fluorides exist in the form of monomers. Nothing of strict validity can be said about tendencies to undergo dimerization, oligomerization, and polymerization, but much can be explained by comparisons, and even predictions are possible. An early attempt to elucidate this problem was the formulation of the double-bond rule (only first row elements will form double bonds) which can no longer be used in such a simple form.

2. The Electron Pair Repulsion Model (VSEPR Theory)

This simple model dates back to 1939[6, 7] and was refined in 1957[8]. A detailed description can be found in [9].

According to the VSEPR theory the molecular state of a compound AF_x or AO_xF_y is determined by the repulsion of the bonding and nonbonding valence electron pairs. The electron pairs, and hence the ligands, arrange themselves in such a way that they are as far from one another as possible. Thus definite structures are obtained, such as triangles (BF_3, COF_2), tetrahedra (CF_4, SO_2F_2, NF_3), trigonal bipyramids (PF_5, SF_4, ClF_3), octahedra (SF_6, IF_5, XeF_4), *etc.* In the case of molecules with different ligands the positions with the smallest available space are always occupied by the most highly electronegative ligands. This is particularly important in the case of the trigonal bipyramid. Deviations from ideal bond angles can also be plausibly explained in many cases. The structural properties of the known nonmetal fluorides and of their cationic and anionic derivatives fit into this scheme without any gaps, particularly if sixfold coordination is not exceeded. The same structural predictions can be obtained by simple Hückel approximation calculations[10]; the advantage of the VSEPR method is mainly its didactic simplicity.

The "steric effect of the nonbonding electron pair"—a unique feature of the VSEPR model—decreases with increasing size and increasing number of ligands. This is clear in the case of compounds such as XeF_6, XeF_8^{2-}, or $TeCl_6^{2-}$: in the presence of eight fluorine or six chlorine ligands the free electron pairs cease to have more than a slight steric effect. Thus, the ions $SeCl_6^{2-}$, $TeCl_6^{2-}$, $PoCl_6^{2-}$, $SbCl_6^{3-}$, and $BiCl_6^{3-}$ have an octahedral structure ("sterically inactive s-electron pair"). However, many of these salts show effects that can be explained by a dynamic distortion of the octahedron[11].

The existence of nonrigid transitions here is shown by the series of tellurium chlorides: $TeCl_3^+$ has a pyramidal structure with complete steric activity of the electron pair (and also has three more remote chlorine atoms in the vicinity). Tetrameric $TeCl_4$ has a cubane-like structure and $TeCl_5^-$ is polymeric. In this sequence, tellurium increasingly achieves an octahedral environment by means of six chlorine ligands[12–15]. Finally, $TeCl_6^{2-}$ has an almost or completely octahedral structure[11]. The same transition can be observed in the case of XeF_5^+, XeF_6, and XeF_8^{2-} (see Section 10).

3. Discontinuities in Group-Homologous Compounds

Nonmetals of the first row of the periodic system always have only four orbitals available in the valence shell (*"octet rule"*), which means that the number of ligands and the number of nonbonding valence electrons cannot exceed four. No exceptions to this rule are known[16]. Thus, while the ion NF_4^+ does exist, the hypothetical NF_5 appears to be realized only in the form of $NF_4^+F^-$. *Siebert* pointed out as early as 1953 and *Gillespie* repeated in 1964 that elements of the second and third rows obviously have available only the equivalent of six single bonds[17–19]: the bond orders of the nonmetal-oxygen bonds in the anions PO_4^{3-}, SO_4^{2-}, and ClO_4^- have been calculated as 1.41 (P), 1.52 (S), and 1.48 (Cl).

It seems that a bond order of 1.5 (times 4 = 6 single bonds) is the upper limit for these elements: chlorine cannot achieve the equivalent of seven single bonds. If fluorine is taken in place of oxygen, the situation is still clearer: the ions ClF_6^+ and BrF_6^+ exist, but neither ClF_7 nor BrF_7 has yet been obtained. Thus, six bonds are permitted in the second row, but not seven: AlF_6^{3-}, SiF_6^{2-}, PF_6^-, SF_6, and ClF_6^+ are known.

Exceptions occur in the third row: BrF_6^- and $SeCl_6^{2-}$ exist. It is interesting to note that only SeF_5^- is observed and not SeF_6^{2-}. An explanation is that five fluorine ligands in SeF_5^- imply a strong steric activity of the nonbonding electron pair; here, therefore, the quasi-octahedral arrangement is achieved. Although chlorine is larger than fluorine, because of the greater Se—Cl distance there is more space around the selenium atom, so that a $SeCl_6^{2-}$ species becomes possible. The nonbonding electron pair is supposed to be sterically not very active. For a discussion about BrF_6^-, see Section 9.

In the fourth period of the periodic system the limit of six ligands is finally exceeded: TeF_8^{2-}, IF_7, IF_8^-, and XeF_8^{2-} exist. So far, nine has been found as the maximum number of ligands plus nonbonding electron pairs.

Discontinuities have been observed not only in the maximum coordination number but also in the bond energy, *i.e.* the energy that must be supplied to decompose a gaseous

compound completely into atoms. The bond energy can usually be given accurately for binary compounds.

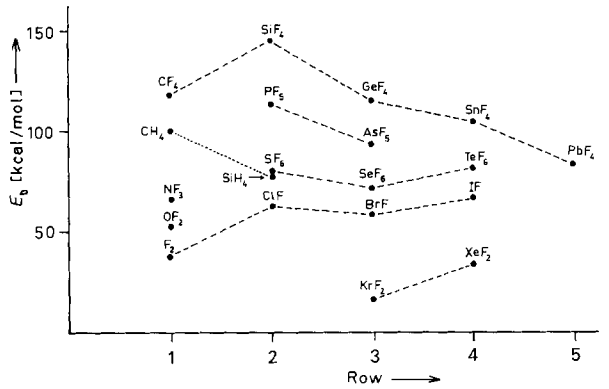


Fig. 1. Mean bond energies E_b of some fluorides (and hydrogen compounds) per bond [20]. The "M" form, with maxima at the elements of the second and fourth period, is characteristic. This is a superposition of size effects (transition-metal contraction, lanthanoid contraction), orbital effects, and increase in metallic character (decrease in electronegativity).

It is appropriate to divide this energy by the number of bonds. If this mean bond energy of some fluorides is plotted in a diagram, the following peculiarities are observed (see Fig. 1): the bond energy passes through two maxima, one at Si, P, S, and Cl, and another—less pronounced—at Sn, Te, I, and Xe. This discontinuity in the bond energy parallels the irregular change in electronegativity (*e.g.* C 2.5, Si 1.7, Ge 2.0, Sn 1.7, Pb 1.8; after *Allred* and *Rochow*).

Some chalcogen fluorides are discussed as examples of further discontinuities. The sensitivity to hydrolysis is found to be $SF_6 \approx SeF_6 \ll TeF_6$. It appears that SF_6 and SeF_6 are similarly insensitive to hydrolysis and the greater instability of SeF_6 must be ascribed simply to its easier reducibility. Thus, SeF_6 is as stable as SF_6 towards concentrated alkali, but not in the presence of I^-[21]. The oxidizing power of the oxo-anions also follows a very irregular sequence: $SO_4^{2-} \ll SeO_4^{2-} > H_4TeO_6^{2-}$. The instability or actual nonexistence of $FOTeF_5$ ($FOSF_5$ and $FOSeF_5$ have long been known) could also be a consequence of atomic size: on attempted synthesis, $FOTeF_5$ decomposed into TeF_6 and $\frac{1}{2}O_2$[22]. By comparison, $FOCF_3$ exists while $FOSiF_3$ does not as yet.

In the series of oxide fluorides F_5SOSF_5, $F_5SeOSeF_5$, and $F_5TeOTeF_5$, the last one shows the greatest bond angle and also the most pronounced shortening of the chalcogen-oxygen bond[23, 24] (see Section 8).

The amine $H_2N—TeF_5$ is less basic than $H_2N—SF_5$, in spite of the lower electronegativity of tellurium[25, 26]. A comparative investigation of the acid strengths of $HOSF_5$, $HOSeF_5$, and $HOTeF_5$ has so far foundered on the corrosiveness of $HOSeF_5$ and the instability of $HOSF_5$[27, 28]. In this connection, mention should be made of the extreme Lewis acidity of the boron compound $B(OTeF_5)_3$[29] in comparison with that of the boron halides. Unfortunately, there are no analogous sulfur and selenium compounds.

The following explanation is offered for these irregular features.

Because of the transition-metal and lanthanoid contraction, the sizes of the atoms change irregularly (see Table 1). The filled d-electron levels just before the elements Ga to Kr and the filled f-electron levels before Hf to Rn lead to a contraction of the atomic volumes.

Table 1. Transition-metal and lanthanoid contraction as shown by the atomic volumes of some main-group elements at 0 K. Volumes in cm^3/g-atom [30].

Mg	Al	Si	P	S	Cl	Ar
13.8	9.9	12.0	black 11.4 violet 13.2 white 15.4	15.0	16.3	23.5
Ca	**Ga**	**Ge**	**As**	**Se**	**Br**	**Kr**
25.6	11.7	13.5	13.0	red 17.2 met. 15.8	19.2	26.5
Sr	**In**	**Sn**	**Sb**	**Te**	**I**	**Xe**
37.0	15.7	tetr. 16.0 gray 20.5	18.1	20.2	24.5	36.0
Ba	**Tl**	**Pb**	**Bi**	**Po**		
37.0	16.0	17.9	21.0	22.4		

Thus, for spatial reasons alone an expansion of the coordination sphere is more difficult for the elements of the third and fifth rows, as compared with those of the elements of the second and fourth rows. The first filling of relatively diffuse 3d- and 4f-orbitals also leads to ineffective screening of the nuclear charge, so that the electrons in the smaller and spherically symmetrical 4s- and 6s-orbitals are bound particularly strongly. Consequently, the oxidation states of five for arsenic and bismuth, six for selenium, and seven for bromine are more unstable than for the group-homologous elements. Indicative of this phenomenon is the fact that the preparation of the perbromates and of arsenic pentachloride was achieved only a few years ago[31–33].

The above-mentioned explanation for discontinuities in group-homologous compounds is a physical reality. Conversely, it is also possible to make the first participation of d- and f-orbitals responsible for the strengthening the bonds of the preceding elements (and not the weakening of the bonds of the following elements; see above). We thus arrive at the bond model of full hybridization.

By means of this model it is possible to explain the properties of the elements Si to Cl by the first appearance of d-orbitals. These can be used to expand the coordination sphere (SiF_6^{2-}) or for a (p→d)π-back bonding (SiF_4). Many peculiarities of Si chemistry, as compared with C chemistry, can be explained in this way; for example, differences in the bond angles or basicities in comparable compounds. (The "reality" of the involvement of d-orbitals will be discussed in Section 4.)

If the abrupt change between the third and fourth rows is to be described by the same bond model, it must be argued that now 4f-orbitals become available for the first time. However, the influence of the f-orbitals has not yet been accurately studied for main group elements. Yet all those arguments which are employed in the dispute concerning the participation of d-orbitals can be used for or against f-orbital involvement. Thus it is conceivable that in a molecule such as TeF_6 because of the high charge of the tellurium, the 4f-orbitals are in an energetically more favorable position than the 5d-orbitals. In an octahedral field, the seven f-orbitals are divided into the classes A_{2u}, T_{1u}, and T_{2u}. In TeF_6, T_{1u}

could give a σ-bond and T_{2u} σ- and π-bonds, while the A_{2u} orbital would be suitable only for a δ-bond. Bonds in more highly coordinated compounds such as TeF_8^{2-} can also be easily explained.

The picture of f-orbital participation must be used with great caution and it should be regarded only as an aid to the understanding of the abruptly changed bonding behavior.

4. Bonding Problems

The participation of d-orbitals in the bonds between main-group elements has received considerable attention in the last twenty years[34-54,61,62]. Some of the arguments have been collected in book form[34]. More precisely, the question is to what extent are d-orbital included in the molecular orbitals of compounds of main-group elements, and how strongly bonding are they? This question is far from physical reality as the description of the total electronic structure of a compound in terms of molecular orbitals is already a simplification. Although no definite judgment can yet be made the following answer may be allowed. The participation of d-orbitals in bonds is very small and becomes appreciable only in compounds that contain the main-group elements in the highest oxidation states[4,5,55]. An indication of d-orbital participation appears to be given by the peculiar structures of F_5SOSF_5 and its homologs[23,24,28] (see Section 8).

The best description of bonding properties is today achieved by using molecular orbitals. This will be shown for the hexafluorides SF_6, SeF_6, and TeF_6. The arrangement of the molecular orbitals with respect to energy has been calculated by several methods. The degree of degeneracy of the orbitals is always obtained from the symmetry of the molecule. However, the MO description is clear only in simple molecules, and in any case it is only a model. Figure 2 shows the MO scheme for SF_6[48]; the arrangement of very close molecular orbitals varies, depending on the method of calculation.

Some check on the calculations is provided by photoelectron spectroscopy, and this method seems to confirm the MO scheme for SF_6, SeF_6, and TeF_6[56,57], assuming the validity of Koopmans' theorem. Figure 2 shows the nonbonding electron pairs at the fluorine atoms ($1e_g$, $1t_{1g}$, $3t_{1u}$, $1t_{2u}$) as well as strong σ-bonds which form the octahedral skeleton ($1a_{1g}$, $1t_{1u}$, $2a_{1g}$, $2t_{1u}$). $1t_{2g}$ and $2e_g$ are weakly bonding; however, it is just these orbitals that contain sulfur 3d-contributions. The d-orbital participation becomes particularly clear in the case of $2e_g$: if no d-character is permitted in the calculation, $2e_g$ lies above $1t_{1g}$[48]. Symmetry requires that $2e_g$ forms a σ-bond and $1g_{2g}$ a π-bond ((p→d)π-back donation).

When the d-orbitals are included in the calculation, the bond becomes less polar. In that respect the expression "back donation" is quite appropriate.

Turning to SeF_6, it is striking that the distance between $2a_{1g}$ and $2t_{1u}$ ("s-p splitting") is substantially greater than that in SF_6; the inadequate screening of the nuclear charge by 3d-electrons is visible here ("transition-metal contraction").

Figure 2 does not show the antibonding orbitals, the lowest of which is probably $3a_{1g}^*$. Since this one is lowered in energy like $2a_{1g}$, the ready reducibility of the selenium compound becomes understandable.

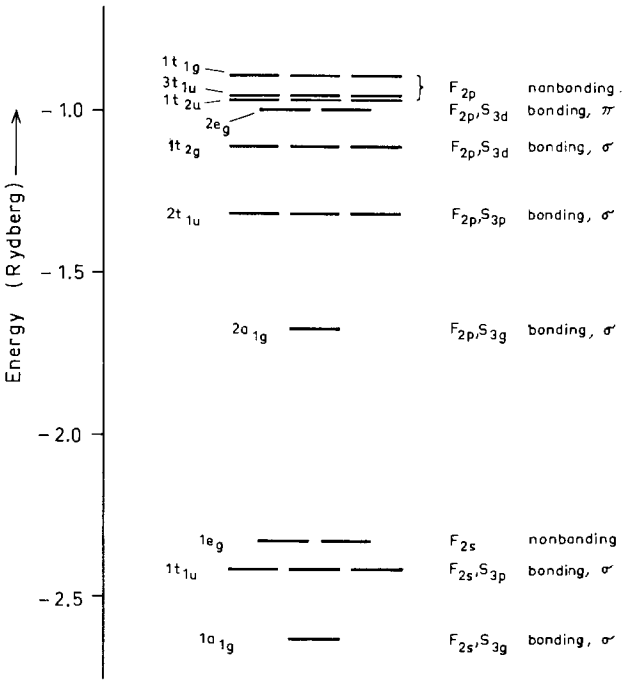


Fig. 2. MO scheme for SF_6 [48]. The figure shows only the occupied orbitals; inner shells (F_{1s}, S_{1s}, S_{2s}, S_{2p}) have been omitted. The distances between the orbitals vary according to the method of calculation; an approximate assignment of the upper orbitals to ionization energies of SF_6 is possible. The main contributions of fictitious atomic orbitals to molecular orbitals are written on the right side. Bonding occurs mainly through $1a_{1g}$, $1t_{1u}$, $2a_{1g}$, and $2t_{1u}$, while $1e_g$, $1t_{2u}$, $3t_{1u}$, and $1t_{1g}$ act as nonbonding electron pairs on the fluorine atoms. A graphical representation of all orbitals, although based on older CNDO calculations omitting the S_{3d} contributions, can be found in [50]. d-Atomic orbitals of sulfur are involved only in $1t_{2g}$ and $2e_g$, and for reasons of symmetry $1t_{2g}$ must be a π-bond [(p→d)π-back-donation] which is energetically lower than $2e_g$ (σ-bond with d-orbital participation).

In TeF_6, the $2a_{1g}$—$2t_{1u}$ distance is normalized again. All the orbitals are now closer together. Taking the 4f-orbitals into account will perhaps enhance this effect still further. However, because of the atomic size of tellurium, the MO calculations must be regarded with great caution.

5. Stability of the Fluorides and the Oxide Fluorides

It can be deduced from the mean bond energies that the bond strengths of the fluorides and oxide fluorides decrease with increasing electronegativity of the central atom (see Fig. 1). The resistance of a compound to decomposition into the elements is also affected by the atomization energies of the elements. The contribution of fluorine (dissociation energy 37 kcal/mol) is the same for all fluorides. The high dissociation energy of oxygen (118 kcal/mol), on the other hand, explains the visibly lower stability of the oxide fluorides and oxides as compared with the pure fluorides. This effect can be seen in the pair XeF_4 (stable) and XeO_4 (explosive). Another example is the decomposition of IOF_5:

$$IOF_5 \xrightarrow{\Delta} IF_5 + \tfrac{1}{2}O_2$$

This reaction clearly demonstrates the high formation tendency of molecular oxygen, which manifests itself in spite of the fact that the I—O bond is stronger than the I—F bond. Since the atomization energy of the noble gases is

zero, XeF_2, XeF_4, and XeF_6 are stable in the presence of one another: reactions such as

$$2\,XeF_2 \rightarrow XeF_4 + Xe$$

therefore have such small heat effects because Xe—F bonds are always approximately equal in strength and the liberation of xenon yields no energy[58]. These reactions are therefore mainly entropy-directed. The case is quite different for the sulfur fluorides: the unstable SF_2 decomposes rapidly into sulfur and SF_4, the driving force being the polymerization energy of the sulfur ($8\,S \rightarrow S_8$)[59]. This phenomenon explains the instability of many fluorides of elements in a lower valence state, such as IF, IF_3, BrF, SF_2, S_2F_2, SeF_2, and Se_2F_2.

6. Bridge Formation and Coordination Problems

CF_4 is a monomer, but under normal conditions CF_2 is a polymer; there are similar pairs, such as IF and $(IF_3)_x$, and SOF_4 and $(TeOF_4)_2$. It is easy to predict approximately whether a given nonmetal fluoride or oxide fluoride will have a monomeric, oligomeric, polymeric, or ionic structure, but accurate predictions are another matter altogether. Furthermore, transitions exist which are observed, in particular, in the case of monomeric molecules with high dipole moments (IF_5). There are also several types of polymeric structures: F-bridged (SbF_5, BrF_3), O-bridged ($Se_2O_2F_{10}$, $I_2O_4F_6$), and central-atom-bridged ($(CF_2)_2$, $(SiF_2)_n$, B_3F_5). Apart from the latter exceptions, the fluorides polymerize through fluorine bridges, while in the case of the oxide fluorides oxygen bridges prevail. However, in the case of the oxide fluorides of the *subgroup* elements fluorine bridges are formed preferentially to oxygen bridges[60].

The weakly interacting molecules found almost exclusively among the fluorides and oxide fluorides of the highest-valent nonmetals are particularly fascinating (see Tables 2 and 3).

Table 2. Weakly interacting fluorides of nonmetals in their highest valence states. Boiling points in °C.

BF_3	−100.4	CF_4	−128.0						
AlF_3	+1272	SiF_4	−95.0	PF_5	−84.0	SF_6	−63.8		
		GeF_4	−36.5	AsF_5	−52.9	SeF_6	−46.6		
		SnF_4	+705	SbF_5	+150	TeF_6	−38.9	IF_7	+4.8
		PbF_4		BiF_5	+550	PoF_6			

Since the replacement of two fluorine atoms by oxygen decreases the coordination number, the weakly interacting monomeric molecules are rarer in the oxide fluorides.

Table 3. Weakly interacting oxide fluorides of nonmetals in their highest valence states. Boiling points in °C.

$(BOF)_3$	COF_2	−83.1	NOF_3	−90.0			
	$(SiOF_2)_n$		POF_3	−39.8	SOF_4	−48.5	
			$(AsOF_3)_n$		$(SeOF_4)_2$		
			$(SbOF_3)_n$		$(TeOF_4)_{2,n}$	IOF_5	<4 XeO_2F_4

Monomeric compounds with central atoms of lower valence frequently have a greatly reduced volatility. The reason for this is a high dipole moment (BrF_5) or dynamic fluorine bridges (SeF_4, XeF_6) (Tables 4 and 5). The transition to fluorine-bridged solids is not rigid, *e.g.*

$$SF_4\ (\text{gaseous}) - SeF_4\ (\text{liquid}) - TeF_4\ (\text{solid})$$

Table 4. Monomeric but strongly interacting fluorides of nonmetals in lower valence states. Boiling points in °C.

$(CF_2)_{2,n}$	NF_3	−129.0						
$(SiF_2)_n$	PF_3	−101.8	SF_4	−40.4	ClF_5	−13.1		
GeF_2	AsF_3	+63	SeF_4	+106	BrF_5	+41.3		
SnF_2	SbF_3	+376	TeF_4		IF_5	+104.5	XeF_6	+75.6
PbF_2	+1293	BiF_3						

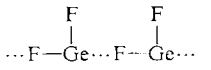
Table 5. Monomeric but strongly interacting oxide fluorides of nonmetals in lower valence states. Boiling points in °C.

CO	−191.5	NOF	−59.9	SOF_2	−43.7	$ClOF_3$	+27 to +29
(SiO)		(POF)		$SeOF_2$	+126	$BrOF_3$	?
(GeO)		$(AsOF)_x$		$(TeOF_2)$		IOF_3	$XeOF_4$ +105

If a molecule is still unknown, its physical properties can be estimated from related compounds. However, care must be taken. Thus, SF_6, SOF_4, and SO_2F_2 and also SeF_6 and even SeO_2F_2 are weak-interaction compounds, but the long-sought $SeOF_4$ appears under normal conditions as the dimer (see Section 8). Fivefold coordination seems to be particularly unfavorable. Accordingly, the dimeric structure of $(IO_2F_3)_2$ was analogous to related selenium and tellurium compounds and was to be expected *a priori*, in contrast to monomeric ClO_2F_3 (see Section 9).

Radical changes in physical properties are most pronounced in the third and fourth groups of the periodic system: thus, BF_3 boils at −100.4 °C and AlF_3 at 1272 °C. CF_4 is such an inert gas that it was possible to detect it as an atmospheric "krypton isotope"[61]. Although SiF_4 and GeF_4 already show a tendency towards expansion of the coordination sphere as in SiF_6^{2-} and GeF_6^{2-}, they are still gases. SnF_4 is the first species to have the structure of a solid with quasi-octahedral environment of the tin by fluorine, as has PbF_4[62].

The difluorides of this group also show interesting transitions. Monomeric CF_2 and SiF_2 are short-lived (SiF_2: 150 s at 0.2 torr)[63]. Both molecules are bent (CF_2 105°, SiF_2 101°)[64–66] and also exist in the isomeric triplet form with two unpaired electrons[67–69]. Polymerization takes place through C—C and Si—Si bonds to give $(CF_2)_n$ and $(SiF_2)_n$. On the other hand, GeF_2 is a fluorine-bridged polymer which can be described approximately as [70]:



The bond angles are in the neighborhood of 90° and the steric activity of the nonbonding electron pair is evident (see Fig. 3). Ge—Ge bonds cannot be detected.

In SnF_2 a highly distorted octahedral environment around the Sn is observed, again with a detectable steric effect of the nonbonding electron pair[71]. PbF_2 exists as a salt (CaF_2 type), with an ionic lattice, where eight fluorine atoms surround each lead atom.

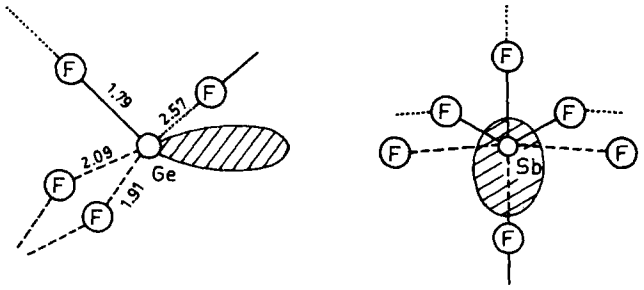


Fig. 3. Solid-state structures of GeF_2 [71] and SbF_3 [91] as examples of the difficulties in the definition of a coordination number. Only one central atom with its coordination sphere is shown. In both cases, the steric effect of a nonbonding electron pair is indicated by hatching. In GeF_2 only one fluorine atom is bound closely to the central atom but still belongs as a bridge to the sphere of another central atom. The environment of the germanium is best described as (distorted) trigonal-bipyramidal. The environment of antimony in SbF_3 is initially pyramidal, as in PF_3, but when three more remote fluorine atoms are taken into account a distorted octahedral arrangement appears.

The structures of GeF_2, and still more that of SnF_2, point out a basic difficulty in the interpretation of crystal structures: it is often impossible to strictly define the environment of the central atom in the form of a coordination number, as it is in the case of molecular compounds and salts. In the lattice the fluorine may occur as a singly bound ligand, as bridge fluorine, and even as a fluoride ion. Depending on the point of view, in GeF_2 and SnF_2 a coordination number of four to five (Ge) or four to seven (Sn) can be given, including the sterically active electron pair in both cases. *Hoppe* has dealt with this general problem in a review[72]. The difficulty of determining the coordination number occurs almost invariably in cationic and anionic derivatives, and particularly seriously in the case of derivatives with heavy elements. Nevertheless, it can be stated that even the more remote coordination sphere is governed by electron-pair repulsion. Nonbonding electron pairs can be detected as free space in the nearer and more distant environment. A well investigated example is, among others, $XeF_3^+Sb_2F_{11}^-$ (see Section 10).

Although there is a very strong double bond in COF_2, no monomeric $SiOF_2$ exists under normal conditions; just as, in general, double bonds of silicon have been detected hitherto only in short-lived intermediates. This appears to be mainly a problem of the coordination sphere: while in POF_3 and SO_2F_2 formal double bonds form without difficulty, since the coordination number remains four, this is not possible in the case of silicon for simple arithmetical reasons. A tetrahedral configuration means either four fluorine ligands (SiF_4) or the formation of oxygen bridges $(-F_2Si-O-SiF_2-O-)_n$. Argumentation by orbital theory is therefore not necessary when the absence of double-bonds at a silicon atom has to be explained. The fact that a similar phenomenon occurs in tellurium (in contrast to sulfur and selenium) with the prohibition of a double bond for the maintenance of the coordination number six (see Section 8) indicates the validity of this argument.

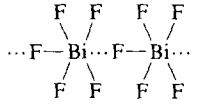
7. Fluorides and Oxide Fluorides of Elements of the Fifth Main Group

NF_5 does not seem to exist, a fact that confirms the octet rule. From the point of view of bonding theory a covalent NF_5 would be conceivable if electron-deficient bonds were permitted. Assuming that the existence of $NF_4^+F^-$ is confirmed[73], this unstable compound is a salt of the NF_4^+ cation[74].

PF_5 is well known; like AsF_5, it has a trigonal-bipyramidal structure[75, 76]. The axial and equatorial bonds are of almost the same length. The axial-equatorial ligand exchange generally takes place the faster, the more equal the bond lengths are; this ligand exchange has been demonstrated by nuclear resonance[77, 78]. In the case of PF_5 and AsF_5 it has not yet been possible to "freeze" this intramolecular fluorine exchange. Ions such as PF_4^+ and PF_6^- are derived from PF_5, while only AsF_6^- is known from AsF_5.

AsF_5, because of its strong Lewis acid character and because of its high volatility, is a valuable reagent in fluorine chemistry. SbF_5, which is probably the strongest Lewis acid, is a high-boiling viscous liquid; NMR investigations have shown that SbF_5 exists in solution as a *cis*-bridged polymer[79–81]. Even in the gaseous state, SbF_5 is still partially polymeric[82–85]. Solid SbF_5, like the ions $Sb_3F_{16}^-$ and $Sb_4F_{21}^-$ in solution, has a *cis*-bridged structure[81, 86], while the salt $Br_2^+Sb_3F_{16}^-$ contains a *trans*-$Sb_3F_{16}^-$ ion[83]. The angles at the bridge fluorine atom vary between 141 and 173°[86–88]. A discussion of the bond angle of fluorine bridges is not profitable.

BiF_5 is a solid, made up of chains of the type[89, 90]:



An exact knowledge of the structure of this fluoride (as also of PbF_4) is important for predicting the properties of the fluorides of polonium, astatine, and radon, which are accessible only with difficulty (see Section 11).

The transitions that have already been described several times appear equally clearly in the case of the trifluorides: NF_3 and PF_3 are pyramidally built gases; AsF_3 is a monomeric liquid whose dipole forces are already sufficient for association, as is frequently the case when nonbonding electron pairs are present at the central atom; SbF_3, a solid, still has the pyramidal structure in the crystal, but already with three additional bridging fluorine atoms which are more distant[91] (see Fig. 3). The Bi atom in BiF_3 is surrounded by eight fluorine atoms, and the free space of the nonbonding electron pair is still visible[92–94]. Many ions are also derived from these trifluorides. The ion $Sb_2F_7^-$ has the form of two axially linked trigonal bipyramids[95], while $Sb_2F_9^{3-}$ consists of two apex-linked octahedra[96] (including the nonbonding electron pairs in each case).

Fluorides of lower molecular weight are known particularly in the case of nitrogen[97]: N_2F_4 exists both in the *trans* and in the *gauche* form[98–101]; even at room temperature it is in equilibrium with $^{\bullet}NF_2$, one of the few stable fluoride free radicals. Fluorine azide N_3F decomposes with formation of N_2 and N_2F_2. The latter exists in *cis* and *trans* forms. Interestingly, the *cis* form is the more reactive and also thermodynamically more stable one[102, 103]. $N{=}NF_2$ is also conceivable[104], but has not yet been isolated. Phosphorus forms P_2F_4[105, 106], which, in contrast to N_2F_4, occurs only in the *trans* form[105, 107], presumably because the small P—P—F

angle in any *cis* or *gauche* form would hinder the fluorine atoms.

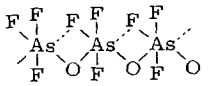
Six nitrogen oxide fluorides have been described: FNO, FNO_2, $FONO_2$, NOF_3, $ONNF_2$, and O_2NNF_2, and some others are also conceivable[108,109]. NOF is of great value as a strong gaseous Lewis base (like AsF_5 as a Lewis acid). The fact that the bonded fluorine is readily given off as F^- is explained directly by the structure of NOF the N—F bond is extremely long (1.51 Å as against 1.36 Å in NF_3), while the N—O bond is extraordinarily short (1.13 Å)[109,110].

NOF_3 is of theoretical importance. It was discovered fairly late[111-113]. The structure can be described formally as $\bar{O}$—$\overset{+}{N}F_3$. However, it must be emphasized that according to the vibrational spectra the molecule has a very strong NO bond; the situation must therefore be explained by hyperconjugation:

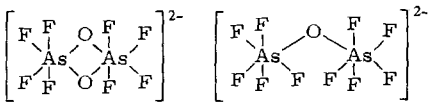
$$O^-—N^+F_3 \leftrightarrow O{=}\overset{+}{N}F_2F^-$$

Indeed, the N—F bonds are weaker than in NF_3. Such problems do not occur in the case of POF_3: the bond to the oxygen can be regarded as a true double bond and the PF bonds in POF_3 (1.52 Å) are actually somewhat shorter than in PF_3 (1.57 Å)[114,115]. It is therefore unnecessary to invoke for POF_3 an ionic-covalent resonance as in NOF_3—formally an indication of the participation of more than four orbitals in the bonds. For a lower phosphorus oxide fluoride with an oxygen bridge, $F_2P—O—PF_2$, cf. [105].

The synthesis of the monomeric $AsOF_3$[116] has not been confirmed. However, it has been possible to obtain polymeric $(AsOF_3)_n$, the structure of which is not yet known in detail[117]. In view of the structures of $(SeOF_4)_2$ and $(TeOF_4)_2$, oxygen bridging should be expected here as well:



This becomes still clearer if the structures of the anions $(AsOF_4)_2^{2-}$ and $F_5AsOAsF_5^{2-}$ are compared[118-120]:



Solution of this problem requires an X-ray structure analysis of solid $(AsOF_3)_n$. Taking into account the marginal existence of monomeric $SeOF_4$, it should perhaps be possible to trap monomeric $AsOF_3$ which, like $SeOF_4$, should polymerize readily. The evidence in favor of a monomeric $AsOF_3$ is the more stable tetrahedral configuration as compared with the trigonal-bipyramid structure of $SeOF_4$. The evidence against its monomeric form is that arsenic is larger than selenium and the polymeric hexacoordination is therefore still more highly favored[*].

The likelihood of monomeric $SbOF_3$ is poor: a polymeric $SbOF_3$ has been obtained[117]. The structural problem is the same as in the case of the arsenic compound—an indication that in the case of the oxide fluorides the similarities between the third and fourth rows are sometimes more pronounced than those between the second and third rows. The anion $(SbOF_4)_3^{3-}$ is trimeric with a ring structure and an octahedral environment around the Sb[121]. It is possible to explain why $(AsOF_4)_2^{2-}$ is dimeric and $(SbOF_4)_3^{3-}$ trimeric. Two forces are in competition: forces of repulsion within a four-membered ring and forces of deformation of the octahedron around As or Sb. Because of its size, antimony can deform the octahedral bond angle—as is necessary for trimerization—more readily than arsenic: a six-membered ring is formed. The smaller arsenic must accept a four-membered ring and the angular deformation of the oxygen in exchange[121].

The anion $F_5SbOSbF_5^{2-}$ has the same structure as the arsenic analogue[121]. Nothing is known about the structure of $BiOF_2$[122]. There are still other oxide fluorides of phosphorus ($F_2PO—O—POF_2$, $(PO_2F)_n$), which all have a tetrahedral structure[123].

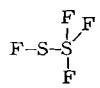
8. Fluorides and Oxide Fluorides of Elements of the Sixth Main Group

The number of fluorides and especially of the oxide fluorides reaches a maximum in the 6th main group. Relatively simple fluorides are formed by oxygen: the certain ones are OF_2 and O_2F_2, and also the radicals OF and O_2F. The existence of O_3F_2 is unclear[124,125], and there is some evidence for the existence of O_4F_2, the dimer of the O_2F radical. O_5F_2 and O_6F_2[126], and also O_3F and O_4F[127], are still less certain; the compounds are said to contain oxygen chains. The synthesis and the properties of the oxygen fluorides have already been reviewed on several occasions[128-130]. The highest formal oxidation state of oxygen so far, +2, has been found in OF_2. However, the existence of $OF_3^+SbF_6^-$ does not appear to be impossible; its formal oxidation number would be +4.

Sulfur fluorides are still more numerous: SF_2, SSF_2, FSSF, FSSSF, FSSSSF, FS—SF_3, SF_4, SF_6, and S_2F_{10}[131]. The general instability of the lower sulfur fluorides has already been explained (see Section 5).

SSF_2 is the sulfur analogue of thionyl fluoride and the existence of two isomers FSSF/S=SF_2 has no parallel in the cases of ClSSCl, HSSH, and ClSSF. These findings have also been confirmed by CNDO calculations[132].

SF_2 has a monomeric structure, and the angle at the sulfur atom (98° 16′)[133] is understandably somewhat smaller than that in OF_2 (103° 4′)[134]. S_2F_4 is not dimeric SF_2, but FS—SF_3, a derivative of SF_4 with the structure:



as has been shown by nuclear magnetic resonance[135,136]. Hindered rotation about the S—S axis is necessary to explain the nonequivalence of the two axial fluorine atoms. A conceivable tetragonal arrangement is probably reserved for the transition state according to the Berry mechanism; FS—SF_3 reacts spontaneously with oxygen to give SOF_2[135].

SF_4 has the expected trigonal-bipyramidal structure with the nonbonding electron pair in the base. Intramolecular fluorine exchange can be frozen out at −20 °C if the last traces

[*] *Note added in proof: A. J. Downs* has presented evidence for monomeric $AsOF_3$ in a matrix: 6th European Fluorine Symposium, Dortmund, 1977.

of HF are eliminated[137]. The ligand exchange takes place strictly by the Berry mechanism[138]. The pentacoordination of SF_4 also determines its chemistry: it converts many oxygen compounds into fluorides with no change in valence; the driving force is the tendency toward the formation of sulfinyl fluoride SOF_2 (with formal tetrahedral configuration). Another variant of the change in coordination is the abstraction of F^- to give SF_3^+ (pyramidal structure) or the addition of F^- to give SF_5^- (with the IF_5 structure).

The kinetic stability of SF_6 can be ascribed to complete screening of the sulfur by the fluorine atoms. Another interesting derivative is $F_5S{-}SF_5$ with a sulfur-sulfur bond, which has no selenium or tellurium analogues so far.

The sulfur oxide fluorides are very numerous (see Table 6). This is because oxygen can form a double bond or a bridge, and because both the tetrahedral and the octahedral arrangements are particularly stable. SOF_4 constitutes the only exception with a coordination number of five. It has a trigonal-bipyramidal structure with the oxygen in an equatorial position. It has not yet been possible to freeze out the intramolecular fluorine exchange. Derivatives such as $SOF_3^+SbF_5^-$ and $Cs^+OSF_5^-$ are known. The anion OSF_5^-, like the homologs $OSeF_5^-$ and $OTeF_5^-$, contains a strong oxygen-sulfur bond which is best explained by ionic-covalent resonance (hyperconjugation)[140-142]. In general, hyperconjugation appears to be possible as an explanation if a double bond is implied.

The noteworthy feature is that the axial fluorine atom, especially in OSF_5^- and $OSeF_5^-$, and to a smaller extent in $OTeF_5^-$, accepts the bulk of the negative charge, and the middle resonance form is therefore particularly important: *trans* effect in the octahedron.

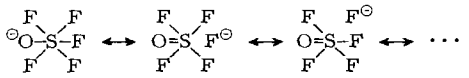


Table 6. Oxide fluorides of hexavalent sulfur [139]. CN = coordination number.

CN	
4	SO_2F_2, FSO_2OSO_2F, $FSO_2(OSO_2)_nOSO_2F$, $FOSO_2F$, FSO_2OOSO_2F, $FOOSO_2F$
5	SOF_4
6	$FOSF_5$, F_5SOSF_5, F_5SOOSF_5, $F_5S{-}OSF_4{-}OSF_5$ (*cis*), $SF_5{-}OSF_4{-}OOSF_5$, $SF_5{-}OSF_4{-}OOSF_4{-}OSF_5$
4+6	FSO_2OSF_5, $F_5SOSO_2OSF_5$, $FSO_2{-}OSF_4{-}OSO_2F$ (*cis*)

The $O{-}SF_4{-}O$ grouping, or in general the $X{-}SF_4{-}X'$ grouping, may occur in the *cis* or the *trans* form. No systematic explanation can yet be given, although there are many examples[143-147]. Any explanation should take into account both the thermodynamic stabilities and the kinetically controlled modes of formation. Thus, it is striking that the radical mode of formation leads predominantly to *cis* systems[148]. The intermediate radical $X{-}O{-}SF_4^{\bullet}$ exists and reacts only in the *cis* form (see Section 12). Most systems with sulfur as the central atom behave similarly. For example, *cis*-$F_5S{-}OSF_4{-}OSF_5$ arises by a radical mechanism[139], while the mode of formation of the homologous *cis*-$F_5Se{-}OSeF_4{-}OSeF_5$ has not yet been elucidated but is presumably not radical[149]. The *trans* isomers of these two compounds are unknown, while the two isomeric tellurium compounds *cis*- and *trans*-$F_5Te{-}OTeF_4{-}OTeF_5$ are produced together by a radical mechanism. These do not undergo rearrangement even at elevated temperatures[150,151]. However, in the case of nucleophilic substitution in TeF_5X to give TeF_4XX' a preferred *cis* orientation has been found[152-154].

Lower selenium and tellurium fluorides have not as yet been reported[*]. Fluorine analogues of the subchlorides, subbromides, and subiodides of tellurium have not yet been found either[155,156].

In contrast to SF_4, SeF_4 is a high-boiling liquid. Fluorine bridges certainly exist. It has been possible to freeze out the fluorine exchange at $-140°C$ and to detect the SeF_4 in dilute solution as a monomer. Thus the SF_4-analogous structure was unambiguously demonstrated[157,158]. SeF_4 forms SeF_3^+ and SeF_5^-; salts of this anion are clearly more stable than SF_5^- salts.

The oxide fluorides of selenium show some special features: coordination numbers smaller than six are rare. $SeOF_4$ exists as a monomer, and the structure is probably the same as that of SOF_4[159,160]. Above $-100°C$, $SeOF_4$ dimerizes to $F_4SeO_2SeF_4$, the structure of which is derived from that of SeF_6 by the edge linkage of two octahedra[160-162], in the same way as $F_5SeOSeF_5$ arises by the apex-linkage of two octahedra[163,164].

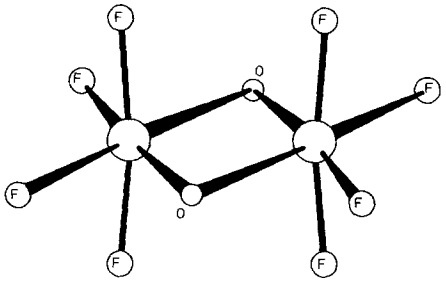


Fig. 4. Molecular structure of $F_4SeO_2SeF_4$ (and $F_4TeO_2TeF_4$), as determined by electron diffraction [162]. In spite of the proximity of the two chalcogen atoms a transannular bond is unlikely.

The dimer $Se_2O_2F_8$ soon became a model substance for other oxide fluorides such as $Te_2O_2F_8$ and $(IO_2F_3)_2$; in addition, the anion $As_2O_2F_8^{2-}$, which has the same structure, was already known. Four-membered ring units of this type appear to occur more frequently than is generally assumed. The long-known salt $K_3Se_2O_6H_3F_2$ also probably has the same type of structure[165]. In fluorine-free systems this structural principle is realized in the anions $[Te_2O_8(OH)_2]^{6-}$ and $[I_2O_8(OH)_2]^{4-}$[166,167].

SeO_2F_2 has the same tetrahedral structure as SO_2F_2, but not its chemical resistance. Already with HF the coordination sphere is enlarged to $HOSeF_5$[168,176].

The other selenium oxide fluoride with a formal tetrahedral structure is $SeOF_2$. Strong dipole forces and fluorine exchange raise the boiling point to 125°C (SOF_2: $-40°C$).

Other oxide fluorides of selenium with an octahedral structure are $F_5SeOOSeF_5$, *cis*-$F_5Se{-}OSeF_4{-}OSeF_5$, $FOSeF_5$, and $F_5SeO{-}SeO{-}OSeF_5$[149,161,162,169-171].

In the chemistry of tellurium the octahedral structure dominates completely. According to the crystal structure analysis, TeF_4 consists of TeF_4 units with steric activity of the nonbonding electron pair linked in the form of chains, and thereby reaches a quasi-octahedral environment around

[*] *Note added in proof: A. Haas* and *H. Willner* report the matrix isolation of unstable SeF_2, Se_2F_2, and FSeSeF: Z. Anorg. Allg. Chem., in press.

Te[172]. Monomeric TeF_4 with an SF_4-type structure has been detected only in a matrix[173]. Steric activity of the nonbonding pair of electrons is also found in the anion TeF_5^-, which, moreover, is a good example of the orientation of even the more remote coordination sphere according to the electron pair repulsion model[174, 175].

TeF_6 is a relatively inert gas, but by no means as resistant to hydrolysis as SF_6 and SeF_6. The hydrolysis takes place in steps[152, 176]. TeF_6 can widen its coordination sphere, forming TeF_7^- and TeF_8^{2-}. These ions probably have pentagonal-bipyramidal and square-antiprismatic structures, respectively[177, 178]. No Te_2F_{10} (with the structure of S_2F_{10}) has so far been reported: the fraction arising by the fluorination of Te/TeO_2 has proved to be $F_5TeOTeF_5$ with a certain amount of $F_5TeOOTeF_5$[22, 179, 180].

All oxide fluorides of tellurium are derived from the octahedral structure (see Table 7 and Figs. 4 and 5). Doubly-bonded oxygen has never been observed here. Hexavalence and hexacoordination alone are responsible for the diversity of the chemistry of purely covalent tellurium compounds.

Table 7. Tellurium oxide fluorides [151].

$F_5TeOTeF_5$	$FTe(OTeF_5)_5$
$F_5TeOOTeF_5$	$Te(OTeF_5)_6$
$F_4TeO_2TeF_4$	$(TeOF_4)_n$
	$Te_6O_5F_{26}$
	$Te(OTeF_5)_4$
trans-$F_5Te{-}OTeF_4{-}OTeF_5$	
cis-$F_4Te(OTeF_5)_2$	
trans-$F_2Te(OTeF_5)_4$	
cis-$F_2Te(OTeF_5)_4$	

The oxygen bridge angle in the oxide fluorides of hexavalent tellurium (with the exception of $F_4TeO_2TeF_4$) is very constant and large—in $F_5TeOTeF_5$ it is 145.5°[23, 24]—but only slightly larger than in $F_5SeOSeF_5$ (142—143°). Since, in spite of steric problems, neighboring fluorine atoms on different chalcogen atoms coincide and the chalcogen-oxygen bonds appear shortened, a possible explanation is $(p\rightarrow d)\pi$ back-donation, which is strongest in the case of $F_5TeOTeF_5$.

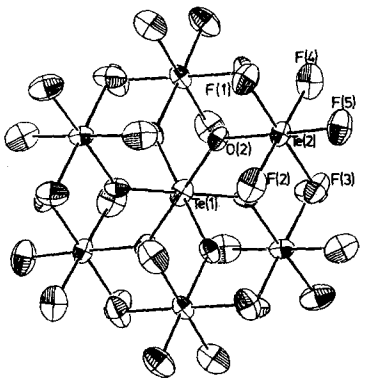
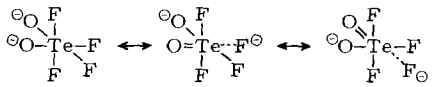


Fig. 5. Crystal structure of $Te(OTeF_5)_6$ [151]. The octahedral environments of the central and peripheral tellurium atoms yield a perfectly screened structure. As a result this oxide fluoride is chemically as inert as TeF_6.

In *trans*-$F_2Te(OTeF_5)_4$ and $Te(OTeF_5)_6$[151, 181, 182] the angle at the oxygen atom is also $139\pm1°$. As in the case of $F_5TeOTeF_5$, this large angle is not caused by steric hindrance.

Monomeric $TeOF_4$ (with doubly-bonded oxygen) does not appear to exist; only the dimer $F_4TeO_2TeF_4$ or a polymer $(TeOF_4)_n$ is observed[29, 160, 183]. However, it is useful to assume formally doubly-bonded oxygen in the form of hyperconjugation in anions such as $TeOF_5^-$ and $TeO_2F_4^{2-}$. The *cis* arrangement of the oxygens in $TeO_2F_4^{2-}$ is best explained by the assumption that a shift of the negative charge to fluorine atoms in the *trans* position is possible only in the *cis* anion[152, 160, 184]. (The electron pair repulsion theory in fact



predicts the *trans* arrangement for the $TeO_2F_4^{2-}$ anion.) On the other hand, $TeOF_4^{2-}$ again has the expected $XeOF_4$-analogous structure[185].

The prohibition of a double bond in hexavalent tellurium must also be regarded as being analogous to prohibition of a double bond on silicon: a double bond leads to a decrease in the size of the coordination sphere (five ligands in the case of "$TeOF_4$", three ligands in the case of "$SiOF_2$") and this decrease appears to be difficult or impossible. Double bonds are easily formed when the favorable coordination number remains six (IOF_5, XeO_2F_4).

9. Fluorides and Oxide Fluorides of Elements of the Seventh Main Group

Among the halogen fluorides and oxide fluorides the wealth of structures decreases. In particular, compounds with oxygen bridges occur only rarely (exceptions are $O_3ClOClO_3$ and $(IO_2F_3)_2$).

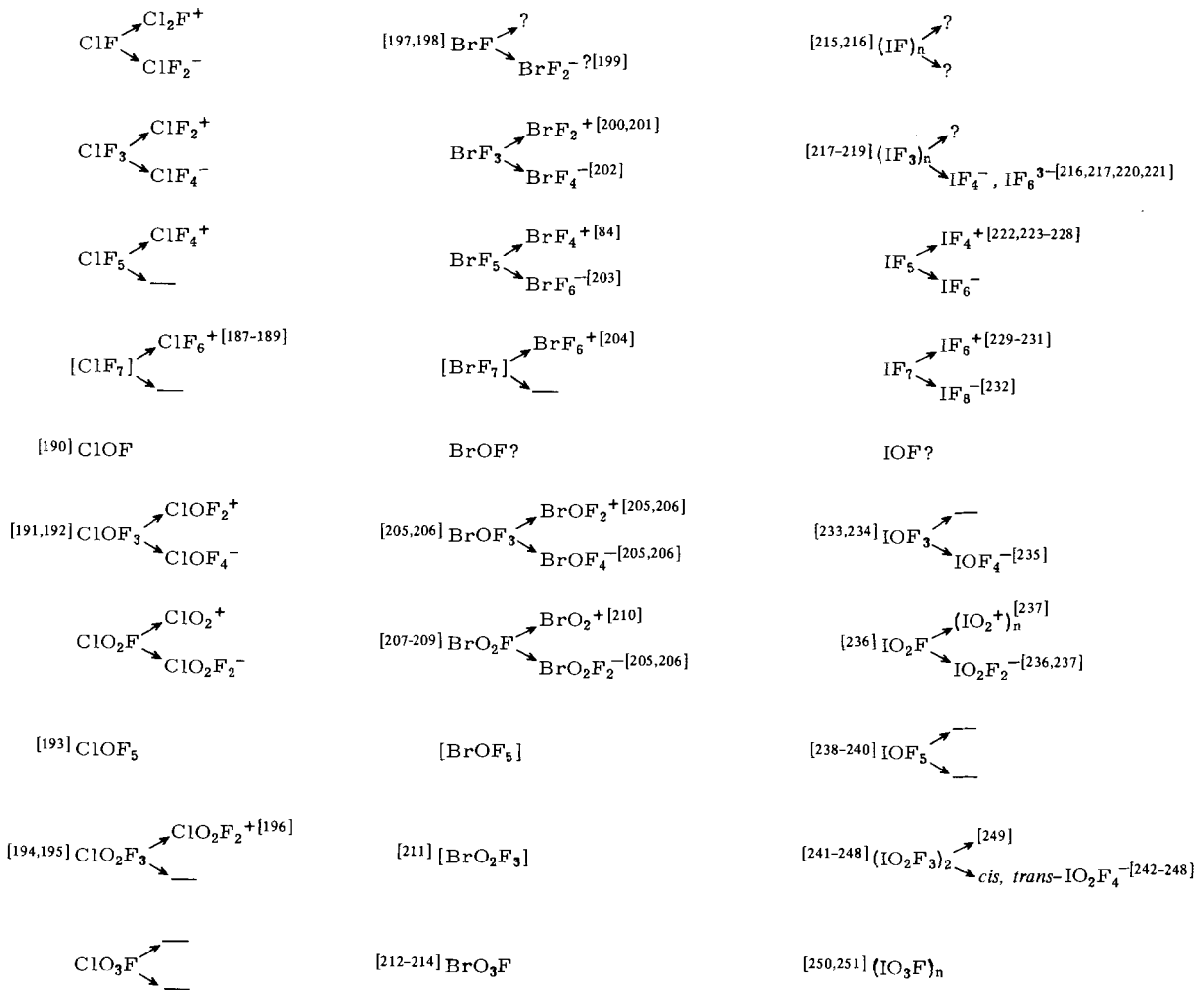
On the other hand, oxidation states of 1 to 7 are now possible, so that the number of compounds is again large (see Table 8). In their structural relationships all the compounds obey the VSEPR theory—an astonishing success of this method. Cationic or anionic derivatives of most of the compounds are known (see Table 8).

Chlorine, bromine, and iodine form fluorides of the types XF, XF_3, and XF_5, and iodine also forms IF_7. ClF is the best source of partially positive chlorine and is therefore gaining increasing importance for preparative chemistry. However, pure Cl^+ does not occur. Thus, ClF reacts with fluoride acceptors not to form $Cl^+SbF_6^-$, but $Cl_2F^+SbF_6^-$[252, 253]. The cation Cl_2F^+ is unsymmetrical and bent:

ClF_5, first discovered in 1963[254], appears to be coordinatively saturated as is indicated by the low boiling point[255]. It liberates a fluoride ion to give ClF_4^+[256, 257], but in contrast to BrF_5 and IF_5 it does not form ClF_6^-. If ClF_7 (and BrF_7) is ever prepared, it may not have a pentagonal-bipyramidal structure as does IF_7[258]. Only the octahedral cation ClF_6^+ is known[187–189].

Chlorine oxide fluorides have been well investigated but not exhaustively. ClOF probably exists only as an unstable species[190], while ClO_2F is the first detectable hydrolysis

Table 8. Fluorides and oxide fluorides of the halogens [186].



product of the chlorine fluorides[259]. $ClOF_3$ like ClF_5, was discovered not long ago[191,192]. The controversy concerning its structure has now been resolved in favor of the expected quasi-trigonal-bipyramidal structure with one fluorine atom, the oxygen atom, and the nonbonding electron pair in the base[260].

The chemical properties of ClO_3F are unexpected. It shows substantial kinetic resistance to hydrolysis; however, it has been possible to replace the fluorine atom. Also $ClOF_5$ has been reported[193], even though a strict proof of its existence is still lacking[186]. The nuclear magnetic resonance spectrum of $ClOF_5$ cannot be predicted with certainty. Because of the almost octahedral structure of the molecule, a considerable line broadening by quadrupole relaxation, as in ClO_3F, is conceivable. The preparation of $ClOF_5$ in a pure state is desirable because it stands in a similar relationship to the well-known IOF_5 as does NOF_3 to POF_3 (see Section 7). The chlorine-oxygen bond is probably strengthened at the expense of the axial fluorine-chlorine bond.

ClO_2F_3 and its cation $ClO_2F_2^+$ have been thoroughly studied[194-196]. To prepare ClO_2F_3 or its cation, ClO_2F must be fluorinated with PtF_6. The anion $ClO_2F_4^-$ does not appear to be stable[195,196].

The nature of the unstable blue, violet, and green reaction products of O_2F_2 with ClF (or BrF_3 or SF_4) is still obscure. They are probably radical oxygen-fluorine compounds[261-264].

The bromine fluorides are thermodynamically more stable than the chlorine fluorides, but BrF cannot be obtained in a pure state because it decomposes into bromine and bromine trifluoride[197,198].

BrF_3, a high-boiling yellow liquid, is also strongly bridged in the liquid state. In contrast to ClF_3 and SeF_4 it has not yet been possible to freeze the fluorine exchange out by a suitable choice of the solvent; only one signal is always found. On the other hand, fluorine exchange ("self-dissociation") makes BrF_3 a good solvent that in a broader sense can be included among the "water-like solvents". The same applies to IF_5, SeF_4, and XeF_6.

As a quasi-octahedral molecule, BrF_5 gives up a fluoride ion only with difficulty and forms $BrF_4^+Sb_2F_{11}^-$; fluoride acceptors other than SbF_5 are not strong enough. The nonbonding electron pair in the BrF_4^+ cation can be detected because of angular deformation in spite of the presence of two fluorine bridges[88]. It is surprising that BrF_5, in contrast to ClF_5, also accepts F^- to form BrF_6^-[203]. Unfortunately, little is

known about the structure of this anion apart from the fact that it is not an octahedral one. If BrF_6^- does actually exist as an isolated anion with a nonbonding electron pair, this will be the only one of the derivatives described here, in which an element of the third period has a higher coordination number than six. Possibly, however, it represents an adduct, $BrF_5 \cdot F^-$. The BrF_6^- ion is isoelectronic with XeF_6, which in the solid state can also be regarded as $(XeF_5^+F^-)_n$. In any event, a complete crystallographic investigation of $Cs^+BrF_6^-$ would be of great interest.

BrF_5 is important as a strong fluorinating agent that is nevertheless easy to handle because of its low boiling point. Still, it can itself be fluorinated with KrF^+ (or $Kr_2F_3^+$) to the cation BrF_6^+[204]. This fluorination cannot be performed with PtF_6 (which fluorinates ClF_5 to ClF_6^+), which shows once again the difficulty of achieving the heptavalent state of bromine. BrF_6^+ has a strictly octahedral structure. The synthesis of BrF_7 from BrF_6^+ proved impossible; the report of a direct fluorination of BrF_5 to BrF_7 is probably erroneous[265].

The bromine oxide fluorides have not been investigated completely; they appear to be equivalent to those of chlorine. The lower resistance of BrO_3F to hydrolysis may be a coordinative effect of the somewhat larger bromine. There is already a mass-spectroscopic indication of the existence of BrO_2F_3[211]. Since it is a homologue of ClO_2F_3, $(IO_2F_3)_2$, and $(SeOF_4)_2$, it could exist either in the monomeric form (like ClO_2F_3) or as a dimer with two oxygen bridges (like $(IO_2F_3)_2$).

Among the iodine fluorides, IF and IF_3 have been investigated more closely only in the last few years[215-219]. Both are polymerized through fluorine bridges. It is also interesting that the yellow IF_3 first disproportionates into IF_5 and IF, the latter decomposing, in turn, into I_2 and IF_5. From IF_3 are derived not only an IF_4^- but also an IF_6^{3-}[220]; concerning its structure we know so far only that it is not octahedral.

IF_5, the least aggressive halogen fluoride, is a molecular compound. Dipole forces raise the boiling point to 104.5 °C. IF_5 has the well known tetragonal-pyramidal structure, like BrF_5 and ClF_5, the steric activity of the nonbonding electron pair being so great that it displaces the four fluorine atoms in the base appreciably toward the axial fluorine atom[266, 267]; axial and equatorial bonds are of almost the same length. IF_5 readily forms IF_4^+, IF_6^-, and $I_3F_{16}^-$ (see Table 8). IF_6^- is likewise not octahedral and certainly has a less symmetrical structure than BrF_6^-.

IF_7 is a completely unbridged compound. Because of an incomplete measurement of the IR spectrum and the low informative value of the ^{19}F-NMR spectrum, its structure was long disputed. Today it is clear that it has a pentagonal-bipyramidal structure[231, 268, 269]. The axial and equatorial fluorine atoms exchange rapidly even at very low temperatures. Therefore the ^{19}F-NMR spectrum shows no fine structure. The very broad resonance line must be ascribed to coupling with the nuclear spin of the iodine (5/2) which, because of the quadrupole relaxation of the almost spherical IF_7 molecule, leads only to a broadening with a weak structure. The contour of this signal resembles that of ClO_3F and MnO_3F[270]. IF_7 forms a stable cation IF_6^+, which—as expected—shows a distinct ^{129}I-^{19}F coupling sextet in the ^{19}F-NMR spectrum[229-231]. The preparation of IF_8^- was finally achieved in 1974; its structure is still unknown, but it may be a tetragonal antiprism[232]. The solid-state structure of IF_7 should be redetermined. It will be interesting to know how the molecule is arranged in the crystal; it probably does not decompose into $IF_6^+F^-$[271] as does the related species XeF_6 in the solid state.

The ^{19}F-NMR spectra of the iodine fluorides IF_5, IOF_5, IF_7, and IF_6^+ show a clear transition from faster to slower quadrupole relaxation of the ^{127}iodine nucleus:

IF_5: Asymmetric structure → rapid relaxation → sharp lines without ^{19}F-^{127}I coupling, but because of the rigid structure F_{ax}-F_{eq} coupling with corresponding fine structure.

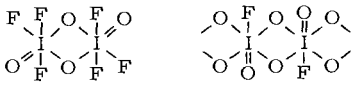
IOF_5: Almost octahedral → slower relaxation → line broadening, $^{19}F_{ax}$-$^{19}F_{eq}$ coupling still visible[238-240, 272].

IF_7: Nonrigid molecule with a (time-averaged) spherically surrounded iodine nucleus → slow relaxation → indication of ^{19}F-^{127}I resolution; because of nonrigidity, no F_{ax}-F_{eq} coupling[272].

IF_6^+: Regular octahedron → very slow relaxation → sharp lines with clear ^{19}F-^{127}I coupling.

With the exception of IOF_5, all iodine oxide fluorides are bridged. The crystal structure of IOF_3[233, 234] still shows molecular IOF_3 units, but at the same time bridges can be observed, so that a coordination number between five and eight may be assumed.

According to the crystal structure analysis, IO_2F_3 is dimeric[241], and the same applies to the compound in the gaseous state[244].

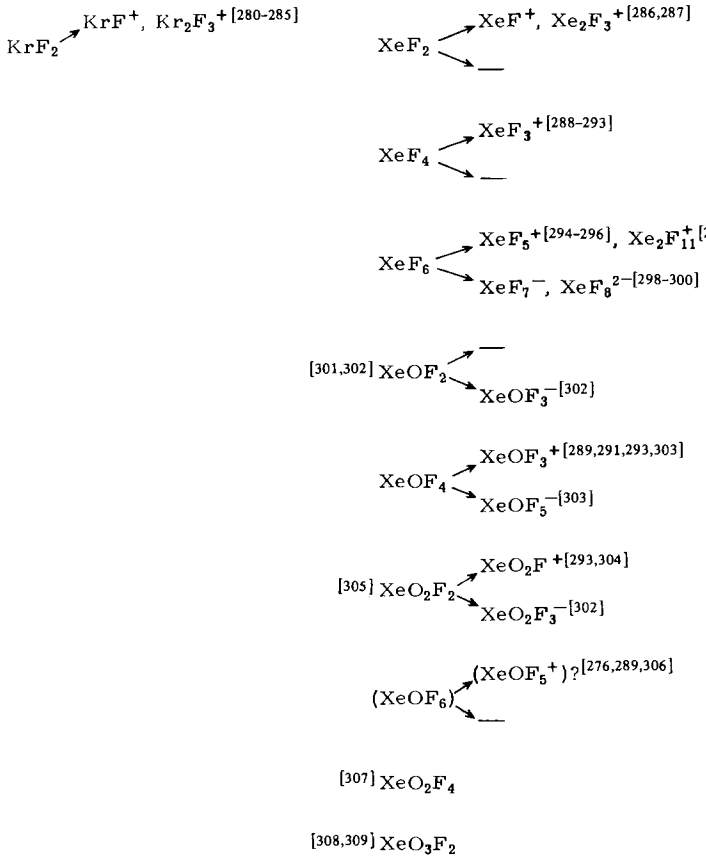


The structure of $(IO_2F_3)_2$ has given rise to much discussion, since the compound was first believed to be monomeric[242, 243], while the nuclear magnetic resonances indicated a trimer[245]. IO_3F[238, 239] probably also has a four-membered ring structure, such as has been proposed for meta-periodic acid[273].

10. Fluorides and Oxide Fluorides of the Noble Gases

The fluorides and oxide fluorides of the noble gases are surprisingly similar in their structural and chemical behavior to the corresponding halogen compounds; hitherto only xenon compounds have been studied extensively. Probably the only accessible argon fluoride would be the cation ArF^+ (perhaps with SbF_6^- as anion)[274]. ArF_2 itself would probably be very unstable. KrF_2 is nowadays easily prepared by a photolysis reaction[275]. KrF_2 and still more its cation KrF^+ are the strongest fluorinating agents known. Thermodynamically, KrF_2 is a fluorinating agent about 13 kcal/mol stronger than elemental fluorine. The use of KrF_2 enabled BrF_6^- and AuF_5 to be prepared for the first time[204, 276]. A report on the detection of KrF_4[277] has proven to be erroneous[278]; likewise krypton-oxygen compounds do not exist; their supposed observation must obviously be ascribed to xenon contamination of the krypton gas used[279].

Table 9. Fluorides and oxide fluorides of the noble gases.



Surprisingly XeF_2 and XeF_4 do not form anions. The hypothetical XeF_3^- will probably be T-shaped[310]. The crystal structures of many xenon-fluorine cations again show the problem of the coordination number in the solid state very distinctly[72]. Compounds of the type $XeF_2 \cdot AF_5$ exhibit all transitions between $F—Xe^+ \cdots AF_6^-$ (ion), $F—\overset{\delta+}{Xe}\cdots\overset{\delta-}{F}\cdots AF_5$ (bridge), and $F—Xe—F \cdots AF_5$ (adduct). The coordination number (including the three nonbonding electron pairs of xenon) thus ranges between four and five. In XeF_3^+ and XeF_5^+ the steric activity of the nonbonding electron pairs is indirectly visible from the the space that is avoided by any F atoms even at relatively large distances from the xenon atom[290,292].

The chemistry of tetravalent xenon has been investigated the least. Pure XeF_4 can now be prepared in quantitative yield by irradiating XeF_6[311]. The oxide fluoride $XeOF_2$ is very unstable; most likely, the oxygen atom forms a bridge instead of a double bond[301,302].

The structure of XeF_6 has roused much controversy. The structure of the gaseous (monomeric) XeF_6 molecule is certainly not octahedral (see Fig. 6a). The most probable structure is one in which the nonbonding electron pair is located on a surface or an edge of an octahedron and correspondingly distorts the octahedral arrangement to C_{3v} and C_{2v} symmetry. These structures interconvert very rapidly with very low potential barriers. Because of this nonrigid arrangement, the xenon is on average in an almost spherical environment. All physical properties are in agreement with this structural model[312]. The other explanation of the structure, in which XeF_6 forms three electronic isomers[313] which are transformed into one another in times reckoned in minutes, can probably be rejected. In the liquid state XeF_6 is fluorine-bridged; XeF_5^+ and XeF_7^- ions certainly occur as intermediates[314]. In dilute solutions in chlorofluorocarbons or similar solvents a tetramer Xe_4F_{24} with equivalent xenon and fluorine atoms is observed (Fig. 6b)[311,315,316]. This is supported by ^{19}F- and ^{129}Xe-NMR spectroscopy and confirmed by measurements on enriched $^{129}XeF_6$[316]. The structure of the tetramer is probably tetrahedral; the magnetic equivalence of 24 fluorine atoms is explained by a rapid rearrangement of all the fluorines in the manner of a cog-wheel mechanism. The cohesion of the tetramer can be explained in terms of flexible fluorine bridges and probably also of

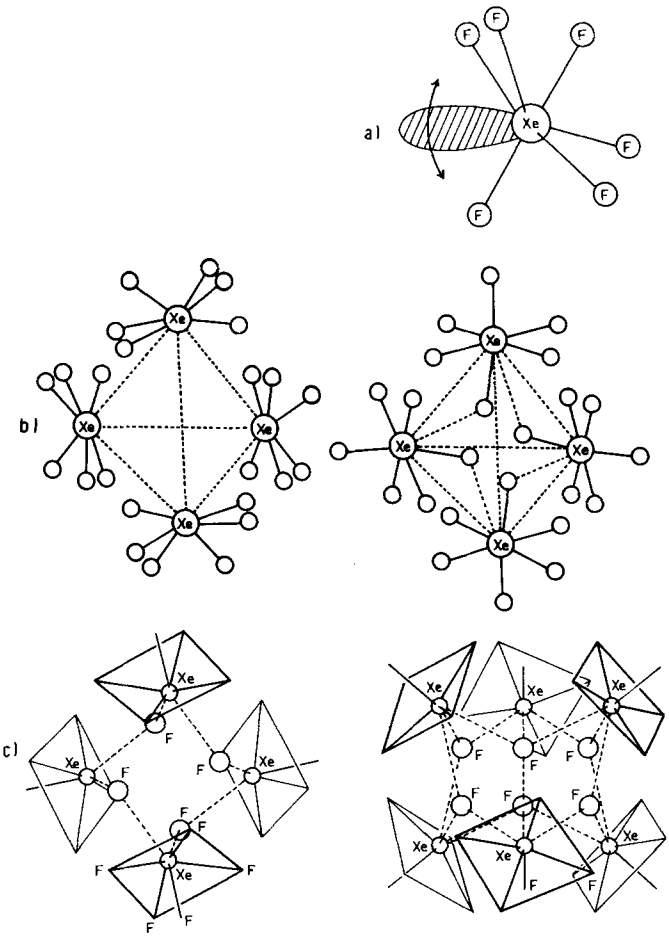


Fig. 6. The structure of XeF_6.
a) In the gaseous state the directed free electron pair moves mainly between a position over a face and over an edge of the dynamically distorted octahedron [312].
b) Tetramerization takes place in non-bridging solvents (CF_2Cl_2, CF_3Cl, SO_2ClF, F_5SOSF_5). The xenon atoms probably form a tetrahedron. The 24 fluorine atoms are all found to be magnetically equivalent. It follows that all the fluorine atoms take part in a rearrangement, but do not leave the sphere of the tetrahedron. The cohesion of the Xe_4F_{24} cluster must be ascribed not only to dynamic fluorine bridges but perhaps also to (weak) xenon-xenon interactions [311, 315, 316]. The high-temperature form of $Rh_4(CO)_{12}$ has a comparable dynamic structure (*F. A. Cotton, C. Kruczynski,* and *B. C. Shapiro,* J. Am. Chem. Soc. *94*, 6191 (1972); *J. Evans, B. F. G. Johnson, J. Lewis, J. R. Norton,* and *F. A. Cotton,* J. Chem. Soc. Chem. Commun. *1973*, 807).
c) Crystal structure of XeF_6. Here the tetrameric Xe_4F_{24} units are frozen out and are best described as $(XeF_5^+F^-)_4$. Hexameric units $(XeF_5^+F^-)_6$ also occur in the cubic modification [318—320].

xenon-xenon interactions. Thus, electron-deficient bonds on the tetrahedral surfaces can be assumed, as in B_4Cl_4, or the problem can be treated according to a simple MO model for four-atom polyhedra[317]. The structure in the liquid state has some correspondence with the crystal structure (Fig. 6c)[318-320]. Four crystalline modifications are known; the cubic one has been investigated in detail[320]. $(XeF_5^+F^-)_4$ and $(XeF_5^+F^-)_6$ units are observed, the xenon atoms occupying the corners of the tetrahedra and octahedra. The other three modifications appear to be constructed of tetrahedral units only. This common tetrahedral unit can be regarded as a frozen cluster of the dynamic liquid structure Xe_4F_{24}. In its complexity, the structure of XeF_6 has no analogues among any of the structures presented in this paper. The steric activity of the free electron pair, dominating in XeF_5^+ and still visible in XeF_6, nevertheless disappears almost completely in XeF_8^{2-}[299]. XeF_8, although reported[321], does not seem to exist[322]; it can be estimated that it would in fact decompose into XeF_6 with liberation of two fluorine atoms, so that any kinetic stability is questionable.

The oxide fluorides of octavalent xenon are also very unstable. The reaction of XeO_4 with XeF_6 gives both XeO_3F_2[308,309] and XeO_2F_4[307]; the latter has been detected only by mass spectroscopy. The cation $XeOF_5^+$, a derivative of the hypothetical $XeOF_6$[289], proved to be the adduct $XeF_5^+ \cdot XeOF_4$[276,306]. The octavalent state of xenon is obviously very difficult to achieve except in the stable perxenates.

11. Fluorides and Oxide Fluorides of Polonium, Astatine, and Radon

Bismuth is followed by three radioactive elements which have been little studied because of their short half-lives. By analogy with tellurium, polonium should form a tetrafluoride and perhaps also a hexafluoride. While a substantially ionic structure may be expected for the tetrafluoride, the hexafluoride, if it exists at all, could exist both in monomeric form and also dimerized or polymerized through fluorine bridges. Because of the high α-activity of all long-lived polonium isotopes, self-decompositions may also be observed (as in the case of plutonium hexafluoride)[323].

^{210}Po, which is readily obtained in a reactor ($t_{1/2}=138$ days) could not be fluorinated to PoF_6[324]. On the other hand, ^{208}Po ($t_{1/2}=2.9$ years) has apparently been fluorinated successfully to give a volatile fluoride, *i.e.* a hexafluoride[325]. Since a relatively stable ^{209}Po ($t_{1/2}=103$ years) can be obtained from bismuth in a cyclotron[326], our knowledge in this field could improve.

The same certainly does not hold for astatine. The longest-lived isotope, ^{210}At, has a half-life of only 8.3 h. If ^{211}At ($t_{1/2}=7.2$ h) is treated with ClF_3, a nonvolatile fluoride is obviously formed, *i.e.* not AtF_7[327]. The stability of the highest valence states apparently falls off steadily in the lowest row of the periodic system: $TlF_3 > PbF_4 > BiF_5 > PoF_6$, as a consequence of the deficient screening by the complete 4f shell (lanthanide contraction). We cannot, therefore, expect an RnF_8. When ^{222}Rn ($t_{1/2}=3.8$ days) is fluorinated under the most diverse conditions, obviously the same radon fluoride is always formed[328], probably RnF_2. The chemical behavior of radon fluoride is similar to that of XeF_2. Thus, it reacts with water to give elemental Rd, it forms no oxo-anions, and it always coprecipitates with XeF_2[329]. The Rn—F bond is unquestionably more ionic than the Xe—F bond. This also explains why, presumably, no RnF_4 is formed, since it must be kinetically very difficult to fluorinate a substantially ionic RnF_2[330]. The application of relativistic quantum mechanics to the bonding problem of radon fluorides confirms the highly ionic nature of radon difluoride[331,332]. Whether monovalent ionic fluorides Rn^+F^- or $^{118}E^+F^-$ exist, as discussed in this theoretical paper, is uncertain. The radical fluorides KrF and XeF are very unstable; however, they do not have an ionic structure[333,334]. If radon fluoride does in fact contain monovalent radon, this could be easily detected by ESR spectroscopy.

Suggestions have already been made that cesium or francium could occur in valence states higher than 1. Francium appears to be less suitable for this than cesium if the chemistry of xenon is compared with that of radon, but even a CsF_3 would decompose spontaneously into CsF and F_2[335]. Only $Cs^+F_3^-$ has so far been detected *in* matrix[336].

12. Free Radicals

The hypothesis concerning Rn^+F^- reminds us that free radical fluorides also exist.

Only a few stable radicals are known: NF_2[97], SO_3F[337-339], and perhaps also O_2F[340] and PF_2[105]. These exist in equilibrium with the dimers N_2F_2, $FSO_2—O—O—SO_2F$, O_4F_2, and P_2F_4. The O_2F radical, from which the stable cation O_2^+ is derived[341,342], is perhaps stable even at room temperature[343]. The radical PO_2F_2 has not yet been confirmed[344]; the UV spectrum published is identical with that of ClO_2.

Most other free radicals have only been detected in matrix. A good review of this technique and the results is given in [345]. The large number of unstable free radicals has mainly been produced in matrix by γ or UV radiation and detected by ESR, IR, or Raman spectroscopy.

The present discussion will be limited to a few cases. In the photolysis of a $ClF/F_2/Ar$, $ClF/F_2/N_2$, or ClF_3/Ar matrix at 15 K it is possible to detect ClF_2[346]. On the basis of the chlorine isotope splitting in the IR spectrum a bond angle of about 136° may be assumed. This bond angle lies between that in ClF_2^+ (about 100°) and that in ClF_2^- (180°)[347-349]. It therefore appears that here again the VSEPR theory applies, *i.e.* that even a single electron is sterically active, although not so strongly as a nonbonded electron pair. A nonplanar structure (similar to that of SF_4) would then be expected for ClF_4, even though the deviation from planarity should be smaller than that from linearity in ClF_2, because the spatial requirements of the four fluorine atoms can be satisfied better in a more planar structure. Indeed, ClF_4 has been detected[350]; the ESR results are, however, compatible with a planar structure. The free radical ClF_6[351,352] and the free radicals BrF_6 and IF_6[352] probably have an almost or a completely octahedral structure. Dynamic effects like those operative in XeF_6 and $TeCl_6^{2-}$ are difficult to detect by ESR.

In the cases mentioned, as well as in the isoelectronic species SF_6^-, SeF_6^-, and TeF_6^-[354], it can be shown by means of the hyperfine structure in the ESR spectrum that the unpaired

electron undergoes an interaction with the central atom and the fluorine ligands. In the related free radicals $SeOF_5$ and $TeOF_5$, however, which are stable to $-30°C$, the unpaired electron is mainly localized on the central atom and on the oxygen[22].

As assumed, the free radical SF_5 has a square-pyramidal structure, and the same arrangement is obtained for CF_3—OSF_4, the ligand O—CF_3 assuming an equatorial position. A consequence of this structure is that this free radical reacts to form the *cis* isomer CF_3O—SF_4—X[353] (see Section 8).

Free radicals always seem to have qualitatively the same structure as their parent molecules or ions which have one more electron[345]. Pairs like ClF_2/ClF_2^-, NO_2/NO_2^-, and SF_5/SF_5^- prove this rule. A more detailed study of this point would be of general interest.

13. Outlook

As shown by this survey, the field of main group fluorides and oxide fluorides has been extensively investigated and an overall picture of the structural problems is clearly emerging. Gaps in this picture are, for example, the compounds of heptavalent bromine, such as BrO_2F_3 and $BrOF_5$, while the existence of BrF_7 and ClF_7 seems unlikely. It is also not entirely understandable why the chemistry of radon is so underdeveloped compared with that of xenon, even though octavalent compounds of radon are not to be expected. The synthesis of an argon compound would be an important synthetic breakthrough. However, the solution of all these problems is fraught with grave experimental difficulties. Each one of these problems will require the development of a highly sophisticated experimental method.

Many of the fluorides and oxide fluorides described are starting compounds for an extensive chemistry; the ligands —OSO_2F, —$OTeF_5$, —$OSeF_5$, —$OPOF_2$, and —ClO_3 may be cited as examples. The use of PF_5, AsF_5, and SbF_5 as fluoride ion acceptors has already become a standard procedure.

With few exceptions, new developments are to be expected not so much in the synthesis of individual compounds of this class, but rather from their chemical applications.

Many colleagues deserve my gratitude for their contributions to valuable discussions. The author's own work cited here has been generously supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

Received: February 1, 1978;
supplemented: August 16, 1978 [A 260 IE]
German version: Angew. Chem. 91, 199 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] Advances in Fluorine Chemistry, Butterworths, London.
[2] Fluorine Chemistry Reviews, Marcel Dekker, New York.
[3] Fluorine Chemistry, Academic Press, New York.
[4] *D. P. Craig, E. A. Magnussen*, Disc. Faraday Soc. *26*, 116 (1958).
[5] *D. W. J. Cruickshank, B. C. Webster, D. F. Mayer*, J. Chem. Phys. *40*, 3733 (1964).
[6] *R. Tsuchida*, Rev. Phys. Chem. Jpn. *13*, 31, 61 (1939).
[7] *R. Tsuchida*, Bull. Chem. Soc. Jpn. *14*, 101 (1939).
[8] *R. J. Gillespie, R. S. Nyholm*, Q. Rev. Chem. Soc. *11*, 339 (1957).
[9] *R. J. Gillespie*, Angew. Chem. *79*, 885 (1967); Angew. Chem. Int. Ed. Engl. *6*, 819 (1967).
[10] *L. S. Bartell*, Inorg. Chem. *5*, 1635 (1966); *M. B. Hall, ibid. 17*, 2261 (1978).
[11] A short review on the structure of the hexachloro anions: *D. J. Stufkens*, Rec. Trav. Chim. Pays-Bas *89*, 1185 (1970).
[12] *B. Krebs, B. Buss, W. Wagner*, Z. Anorg. Allg. Chem. *397*, 1 (1973).
[13] *B. Buss, B. Krebs*, Angew. Chem. *82*, 446 (1970); Angew. Chem. Int. Ed. Engl. *9*, 463 (1970).
[14] *B. Buss, B. Krebs*, Inorg. Chem. *10*, 2795 (1971).
[15] *P. H. Collins, M. Webster*, Acta Crystallogr. *B 28*, 1260 (1972).
[16] In the boranes and carboranes the boron and the hydrogen are bound to five or six other atoms; the number of bonding electron pairs is, however, only four.
[17] *H. Siebert*, Z. Anorg. Allg. Chem. *274*, 35 (1953).
[18] *H. Siebert*, Z. Anorg. Allg. Chem. *275*, 221, 225 (1954).
[19] *R. J. Gillespie, E. A. Robinson*, Can. J. Chem. *42*, 2496 (1964).
[20] *A. J. Downs, C. J. Adams* in: Comprehensive Inorganic Chemistry. Vol. 2. Pergamon Press, Oxford 1973, p. 1259.
[21] *A. A. Banks, A. J. Rudge*, Nature *171*, 390 (1953).
[22] *K. Seppelt, D. Nöthe*, Inorg. Chem. *12*, 2727 (1973).
[23] *H. Oberhammer, K. Seppelt*, Angew. Chem. *90*, 66 (1978); Angew. Chem. Int. Ed. Engl. *17*, 69 (1978).
[24] *H. Oberhammer, K. Seppelt*, Inorg. Chem. *17*, 1435 (1978).
[25] *A. F. Clifford, L. C. Duncan*, Inorg. Chem. *5*, 692 (1966).
[26] *K. Seppelt*, Inorg. Chem. *12*, 2837 (1973).
[27] *W. Porcham, A. Engelbrecht*, Monatsh. Chem. *102*, 333 (1971).
[28] *K. Seppelt*, Z. Anorg. Allg. Chem. *428*, 35 (1977).
[29] *F. Sladky, H. Kropshofer, O. Leitzke*, J. Chem. Soc. Chem. Commun. *1973*, 134.
[30] Landolt-Börnstein: Zahlenwerte und Funktionen aus Physik, Chemie, Astronomie, Geophysik und Technik. Springer, Berlin 1955, Vol. 1, Part 4, p. 519.
[31] *E. H. Appelman*, J. Am. Chem. Soc. *90*, 1900 (1968).
[32] *K. Seppelt*, Angew. Chem. *88*, 806 (1976); Angew. Chem. Int. Ed. Engl. *15*, 771 (1976).
[33] *K. Seppelt*, Z. Anorg. Allg. Chem. *434*, 5 (1977).
[34] *H. Kwart, K. G. King*: d-Orbitals in the Chemistry of Silicon, Phosphorus and Sulfur. Springer, Berlin 1977.
[35] *D. W. J. Cruickshank*, J. Chem. Soc. *1961*, 5486.
[36] *R. E. Rundle*, Rec. Chem. Prog. *23*, 195 (1962).
[37] *R. E. Rundle*, Surv. Prog. Chem. *1*, 81 (1963).
[38] *R. E. Rundle*, J. Am. Chem. Soc. *85*, 112 (1963).
[39] *C. S. Bartell*, Inorg. Chem. *5*, 1635 (1966).
[40] *J. J. Musher*, Angew. Chem. *81*, 68 (1969); Angew. Chem. Int. Ed. Engl. *8*, 54 (1969).
[41] *C. A. Coulson*, Nature *221*, 1106 (1969).
[42] *R. S. Berry, M. Taneres, C. J. Ballhausen, H. Johansen*, Acta Chem. Scand. *22*, 231 (1968).
[43] *B. M. Deb, C. A. Coulson*, J. Chem. Soc. *A 1971*, 958.
[44] *J. J. Musher*, J. Am. Chem. Soc. *94*, 1370 (1972).
[45] *A. L. Companion*, Theor. Chim. Acta *25*, 268 (1972).
[46] *V. B. Kontecky, J. J. Musher*, Theor. Chim. Acta *33*, 227 (1973).
[47] *H. Nakatsji, J. J. Musher*, Chem. Phys. Lett. *14*, 77 (1974).
[48] *N. Rösch, V. H. Smith, M. H. Wangbo*, Inorg. Chem. *15*, 1768 (1976); J. Am. Chem. Soc. *96*, 5984 (1974). Earlier MO calculations of SF_6 are exhaustively discussed in these papers.
[49] *F. J. Marsh, M. S. Gordon*, J. Mol. Struct. *31*, 345 (1976).
[50] *K. Siegbahn, C. Nordling, G. Johansson, J. Hedman, P. F. Heden, K. Hamrin, U. Gelius, T. Bergmark, L. O. Werne, R. Manne, Y. Baer*: ESCA Applied to Free Molecules. North Holland, Amsterdam 1969.
[51] *W. L. Jolly, W. B. Parry*, J. Electron Spectrosc. Rel. Phenom. *4*, 219 (1974).
[52] *C. K. Jørgensen*, Struct. Bonding *6*, 94 (1969).
[53] *R. S. Mulliken, B. Liu*, J. Am. Chem. Soc. *93*, 6738 (1971).
[54] The problem of d-orbitals participation is discussed exhaustively in [52] and [53].
[55] *U. Gelius, B. Roos, P. Siegbahn*, Chem. Phys. Lett. *4*, 471 (1970).
[56] *J. C. Delmer*, J. Chem. Phys. *56*, 4496 (1972).
[57] *A. W. Potts, H. J. Lemka, D. G. Streets, W. C. Price*, Philos. Trans. R. Soc. London *268*, 59 (1970).
[58] *B. Weinstock, E. E. Weaver, C. P. Knop*, Inorg. Chem. *5*, 2189 (1966).
[59] *F. Seel*, Adv. Inorg. Chem. Radiochem. *16*, 297 (1974).
[60] As examples we may mention the structures of the oxide fluorides WOF_4, $MoOF_4$, $ReOF_4$, and $TcOF_4$: *A. J. Edwards, G. R. Jones, B. R. Stevenson*, Chem. Commun. *1967*, 462.
[61] *M. Gassmann*, Naturwissenschaften *61*, 127 (1974).
[62] *R. Hoppe, W. Dähne*, Naturwissenschaften *49*, 254 (1962).
[63] *J. L. Margrave, K. G. Sharp, P. W. Wilson*, Fortschr. Chem. Forsch. *26*, 1 (1972).
[64] *C. W. Matthews*, J. Chem. Phys. *45*, 1068 (1966).
[65] *F. X. Powell, D. R. Lide, Jr.*, J. Chem. Phys. *45*, 1067 (1966).
[66] *V. M. Rao, R. F. Curl, Jr., P. L. Timms, J. L. Margrave*, J. Chem. Phys. *43*, 2557 (1965).
[67] *O. F. Zeck, Y.-Y. Su, Y.-N. Tang*, J. Chem. Soc. Chem. Commun. *1975*, 156.
[68] *N. Cohen, J. Heicklen*, J. Chem. Phys. *70*, 3082 (1966).

[69] *N. Cohen, V. Knight*, J. Chem. Phys. *70*, 3893 (1966).
[70] *J. Trotter, M. Akhtar, N. Bartlett*, J. Chem. Soc. *A 1966*, 30.
[71] *R. C. McDonald, H. Ho-Kuen Hau, K. Eriks*, Inorg. Chem. *15*, 762 (1976).
[72] *R. Hoppe*, Angew. Chem. *82*, 7 (1970); Angew. Chem. Int. Ed. Engl. *9*, 25 (1970).
[73] *C. T. Goetschel, V. A. Campanile, R. M. Curtis, K. R. Loos, C. D. Wagner, J. N. Wilson*, Inorg. Chem. *11*, 1696 (1972).
[74] For a brief review of the NF_4^+ cation, see: *K. O. Christe, R. D. Wilson, A. E. Axworthy*, Inorg. Chem. *12*, 2478 (1972); see also *W. E. Tollberg, R. T. Rewick, S. S. Stringham, M. E. Hill, ibid. 6*, 1156 (1967); *K. O. Christe, J. P. Guertin, A. E. Pavlath, W. Sawodny, ibid. 6*, 533 (1967); *J. P. Guertin, K. O. Christe, H. Pavlath, ibid. 5*, 1921 (1966); *K. O. Christe, ibid. 16*, 2238 (1977).
[75] *K. W. Hansen, L. S. Bartell*, Inorg. Chem. *4*, 1775 (1965).
[76] *L. S. Bartell, V. Plato*, J. Am. Chem. Soc. *95*, 3097 (1973).
[77] For rearrangement reactions at pentacoordinated phosphorus see *R. S. Berry*, J. Chem. Phys. *32*, 933 (1960) and [78].
[78] *P. Gillespie, P. Hoffmann, H. Klusaak, D. Marquarding, S. Pfohl, F. Ramirez, E. A. Tsolis, I. Ugi*, Angew. Chem. *83*, 691 (1971); Angew. Chem. Int. Ed. Engl. *10*, 687 (1971).
[79] *C. J. Hoffmann, B. E. Holder, J. W. Jolly*, J. Phys. Chem. *62*, 364 (1958).
[80] *J. Bacon, P. A. W. Dean, R. J. Gillespie*, Can. J. Chem. *48*, 3413 (1970).
[81] *T. K. Davies, K. C. Mors*, J. Chem. Soc. *A 1970*, 1054.
[82] *A. Müller, H. W. Roesky, D. Böhler*, Z. Chem. *7*, 469 (1967).
[83] *E. W. Lawless*, Inorg. Chem. *10*, 2084 (1971).
[84] *M. J. Vasile, G. R. Jones, W. E. Falconer*, Chem. Commun. *1971*, 1355.
[85] *M. J. Vasile, W. E. Falconer*, Inorg. Chem. *11*, 2282 (1972).
[86] *A. J. Edwards, P. Taylor*, Chem. Commun. *1971*, 1376.
[87] *A. J. Edwards, G. R. Jones*, J. Chem. Soc. *A 1971*, 2318.
[88] *M. D. Lind, K. O. Christe*, Inorg. Chem. *11*, 608 (1972).
[89] *C. Hebecker*, Z. Anorg. Allg. Chem. *384*, 111 (1971).
[90] *J. Fischer, E. Rudsikis*, J. Am. Chem. Soc. *81*, 6375 (1959).
[91] *A. J. Edwards*, J. Chem. Soc. *A 1970*, 2751.
[92] *F. Hund, B. Fricke*, Z. Anorg. Allg. Chem. *258*, 198 (1949); *B. Aurivillius*, Acta Chem. Scand. *9*, 1206 (1955).
[93] *A. Zalkin, D. H. Templeton*, J. Am. Chem. Soc. *75*, 2453 (1953).
[94] *A. K. Cheetham, N. Norman*, Acta Chem. Scand. *A 28*, 55 (1974).
[95] *R. R. Ryan, S. H. Mastin, A. C. Larson*, Inorg. Chem. *10*, 2793 (1971).
[96] *D. R. Schroeder, R. A. Jacobson*, Inorg. Chem. *12*, 515 (1973).
[97] For a survey of nitrogen fluorides, see: *C. B. Colburn*, Adv. Fluorine Chem. *3*, 92 (1963).
[98] *C. B. Colburn, F. A. Johnson, C. Haney*, J. Chem. Phys. *43*, 4526 (1965).
[99] *M. J. Cardillo, S. H. Bauer*, Inorg. Chem. *8*, 2086 (1969).
[100] *M. M. Gilbert, G. Gundersen, K. Hedberg*, J. Chem. Phys. *56*, 1691 (1972).
[101] *Z. Slanina*, J. Fluorine Chem. *6*, 465 (1975).
[102] *C. T. Armstrong, S. Maranth*, J. Chem. Phys. *38*, 169 (1963).
[103] *R. K. Bahn, S. H. Bauer*, Inorg. Chem. *6*, 309 (1967).
[104] *R. H. Sanborn*, J. Chem. Phys. *33*, 1855 (1960).
[105] *R. W. Rudolph, R. C. Taylor, R. W. Parry*, J. Am. Chem. Soc. *88*, 3729 (1966).
[106] *M. Lustig, J. K. Ruff, C. B. Colburn*, J. Am. Chem. Soc. *88*, 3875 (1973).
[107] *H. L. Hodges, L. S. Su, L. S. Barker*, Inorg. Chem. *14*, 599 (1975).
[108] *P. S. Ganguli, A. H. McGee*, Inorg. Chem. *11*, 3071 (1972).
[109] *D. W. J. Magnuson*, J. Chem. Phys. *19*, 1071 (1951).
[110] *W. Sawodny, A. Fadini, K. Ballein*, Spectrochim. Acta *21*, 995 (1965).
[111] *N. Bartlett, J. Passmore, E. G. Wells*, Chem. Commun. *1966*, 214.
[112] *W. B. Fox, J. S. MacKenzie, N. Vanderkooj, B. Sukornick, C. A. Wamser, J. R. Holmes, R. E. Eibeck, B. B. Steward*, J. Am. Chem. Soc. *88*, 2604 (1966).
[113] *E. C. Curtis, D. Pilipovich, W. H. Moberly*, J. Chem. Phys. *46*, 2904 (1967).
[114] *Y. Morino, K. Kuchitzu, T. Moritani*, Inorg. Chem. *8*, 867 (1969).
[115] *K. Kuchitzu, T. Moritani, Y. Morino*, Inorg. Chem. *10*, 344 (1971).
[116] *G. Mitra*, J. Am. Chem. Soc. *80*, 5639 (1958).
[117] *K. Dehnicke, J. Weidlein*, Z. Anorg. Allg. Chem. *342*, 225 (1966).
[118] *W. Haase*, Chem. Ber. *106*, 734 (1973).
[119] *W. Haase*, Chem. Ber. *107*, 1009 (1974).
[120] *W. Haase*, Z. Anorg. Allg. Chem. *397*, 258 (1973).
[121] *W. Haase*, Acta Crystallogr. *B 30*, 2465, 2508 (1974).
[122] *V. Gutmann, H. J. Emeléus*, J. Chem. Soc. *1950*, 1046.
[123] For a review of phosphorus fluoride and oxide fluoride derivatives, see *R. Schmutzler*, Adv. Fluorine Chem. *5*, 31 (1965).
[124] *I. J. Solomon, J. K. Raney, A. J. Kacmarek, R. G. Maguise, G. A. Noble*, J. Am. Chem. Soc. *89*, 2015 (1967).
[125] *I. J. Solomon, J. N. Keith, A. J. Kacmarek, J. K. Raney*, J. Am. Chem. Soc. *90*, 5408 (1968).
[126] *A. G. Streng, A. V. Grosse*, J. Am. Chem. Soc. *88*, 169 (1966).
[127] *A. Arkell*, J. Am. Chem. Soc. *87*, 4057 (1965).
[128] *A. G. Streng*, Chem. Rev. *63*, 607 (1963).
[129] *E. W. Lawless, I. C. Smith*: Inorganic High-Energy Oxidizers. Arnold and Dekker, New York 1968.
[130] *E. A. V. Ebsworth, J. A. Como, J. J. Turner* in: Comprehensive Inorganic Chemistry. Vol. 2. Pergamon Press, Oxford 1973, p. 747.
[131] For reviews, see [59].
[132] *B. Solouki, H. Bock*, Inorg. Chem. *16*, 665 (1977).
[133] *D. R. Johnson, F. X. Powell*, Science *164*, 950 (1969).
[134] *Y. Morino, S. Saito*, J. Mol. Spectrosc. *19*, 439 (1966).
[135] *F. Seel, R. Budenz, W. Gombler*, Chem. Ber. *97*, 3374 (1974).
[136] *F. Seel, R. Budenz*, J. Fluorine Chem. *1*, 117 (1971/72).
[137] *J. A. Gibson, D. G. Ibott, A. F. Janzen*, Can. J. Chem. *51*, 3203 (1973); *F. Seel, W. Gombler*, J. Fluorine Chem. *4*, 327 (1974).
[138] *W. G. Klemperer, J. K. Krieger, M. D. McCreary, E. C. Muetterties, D. D. Traficante, G. M. Whitesides*, J. Am. Chem. Soc. *97*, 7023 (1975).
[139] Review: *S. M. Williamson*, Progr. Inorg. Chem. *7*, 39 (1966).
[140] *K. Seppelt*, Z. Anorg. Allg. Chem. *399*, 87 (1973).
[141] *K. O. Christe, C. J. Schack, D. Pilipovich, E. C. Curtis, W. Sawodny*, Inorg. Chem. *12*, 620 (1973).
[142] *E. Mayer, F. Sladky*, Inorg. Chem. *14*, 589 (1975).
[143] *R. Höfler, O. Glemser*, Angew. Chem. *85*, 1105 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1000 (1973).
[144] *L. C. Duncan, G. H. Cady*, Inorg. Chem. *3*, 850 (1964).
[145] *L. C. Duncan, G. H. Cady*, Inorg. Chem. *3*, 1045 (1964).
[146] *A. L. Logothetis, G. N. Sanzen, R. J. Schozda*, Inorg. Chem. *2*, 173 (1963).
[147] *T. Abe, J. M. Shreeve*, Inorg. Nucl. Chem. Lett. *9*, 465 (1973).
[148] *J. R. Morton, K. F. Preston*, Chem. Phys. Lett. *18*, 98 (1973).
[149] *D. Lentz, K. Seppelt*, unpublished.
[150] *D. Lentz, H. Pritzkow, K. Seppelt*, Angew. Chem. *89*, 741 (1977); Angew. Chem. Int. Ed. Engl. *16*, 729 (1977).
[151] *D. Lentz, H. Pritzkow, K. Seppelt*, Inorg. Chem. *17*, 1926 (1978). Review of the Te—O—F system.
[152] *G. W. Fraser, G. Meikle*, J. Chem. Soc. Chem. Commun. *1974*, 625.
[153] *G. W. Fraser, J. B. Millar*, J. Chem. Soc. Dalton Trans. *1974*, 2029.
[154] *D. R. Armstrong, G. W. Fraser, G. D. Meikle*, Inorg. Chim. Acta *15*, 39 (1975).
[155] *R. Kniep, D. Mootz, A. Rabenau*, Angew. Chem. *85*, 504 (1973); Angew. Chem. Int. Ed. Engl. *12*, 499 (1973).
[156] *A. Rabenau, H. Rau*, Z. Anorg. Allg. Chem. *395*, 273 (1973).
[157] *V. E. Ewing, C. E. Sutton*, Trans. Faraday Soc. *49*, 1241 (1963).
[158] *K. Seppelt*, Z. Anorg. Allg. Chem. *416*, 12 (1975).
[159] *K. Seppelt*, Angew. Chem. *86*, 103 (1974); Angew. Chem. Int. Ed. Engl. *13*, 91 (1974).
[160] *K. Seppelt*, Z. Anorg. Allg. Chem. *406*, 287 (1974); *M. J. Vasile, F. A. Stevie, K. Seppelt*, J. Fluorine Chem., in press.
[161] *K. Seppelt*, Angew. Chem. *86*, 104 (1974); Angew. Chem. Int. Ed. Engl. *13*, 92 (1974).
[162] *H. Oberhammer, K. Seppelt*, Inorg. Chem., in press.
[163] *K. Seppelt*, Chem. Ber. *106*, 157 (1973).
[164] *W. C. Reichert, G. H. Cady*, Inorg. Chem. *12*, 749 (1973).
[165] *R. F. Einland, J. Alfa*, Z. Anorg. Allg. Chem. *21*, 43 (1899).
[166] *O. Lindguist*, Acta Chem. Scand. *23*, 3062 (1969).
[167] *H. Siebert, H. Wegener*, Angew. Chem. *77*, 507 (1965); Angew. Chem. Int. Ed. Engl. *4*, 523 (1965).
[168] *K. Seppelt*, Z. Anorg. Allg. Chem. *428*, 35 (1977).
[169] *G. Mitra, G. H. Cady*, J. Am. Chem. Soc. *81*, 2646 (1959).
[170] *J. E. Smith, G. H. Cady*, Inorg. Chem. *9*, 1442 (1970).
[171] *K. Seppelt*, Chem. Ber. *106*, 1920 (1973).
[172] *A. J. Edwards, F. J. Hewaidy*, J. Chem. Soc. *A 1968*, 2977.
[173] *C. J. Adams, A. J. Downs*, Spectrochim. Acta *28*, 1841 (1972).
[174] *S. H. Mastin, R. R. Ryan, C. B. Asprey*, Inorg. Chem. *9*, 2100 (1970).
[175] *A. J. Edwards, M. A. Monty*, J. Chem. Soc. *A 1969*, 703.
[176] *U. Elgad, H. Selig*, Inorg. Chem. *14*, 140 (1975).
[177] *E. C. Muetterties*, J. Am. Chem. Soc. *79*, 1004 (1957).
[178] *H. Selig, S. Sarig, S. Abramowitz*, Inorg. Chem. *13*, 1508 (1974).
[179] *A. Engelbrecht, W. Loreck, W. Nehoda*, Z. Anorg. Allg. Chem. *360*, 88 (1968).
[180] *H. Bürger*, Z. Anorg. Allg. Chem. *368*, 97 (1968).
[181] *H. Pritzkow, K. Seppelt*, Angew. Chem. *88*, 846 (1976); Angew. Chem. Int. Ed. Engl. *15*, 771 (1976).
[182] *H. Pritzkow, K. Seppelt*, Inorg. Chem. *16*, 2685 (1977).
[183] *J. Beattie, R. Crocombe, A. German, P. Jons, C. Marsden, G. van Schalkwyk, A. Bukowsky*, J. Chem. Soc. Dalton Trans. *1975*, 1659.
[184] *A. Clouston, R. D. Peacock, G. R. Fraser*, Chem. Commun. *1970*, 1197.
[185] *J. B. Milne, D. Moffett*, Inorg. Chem. *12*, 2240 (1973).
[186] A list of the cationic and anionic derivatives of chlorine fluorides and oxide fluorides with an exhaustive collection of references will be found in: *K. O. Christe, C. J. Schack*, Adv. Inorg. Chem. Radiochem. *18*, 319 (1976); *K. O. Christe, C. J. Schack, D. Pilipovich*, Inorg. Chem.

11, 2205 (1972); *K. O. Christe, J. F. Hon, D. Pilipovich, ibid. 12*, 84 (1973).
[187] *K. O. Christe*, Inorg. Nucl. Chem. Lett. *8*, 741 (1972).
[188] *F. Q. Roberto*, Inorg. Nucl. Chem. Lett. *8*, 737 (1972).
[189] *K. O. Christe*, Inorg. Chem. *12*, 1580 (1973).
[190] *L. Andrews, F. K. Chi, A. Arkell*, J. Am. Chem. Soc. *96*, 1997 (1974).
[191] *R. Bougon, J. Isabey, P. Plurien*, C. R. Acad. Sci. *C 271*, 1366 (1970).
[192] *D. Pilipovich, C. B. Lindahl, C. J. Schack, R. D. Wilson, K. O. Christe*, Inorg. Chem. *11*, 2189 (1972).
[193] *K. Züchner, O. Glemser*, Angew. Chem. *84*, 1147 (1972); Angew. Chem. Int. Ed. Engl. *11*, 1094 (1972).
[194] *K. O. Christe*, Inorg. Nucl. Chem. Lett. *8*, 457 (1972).
[195] *K. O. Christe, R. D. Wilson*, Inorg. Chem. *12*, 1356 (1973).
[196] *K. O. Christe, R. D. Wilson, E. C. Curtis*, Inorg. Chem. *12*, 1358 (1973).
[197] *L. Stein:* Halogen Chemistry. Vol. 1. Academic Press, London 1967.
[198] *D. Naumann, E. Lehmann*, J. Fluorine Chem. *5*, 307 (1975).
[199] *T. Surles, L. A. Quarterman, H. H. Hyman*, J. Inorg. Nucl. Chem. *35*, 668 (1973).
[200] *A. J. Edwards, G. R. Jones*, Chem. Commun. *1967*, 1304.
[201] *A. J. Edwards, G. R. Jones*, J. Chem. Soc. *A 1969*, 1467.
[202] *A. J. Edwards, G. R. Jones*, J. Chem. Soc. *A 1969*, 1936.
[203] *R. Bougon, P. Charpin, J. Soziano*, C. R. Acad. Sci. *C 272*, 565 (1971), and references cited therein.
[204] *R. J. Gillespie, G. J. Schrobilgen*, Inorg. Chem. *13*, 1230 (1974).
[205] *R. J. Gillespie, P. Spekkens*, 6th European Fluorine Symposium, Dortmund 1977.
[206] *M. Adelhelm, E. Jacob*, 6th European Fluorine Symposium, Dortmund 1977.
[207] *M. Schmeisser, E. Paumer*, Angew. Chem. *69*, 781 (1957).
[208] *R. J. Gillespie, P. Spekkens*, J. Chem. Soc. Chem. Commun. *1975*, 314.
[209] *E. Jacob*, Z. Anorg. Allg. Chem. *433*, 255 (1977).
[210] *E. Jacob*, Angew. Chem. *88*, 189 (1976); Angew. Chem. Int. Ed. Engl. *15*, 158 (1976).
[211] *E. N. Sloth, C. Stein, C. W. Williams*, J. Phys. Chem. *73*, 278 (1969).
[212] *E. H. Appelman, M. H. Studier*, J. Am. Chem. Soc. *91*, 4561 (1969).
[213] *E. J. Baran, P. J. Aymonino*, Z. Naturforsch. *276*, 1568 (1972).
[214] *N. H. Claassen, E. H. Appelman*, Inorg. Chem. *9*, 622 (1970).
[215] *M. Schmeisser, P. Sartori, D. Naumann*, Chem. Ber. *103*, 590 (1970).
[216] *M. Schmeisser, P. Sartori, D. Naumann*, Chem. Ber. *103*, 880 (1970).
[217] *M. Schmeisser, W. Ludowici, D. Naumann, P. Sartori, E. Scharf*, Chem. Ber. *101*, 4214 (1968).
[218] *M. Schmeisser, D. Naumann, E. Lehmann*, J. Fluorine Chem. *3*, 441 (1973/74).
[219] *E. Lehmann, D. Naumann, M. Schmeisser*, J. Fluorine Chem. *7*, 33 (1976).
[220] *K. O. Christe, D. Naumann*, Inorg. Chem. *12*, 59 (1973).
[221] *G. B. Hargreaves, R. D. Peacock*, J. Chem. Soc. *1960*, 2373.
[222] *A. J. Edwards, P. Taylor*, J. Chem. Soc. Dalton Trans. *1975*, 2174.
[223] *K. O. Christe*, Inorg. Chem. *11*, 1215 (1972).
[224] *K. O. Christe, J. P. Guertin, W. Sawodny*, Inorg. Chem. *7*, 626 (1968).
[225] *S. P. Beaton, D. W. A. Sharp, A. J. Perkins, I. Sheft, H. H. Hyman, K. O. Christe*, Inorg. Chem. *7*, 2174 (1968).
[226] *H. Klamm, H. Meinert, P. Reich, K. Wittke*, Z. Chem. *8*, 393 (1968).
[227] *H. Klamm, H. Meinert, P. Reich, K. Wittke*, Z. Chem. *8*, 469 (1968).
[228] *S. Bukshpan, J. Soriano, J. Shamir*, Chem. Phys. Lett. *4*, 241 (1969).
[229] *F. Seel, O. Dettmer*, Z. Anorg. Allg. Chem. *301*, 113 (1959).
[230] *F. A. Hohorst, L. Stein, F. Gebert*, Inorg. Chem. *14*, 2233 (1975).
[231] *M. Brownstein, H. Selig*, Inorg. Chem. *11*, 656 (1972).
[232] *C. J. Adams*, Inorg. Nucl. Chem. Lett. *10*, 831 (1974).
[233] *J. W. Viers, H. W. Baisch*, Chem. Commun. *1967*, 1093.
[234] *A. J. Edwards, P. Taylor*, J. Fluorine Chem. *4*, 173 (1974).
[235] *R. R. Ryan, L. B. Asprey*, Acta Crystallogr. *B 28*, 979 (1972).
[236] *C. Helmholtz, M. Rogers*, J. Am. Chem. Soc. *62*, 1537 (1940).
[237] *H. A. Carter, F. Aubke*, Inorg. Chem. *10*, 2296 (1971).
[238] *R. J. Gillespie, J. W. Quail*, Proc. Chem. Soc. London *1963*, 278.
[239] *L. G. Alexakos, C. D. Cornwell, S. B. Pierce*, Proc. Chem. Soc. London *1963*, 341.
[240] *N. Bartlett, L. F. Levchuck*, Proc. Chem. Soc. London *1963*, 342.
[241] *L. E. Smart*, J. Chem. Soc. Chem. Commun. *1977*, 519.
[242] *A. Engelbrecht, P. Peterfy*, Angew. Chem. *81*, 753 (1969); Angew. Chem. Int. Ed. Engl. *8*, 768 (1969).
[243] *A. Engelbrecht, P. Peterfy, E. Schandara*, Z. Anorg. Allg. Chem. *384*, 202 (1971).
[244] *M. J. Vasile, W. E. Falconer, F. A. Stevie, J. R. Beattie*, J. Chem. Phys., in press.
[245] *R. J. Gillespie, J. P. Krasznai*, Inorg. Chem. *15*, 1251 (1976).
[246] *J. R. Beattie, G. J. von Schalkwyk*, Inorg. Nucl. Chem. Lett. *10*, 343 (1974).
[247] *A. Engelbrecht, O. Mayer, G. Ziller, E. Schandara*, Monatsh. Chem. *105*, 796 (1974).
[248] *H. A. Carter, N. J. Ruddick, J. R. Sanes, F. Aubke*, Inorg. Nucl. Chem. Lett. *11*, 29 (1975).
[249] *R. J. Gillespie, J. P. Krasznai*, Inorg. Chem. *16*, 1384 (1977).
[250] *M. Schmeisser, K. Lang*, Angew. Chem. *67*, 156 (1955).
[251] *M. Schmeisser, K. Brändle*, Adv. Inorg. Chem. Radiochem. *5*, 41 (1963).
[252] *K. O. Christe, W. Sawodny*, Inorg. Chem. *8*, 212 (1969).
[253] *R. J. Gillespie, M. J. Morton*, Inorg. Chem. *9*, 811 (1970).
[254] *D. F. Smith*, Science *141*, 1039 (1963).
[255] *D. Pilipovich, W. Maya, E. A. Lawton, H. F. Bauer, D. F. Shekan, N. N. Grimoldi, R. D. Wilson, F. C. Gunderloy, V. E. Bedwell*, Inorg. Chem. *6*, 1918 (1967).
[256] *K. O. Christe, D. Pilipovich*, Inorg. Chem. *8*, 391 (1969).
[257] *K. O. Christe, W. Sawodny*, Inorg. Chem. *12*, 2879 (1973).
[258] *B. M. Deb, C. A. Coulson*, J. Chem. Soc. *A 1971*, 958.
[259] *K. O. Christe*, Inorg. Chem. *11*, 1220 (1972).
[260] *K. O. Christe, E. Curtis*, Inorg. Chem. *11*, 2196 (1972).
[261] *A. G. Streng*, Chem. Rev. *63*, 607 (1963).
[262] *A. G. Streng*, J. Am. Chem. Soc. *85*, 1380 (1963).
[263] *D. J. Gardiner*, J. Fluorine Chem. *3*, 226 (1973/74).
[264] *K. O. Christe, R. D. Wilson, I. B. Goldberg*, J. Fluorine Chem. *7*, 543 (1976).
[265] *C. E. Fogh, R. T. Rewick*, US-Pat. 3615206 (1971).
[266] *A. G. Robiette, R. H. Bradley, P. N. Brier*, Chem. Commun. *1971*, 1567.
[267] *R. D. Burbank, G. R. Jones*, Inorg. Chem. *13*, 1071 (1974).
[268] *H. H. Claassen, E. C. Gasner, H. Selig*, J. Chem. Phys. *49*, 1803 (1969).
[269] *H. H. Eysel, K. Seppelt*, J. Chem. Phys. *56*, 5081 (1972).
[270] *J. Bacon, R. J. Gillespie, J. W. Quail*, Can. J. Chem. *41*, 3063 (1963).
[271] *R. D. Burbank, F. N. Bensey, Jr.*, J. Chem. Phys. *27*, 981 (1957).
[272] *N. Bartlett, S. Beaton, L. W. Reeves, E. J. Wells*, Can. J. Chem. *42*, 2531 (1964).
[273] *H. Siebert, U. Woerner*, Z. Anorg. Allg. Chem. *429*, 34 (1977); *R. C. Paul, K. K. Paul, K. C. Malhotra*, Indian J. Chem. *8*, 1030 (1970).
[274] *J. F. Liebmann, C. C. Allen*, Chem. Commun. *1969*, 1335.
[275] *J. Slivnik, A. Smalc, K. Lutar, B. Zemva, B. Frlec*, J. Fluorine Chem. *5*, 273 (1975).
[276] *J. H. Holloway, G. J. Schrobilgen*, J. Chem. Soc. Chem. Commun. *1975*, 623.
[277] *A. V. Grosse, H. D. Kirschenbaum, A. G. Streng, L. V. Streng*, Science *139*, 1047 (1963).
[278] *F. Schreiner, J. G. Malm, J. C. Hindman*, J. Am. Chem. Soc. *87*, 25 (1965).
[279] *A. G. Streng, A. V. Grosse*, Science *143*, 242 (1964).
[280] *H. Selig, R. D. Peacock*, J. Am. Chem. Soc. *86*, 3895 (1964).
[281] *D. E. McKee, C. J. Adams, A. Zalkin, N. Bartlett*, J. Chem. Soc. Chem. Commun. *1973*, 26.
[282] *R. J. Gillespie, G. J. Schrobilgen*, J. Chem. Soc. Chem. Commun. *1974*, 90.
[283] *B. Frlec, J. H. Holloway*, J. Chem. Soc. Chem. Commun. *1974*, 89.
[284] *R. J. Gillespie, G. J. Schrobilgen*, Inorg. Chem. *15*, 22 (1976).
[285] *B. Frlec, J. H. Holloway*, Inorg. Chem. *15*, 1263 (1976).
[286] *V. M. McRae, R. D. Peacock, D. R. Russell*, Chem. Commun. *1969*, 62.
[287] *N. Bartlett, B. G. De Boer, F. J. Hollander, F. O. Sladky, D. H. Templeton, A. Zalkin*, Inorg. Chem. *13*, 780 (1974).
[288] *R. J. Gillespie, B. Landa, G. J. Schrobilgen*, J. Chem. Soc. Chem. Commun. *1971*, 1543.
[289] *D. E. McKee, C. J. Adams, A. Zalkin, N. Bartlett*, J. Chem. Soc. Chem. Commun. *1973*, 26.
[290] *D. E. McKee, A. Zalkin, N. Bartlett*, Inorg. Chem. *12*, 1713 (1973).
[291] *D. E. McKee, C. J. Adams, N. Bartlett*, Inorg. Chem. *12*, 1722 (1973).
[292] *P. Boldrini, R. J. Gillespie, P. R. Ireland, G. J. Schrobilgen*, Inorg. Chem. *13*, 1690 (1974).
[293] *R. J. Gillespie, G. J. Schrobilgen*, Inorg. Chem. *13*, 2370 (1974).
[294] *K. Leary, D. H. Templeton, A. Zalkin, N. Bartlett*, Inorg. Chem. *12*, 1726 (1973).
[295] *N. Bartlett, M. Gennis, D. D. Gibler, B. K. Morrell, A. Zalkin*, Inorg. Chem. *12*, 1717 (1973).
[296] *N. Bartlett, B. De Boer, F. J. Hollander, F. O. Sladky, D. H. Templeton, A. Zalkin*, Inorg. Chem. *13*, 780 (1974).
[297] *K. Leary, A. Zalkin, N. Bartlett*, Inorg. Chem. *13*, 775 (1974).
[298] *R. D. Peacock, H. Selig, J. Sheft*, J. Inorg. Nucl. Chem. *28*, 2561 (1966).
[299] *S. W. Peterson, J. H. Holloway, B. A. Coyle, J. M. Williams*, Science *173*, 1238 (1971).
[300] *G. J. Moody, H. Selig*, Inorg. Nucl. Chem. Lett. *2*, 319 (1966).
[301] *E. Jacob, R. Opferkuch*, Angew. Chem. *88*, 190 (1976); Angew. Chem. Int. Ed. Engl. *15*, 158 (1976).
[302] *R. J. Gillespie, G. J. Schrobilgen*, J. Chem. Soc. Chem. Commun. *1977*, 595.
[303] *H. Selig*, Inorg. Chem. *5*, 183 (1966).
[304] *R. J. Gillespie, B. Landa, G. J. Schrobilgen*, Inorg. Chem. *15*, 1256 (1976).

[305] J. L. Huston, J. Phys. Chem. 71, 333 (1967).
[306] N. Bartlett, K. Seppelt, unpublished.
[307] J. L. Huston, J. Am. Chem. Soc. 93, 5255 (1971).
[308] J. L. Huston, Inorg. Nucl. Chem. Lett. 4, 29 (1968).
[309] H. H. Claassen, J. L. Huston, J. Chem. Phys. 55, 1505 (1971).
[310] J. F. Liebman, J. Fluorine Chem. 7, 531 (1976).
[311] K. Seppelt, H. H. Rupp, Z. Anorg. Allg. Chem. 409, 331 (1974); K. Seppelt, Inorg. Synth., in press.
[312] For exhaustive discussions and literature reviews on the problem of gaseous XeF_6, see S. Y. Wang, C. C. Lohr, Jr., J. Chem. Phys. 60, 3901 (1974); W. H. E. Schwarz, Angew. Chem. 86, 505 (1974); Angew. Chem. Int. Ed. Engl. 13, 454 (1974); S. Y. Wang, C. C. Lohr, Jr., J. Chem. Phys. 61, 4110 (1974); K. S. Pitzer, C. S. Bernstein, ibid. 63, 3849 (1975); W. E. Falconer, M. J. Vasile, F. A. Stevie, ibid. 66, 5335 (1977).
[313] G. L. Goodman, J. Chem. Phys. 56, 5038 (1972).
[314] H. Selig, A. Moortz, Inorg. Nucl. Chem. Lett. 3, 147 (1967).
[315] H. H. Rupp, K. Seppelt, Angew. Chem. 86, 669 (1974); Angew. Chem. Int. Ed. Engl. 13, 613 (1974).
[316] K. Seppelt, N. Bartlett, Z. Anorg. Allg. Chem., in press; G. J. Schrobilgen, J. H. Holloway, P. Granger, C. Breverand, Inorg. Chem. 17, 980 (1978).
[317] C. Glidewell, Inorg. Nucl. Chem. Lett. 11, 761 (1975).
[318] P. A. Agron, C. K. Johnson, H. A. Levy, Inorg. Nucl. Chem. Lett. 1, 145 (1965).
[319] G. R. Jones, R. D. Burbank, W. E. Falconer, J. Chem. Phys. 52, 6450 (1970).
[320] R. D. Burbank, G. R. Jones, Science 171, 485 (1971); 168, 248 (1970); J. Am. Chem. Soc. 96, 43 (1974).
[321] J. Slivnik, B. Volavzek, J. Marsel, V. Vrscaj, A. Smalc, B. Frlec, B. Zemva, Croat. Chim. Acta 35, 81 (1963).
[322] B. Weinstock, E. E. Weaver, C. P. Knop, Inorg. Chem. 5, 2189 (1966).
[323] B. Weinstock, J. G. Malm, J. Inorg. Nucl. Chem. 2, 380 (1956).
[324] H. J. Emeleus, A. G. Maddock, G. C. Miles, A. G. Sharpe, J. Chem. Soc. 1948, 1991.
[325] B. Weinstock, C. C. Cernick, J. Am. Chem. Soc. 82, 4116 (1960).
[326] W. J. Ramler, J. Wing, D. J. Henderson, J. R. Huizenga, Phys. Rev. 114, 154 (1959).
[327] E. H. Appelman, E. N. Sloth, M. H. Studier, Inorg. Chem. 5, 766 (1966).
[328] C. Stein, Science 168, 362 (1970); J. Inorg. Nucl. Chem. 35, 39 (1973).
[329] V. D. Nefedov, M. A. Topova, V. V. Avronin, B. N. Dudkin, Radiokhimiya 14, 930 (1972); V. V. Avronin, V. D. Nefedov, M. A. Toropova, ibid. 16, 261 (1974).
[330] J. F. Liebman, Inorg. Nucl. Chem. Lett. 11, 683 (1975).
[331] K. S. Pitzer, J. Chem. Soc. Chem. Commun. 1975, 760.
[332] K. S. Pitzer, J. Chem. Phys. 63, 1032 (1975).
[333] W. E. Falconer, J. R. Morton, A. G. Streng, J. Chem. Phys. 41, 902 (1964).
[334] J. R. Morton, W. E. Falconer, J. Chem. Phys. 39, 427 (1963).
[335] R. Hoppe, Fortschr. Chem. Forsch. 5, 213 (1965).
[336] B. S. Ault, L. Andrews, J. Am. Chem. Soc. 98, 1591 (1976).
[337] F. B. Dudley, G. H. Cady, J. Am. Chem. Soc. 85, 3375 (1963).
[338] P. M. Nutzkowitz, G. Vinow, J. Am. Chem. Soc. 91, 5956 (1969).
[339] R. A. Steward, S. Furiwara, F. Aubke, J. Chem. Phys. 48, 5524 (1968).
[340] F. Neumayer, V. Vanderkoj, Jr., Inorg. Chem. 4, 1234 (1965).
[341] N. Bartlett, D. H. Lohmann, Proc. Chem. Soc. London 1962, 115.
[342] A. J. Edwards, W. E. Falconer, J. E. Griffiths, W. A. Sunder, M. J. Vasile, J. Chem. Soc. Dalton Trans. 1974, 1129.
[343] N. Bartlett, unpublished.
[344] M. Eisenberg, D. D. DesMarteau, Inorg. Chem. 11, 1901 (1972).
[345] J. R. Morton, K. F. Preston: Fluorine Containing Free Radicals. ACS Symposium Series Band 66 (1978), p. 386.
[346] G. Mamantov, E. J. Vasini, M. C. Moulton, D. C. Vichroy, T. Maekawa, J. Chem. Phys. 54, 3419 (1971).
[347] A. J. Edwards, R. J. C. Sills, J. Chem. Soc. A 1970, 2697.
[348] H. Lynton, J. Passmore, Can. J. Chem. 49, 2539 (1971).
[349] K. O. Christe, W. Sawodny, J. P. Guertin, Inorg. Chem. 6, 7159 (1967).
[350] J. R. Morton, K. F. Preston, J. Chem. Phys. 58, 3112 (1973).
[351] K. Nishikida, F. Williams, G. Mamantov, N. Smyrl, J. Am. Chem. Soc. 97, 3526 (1975).
[352] A. R. Boate, J. R. Morton, K. F. Preston, Inorg. Chem. 14, 3127 (1975).
[353] J. R. Morton, K. F. Preston, J. C. Tait, J. Chem. Phys. 62, 2029 (1975).
[354] A. R. Gregory, S. E. Karavelas, J. R. Morton, K. F. Preston, J. Am. Chem. Soc. 97, 2206 (1975).

Annulenoannulenes

By Masazumi Nakagawa[*]

Annulenoannulenes formally consist of two annulenes fused together. Hitherto, almost all the known representatives of this class of compounds were the strongly dehydrogenated forms, containing a few triple bonds and several cumulated double bonds. Besides *ortho*-annelated dehydroannulenoannulenes also such compounds containing bridges made up of two or four carbon atoms ("acetylene-cumulene" annulenoannulenes) were obtained by multistep syntheses. Most dehydroannulenoannulenes are stable and form colored crystals. In addition to dehydro[$4n+2$]annuleno[$4n+2$]annulenes with 14-, 18-, and 22-membered individual rings, two dehydro[$4n$]annuleno[$4n+2$]annulenes with 16- and 14-, and 16- and 18-membered rings have also been synthesized. Planar combinations of two [$4n$]-rings of this type and size are not known.—The dehydrogentated [14]annuleno[14]annulene containing a bridge of two carbon atoms has been studied in detail; however, the problem of the induction of a diamagnetic ring current in compounds of this type has still not been completely clarified.

1. Introduction

Parallel with the amazing developments recently made in the chemistry of monocyclic and bridged annulenes[1, 2], macrocyclic annulenes fused with benzenoid rings (*e.g.* benzo- and naphthoannelated annulenes) have received a great deal of attention and interesting results have been reported by several research groups[1g, 3–5]. In view of the interesting properties of polycyclic aromatic compounds, annulenoannulenes, fused systems made up of two annulene nuclei, *i.e.* naphthalene-like systems, have deservedly also received considerable attention.

The first examples of macrocyclic annulenoannulenes were reported in 1975 independently by *Cresp* and *Sondheimer*[6] and by the author's group[7].

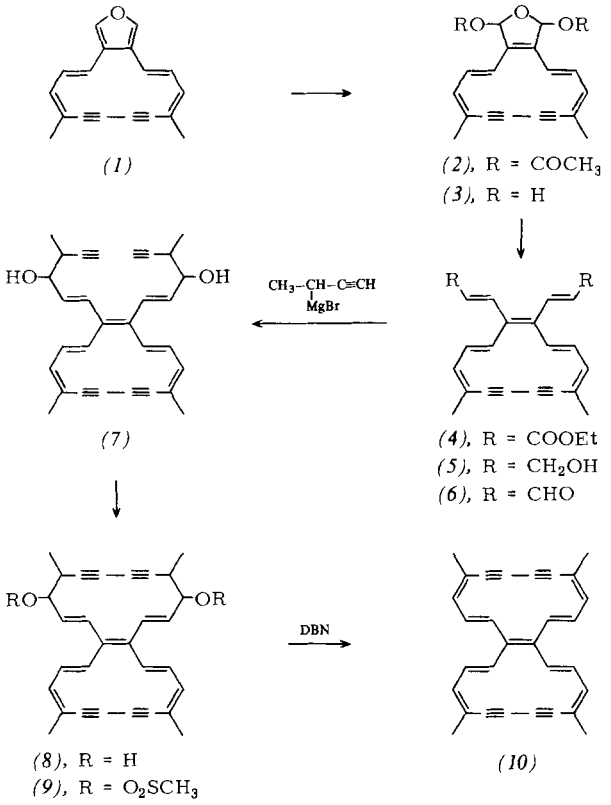
[*] Prof. Dr. Masazumi Nakagawa
Department of Chemistry, Faculty of Science, Osaka University
Toyonaka, Osaka 560 (Japan)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0303-0202 $ 02.50/0

2. Syntheses

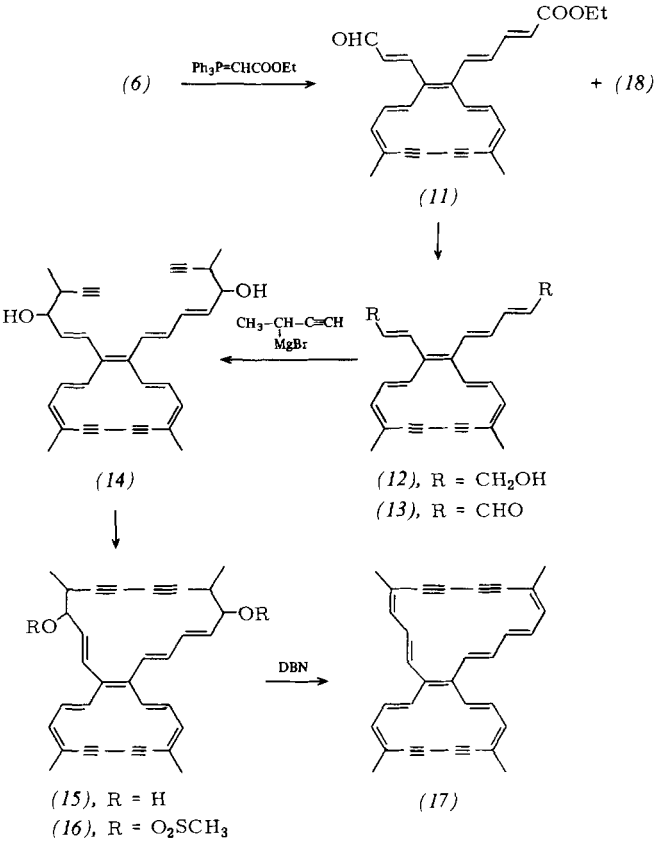
2.1. *ortho*-Annelated Annulenoannulenes[6][*]

The dimethylbisdehydro[14]annuleno[c]furan *(1)*[8], prepared by an improved method, served as starting material for the synthesis of the tetrakisdehydro[14]annuleno[14]-annulene *(10)*. Treatment of *(1)* with lead tetraacetate in acetic acid furnished the diacetate *(2)*, which on hydrolysis gave the hemiacetal *(3)*. Reaction of *(3)* with an excess of (ethoxycarbonylmethylene)triphenylphosphorane afforded

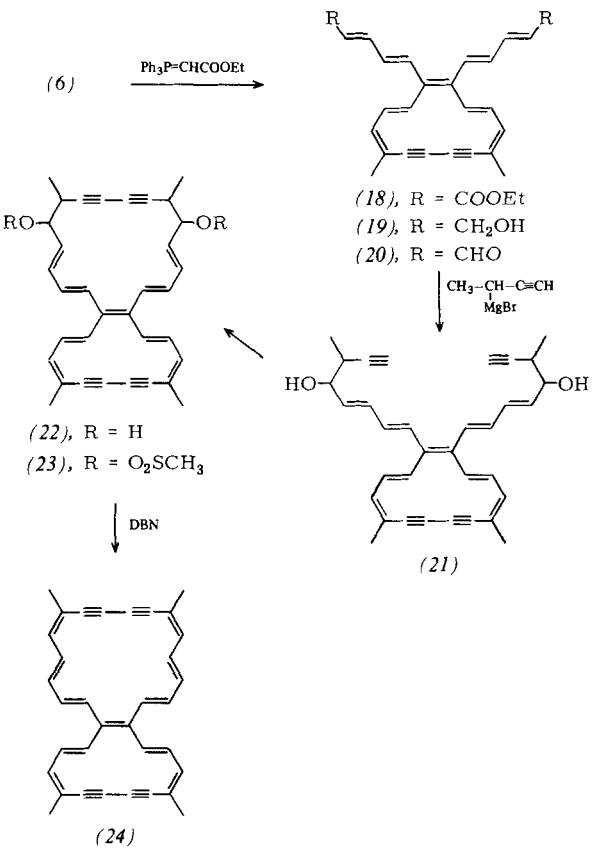


the diester *(4)* (deep-orange crystals). The newly formed double bonds in *(4)* were found to be almost entirely in the desired *trans* configuration. Reduction of the diester *(4)* with diisobutylaluminum hydride and oxidation of the resulting diol *(5)* with manganese dioxide yielded the dialdehyde *(6)* (orange needles). Reaction of *(6)* with the Grignard derivative of 3-bromo-1-butyne[9] led, *via* chain lengthening, to a mixture of the stereoisomeric diols *(7)*. Oxidative coupling of *(7)* with copper(II) acetate in dimethylformamide yielded the bicyclic diol *(8)*. The crude diol *(8)* thus obtained was converted into the corresponding bis(methanesulphonate) *(9)*, which on treatment with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) was converted into the required tetrakisdehydro[14]annuleno[14]annulene *(10)*[**] [dark red-brown prisms, yield *ca.* 5% based on *(6)*].

The dialdehyde *(6)* was used as starting material for the synthesis of the tetrakisdehydro[14]annuleno[16]annulene *(17)*[6b]. Reaction of the dialdehyde *(6)* with one equivalent



of (ethoxycarbonylmethylene)triphenylphosphorane gave the aldehydic ester *(11)* in 56% yield together with 9% of the corresponding diester *(18)*. The aldehydic ester *(11)* was reduced by diisobutylaluminum hydride to the diol *(12)*.



[*] For the nomenclature of the annulenoannulenes according to *Sondheimer* see [6b].

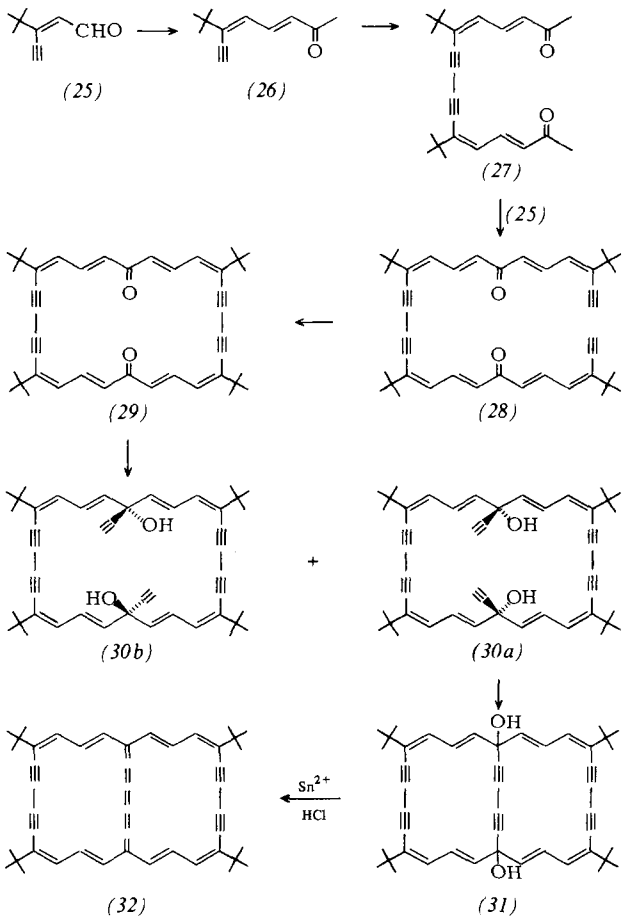
[**] Systematic name of *(10)* according to IUPAC rule A-31: 5,10,18,23-tetramethylbicyclo[12.12.0]hexacosa-1(14),2,4,10,12,15,17,23,25-nonaene-6,8,19,21-tetrayne.

The dialdehyde *(13)*, obtained by the manganese dioxide oxidation of *(12)*, was converted into the diol *(14)* by reaction with the Grignard derivative of 3-bromo-1-butyne. The bicyclic diol *(15)*, obtained by the oxidative coupling of *(14)* with copper(II) acetate in pyridine/ether, was converted into the bis(methanesulphonate) *(16)*, which was transformed on treatment with diazabicyclononene (DBN) into the tetrakisdehydro[14]annuleno[16]annulene *(17)*[*] [deep-purple prisms, yield 3% based on *(13)*].

Compound *(24)* was obtainable in essentially the same manner as *(17)*. The Wittig reaction of *(6)* with an excess of (ethoxycarbonylmethylene)triphenylphosphorane gave the diester *(18)*, which was converted *via (19)* into *(20)* [cf. *(4)*→*(6)*]. The yield of *(20)* was 82% based on *(18)*. The dialdehyde *(20)* could be converted *via* the acyclic diol *(21)*, the cyclic diol *(22)* and the bis(methanesulphonate) *(23)* into the fairly stable tetrakisdehydro[14]annuleno[18]annulene *(24)*[**] (deep-violet crystals, overall yield 20%).

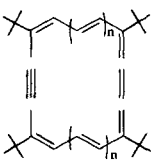
2.2. 'Acetylene-cumulene'-annulenoannulenes[7,15,18,19,25]

In view of the high conformational stability and the strongly diatropic[***] nature of 'acetylene-cumulene'-dehydroannulenes[1g], it was of considerable interest to prepare annulenoannulenes consisting of two fused 'acetylene-cumulene'-dehydroannulenes. For reasons of synthetic convenience, the hexakisdehydro[18]annuleno[18]annulene *(32)* was first synthesized[7]. The ethynyl ketone *(26)*, obtained by the aldol condensation of 3-*tert*-butyl-2-penten-4-ynal *(25)*[10] with acetone, was oxidatively coupled with copper(II) acetate in pyridine to give the diketone *(27)*. Treatment of the diketone *(27)* with an excess of the enyne aldehyde *(25)* in the presence of sodium ethoxide yielded the acyclic diketone *(28)* in 92% yield. Oxidative coupling of *(28)* with copper(II) acetate in pyridine, methanol and ether under high dilution conditions resulted in formation of the 26-membered cyclic diketone *(29)* in almost quantitative yield. Bisethynylation of *(29)* with lithium acetylide-ethylenediamine complex[11] in tetrahydrofuran saturated with acetylene gave a mixture of the diastereomeric cyclic diols *(30a)* and *(30b)* in 88% yield. Subsequent chromatographic separation on alumina yielded a high melting and a low melting isomer (≈4:1). Oxidation of the high melting isomer *(30a)* with copper(II) acetate in pyridine/methanol/ether under high dilution conditions afforded the bicyclic diol *(31)* in 61% yield. In contrast, the low melting isomer *(30b)* gave no bicyclic diol upon attempted oxidative coupling under the same reaction conditions; only the starting material *(30b)* was recovered in 62% yield. The failure of intramolecular oxidative coupling of the low melting isomer *(30b)* is attributable to the unfavorable *trans* disposition of the ethynyl groups in the molecule. (On this basis, we assign the structure *(30a)* to the high melting isomer in which the ethynyl groups are favorably positioned for intramolecular oxidative coupling.)



A solution of *(31)* in ether was mixed at −60°C with a solution of tin(II) chloride dihydrate in ether saturated with hydrogen chloride. The hexakisdehydro[18]annuleno[18]annulene *(32)*[*] was obtained as fairly stable dark-green crystals in 79% yield. The annulenoannulene *(32)* gave a 1:1 CT complex with 2,4,7-trinitrofluorenone.

Since tetra-*tert*-butylbisdehydro[4*n*+2]annulenes *(33)*, *n*=1—5, have already been prepared by the author's group[1f,1g], the synthesis of annulenoannulenes consisting of two bisdehydro[4*n*+2]annulenes *(33)* attracted interest in view of comparing their properties with those of the corresponding monocyclic systems *(33)*.



(33), n = 1,2,3,4,5

The *tert*-butylthiovinyl methyl ketone *(34)*, obtained by the addition of 2-methyl-2-propanethiol to ethynyl methyl ketone in the presence of Triton B[12], was condensed with the *tert*-butylenyne aldehyde *(25)* to give the ethynyltriene ketone *(35)*. Successive treatment of the ethynyl ketone *(35)* with lithium diethylamide in tetrahydrofuran at −78°C and with chloro(trimethyl)silane gave the trimethylsilyl derivative

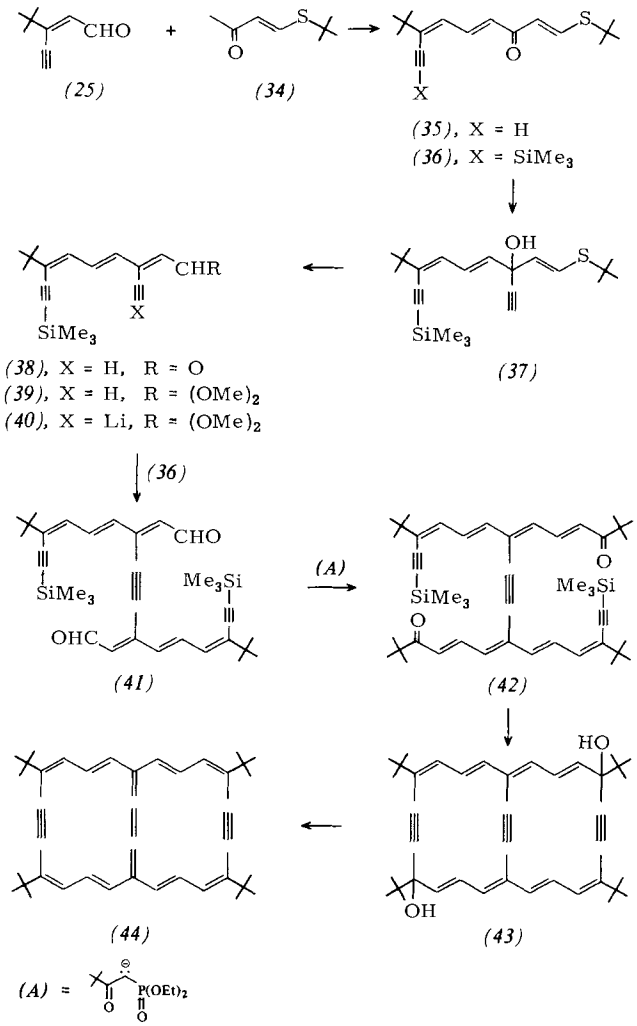
[*] Systematic name of *(17)*: 7,12,20,25-tetramethylbicyclo[14.12.0]octacosa-1(16),2,4,6,12,14,17,19,25,27-decaene-8,10,21,23-tetrayne.

[**] Systematic name of *(24)*: 7,12,22,27-tetramethylbicyclo[16.12.0]triaconta-1(18),2,4,6,12,14,16,19,21,27,29-undecaene-8,10,23,25-tetrayne.

[***] Molecules whose NMR spectra reveal the effect of a diamagnetic ring current are called *diatropic* [1c].

[*] Systematic name of *(32)*: 5,10,18,23-tetra-*tert*-butylbicyclo[12.12.4]triaconta-1(27),2,4,10,12,14(30),15,17,23,25,27,28,29-tridecaen-6,8,19,21-tetrayne.

(36), which was allowed to react with lithium acetylide in tetrahydrofuran[13]. The product *(37)* was treated with an acid to give the aldehyde *(38)*, whose dimethyl acetal *(39)*

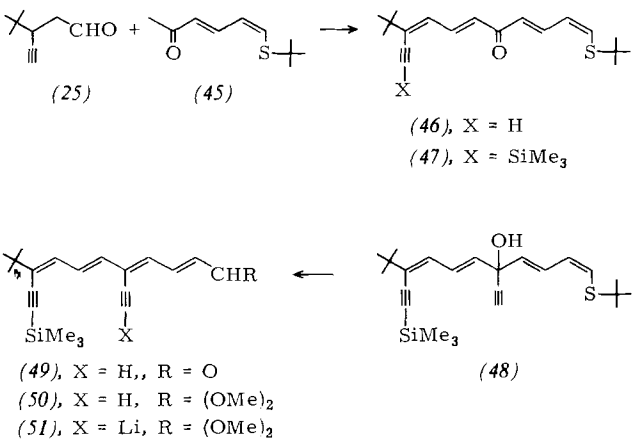


could be lithiated with butyllithium to *(40)*. Reaction of the lithium derivative *(40)* with the trimethylsilyl ketone *(36)*, followed by rearrangement and hydrolysis with an acid, yielded the dialdehyde *(41)* (yellow crystals). Chain-lengthening to give the diketone *(42)* could be achieved by reaction with the carbanion *(A)* derived from diethyl 3,3-dimethyl-2-oxobutanephosphonate[14]; *(42)* (yellow crystals) was obtained in 81% yield. Although cleavage of the trimethylsilyl groups was found to be difficult under the usual conditions, the desired intramolecular reaction could be realized by treatment of the bis(trimethylsilyl) diketone *(42)* with potassium hydroxide in liquid ammonia. A mixture of the diastereomeric bicyclic diols *(43)* (yellow crystals, 94% yield) was obtained.

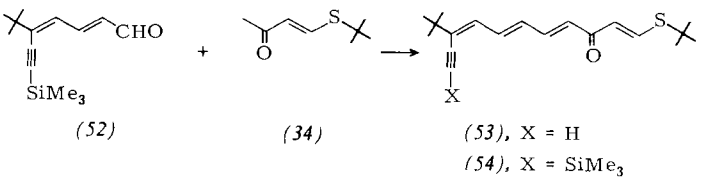
Treatment of *(43)* with tin(II) chloride in ether saturated with hydrogen chloride yielded the trisdehydro[10.10.2][14]-annuleno[14]annulene *(44)*[*] (stable reddish-purple crystals) in 77% yield[15]. The annulenoannulene *(44)* gave a 1:1 CT complex (purple crystals) with 2,4,7-trinitrofluorenone[15].

The successful synthesis and the interesting properties of the [14]annuleno[14]annulene *(44)* (see, Sections 3.1 and 3.2) encouraged us to prepare other members of this series of annulenoannulenes.

tert-Butylthiobutadienyl methyl ketone *(45)* was prepared by addition of 2-methyl-2-propanethiol in the presence of Triton B to 3-hexen-5-yn-2-one, which is readily accessible by the chromium trioxide oxidation of 3-hexen-5-yn-2-ol[16]. The aldol condensation of the diene ketone *(45)* with the enyne aldehyde *(25)*[10] afforded the tetraene ketone *(46)*, which was treated with lithium diethylamide followed by trimethylchlorosilane to give the trimethylsilyl ketone *(47)*. The ketone *(47)* was ethynylated with lithium acetylide in tetrahydrofuran[13] and the product *(48)* treated without isolation



with an acid to give the tetraene aldehyde *(49)* (orange-yellow crystals). The aldehyde *(49)* was converted into the dimethyl acetal *(50)* in the usual way and treated with butyllithium to give the lithium derivative *(51)*, which served as a moiety of construction of the [14]annuleno[18]annulene skeleton.



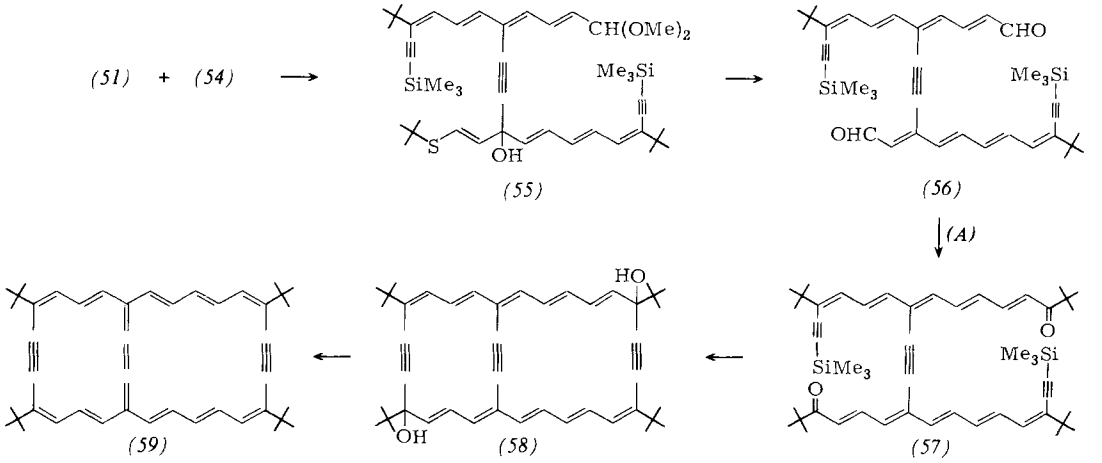
The tetraene ketone *(53)*, obtained by aldol condensation of the dienyne aldehyde *(52)*[17] with the methyl thiovinyl ketone *(34)*, could be silylated into the trimethylsilyl ketone *(54)* by the method used in the transformation of *(46)* to *(47)*. The product *(55)*, obtained by the reaction of *(51)* with *(54)*, was treated with an acid to give the dialdehyde *(56)* (yellow crystals, 68% overall yield). Reaction of *(56)* with the above mentioned carbanion *(A)* yielded the bis(trimethylsilyl) diketone *(57)* in 57% yield. Treatment of the diketone *(57)* without removal of the protective groups with a suspension of potassium hydroxide in liquid ammonia afforded the bicyclic diol *(58)* (yellow crystals 88% yield). The trisdehydro[14.10.2][14]annuleno[18]annulene *(59)*[*] was obtained in 90% yield on treatment of the bicyclic diol

[*] Systematic name of *(44)*: 5,8,16,19-tetra-*tert*-butylbicyclo[10.10.2]tetracosa-1(23),2,4,8,10,12(24),13,15,19,21,23-undecaen-6,17-diyne.

[*] Systematic name of *(59)*: 7,10,20,23-tetra-*tert*-butylbicyclo[14.10.2]octacosa-1(27),2,4,6,10,12,14,16(28),17,19,23,25,27-tridecaen-8,21-diyne.

(58) with tin(II) chloride in ether saturated with hydrogen chloride at low temperature[18]. The annulenoannulene (59) (deep-purple crystals) was found to be a stable compound which forms a 1:1 CT complex (deep-green crystals) with 2,4,7-trinitrofluorenone[18].

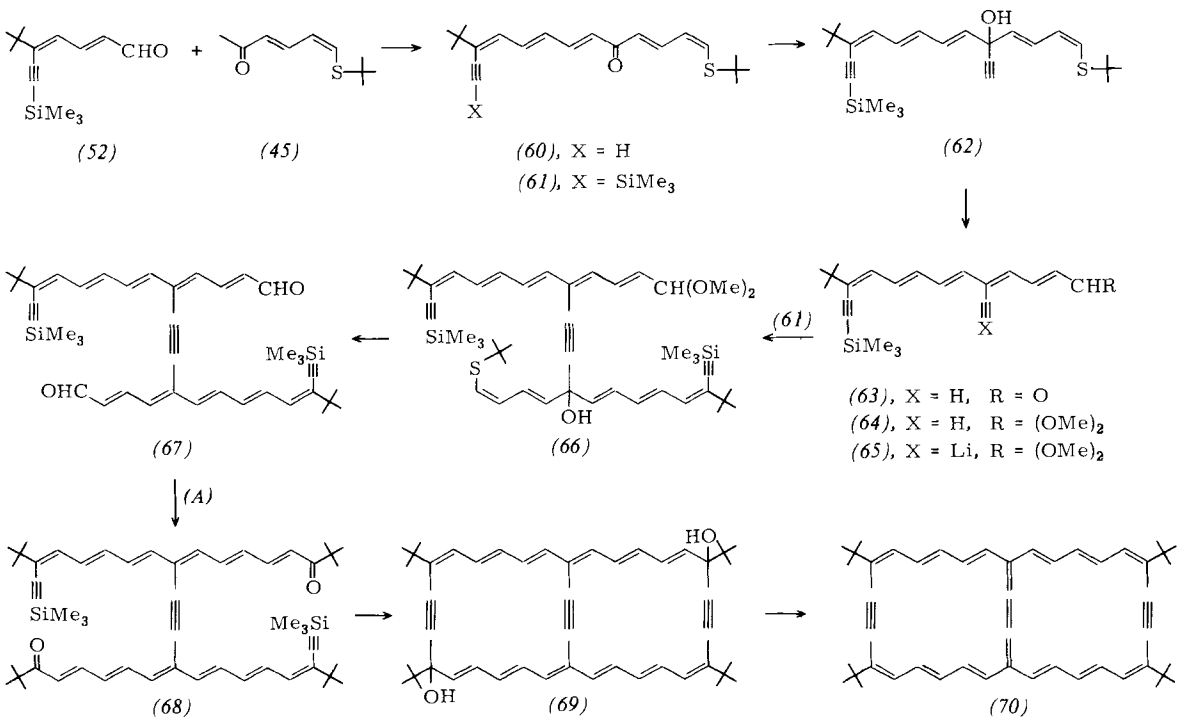
acid. Chain-lengthening with the carbanion (A) afforded the bis(trimethylsilyl) diketone (68) (orange crystals, 65% yield) having the desired skeleton of carbon atoms. On addition of a solution of the diketone (68) in tetrahydrofuran to a suspension of potassium hydroxide in liquid ammonia, the



For the synthesis of the trisdehydro[18]annuleno[18]annulene (70), the pentaenyne ketone (60), obtained by aldol condensation of (52)[17] with (45)[18], was firstly converted into the trimethylsilyl derivative (61) (yellow crystals) by the above-mentioned procedure. The ethynyl alcohol (62), obtained by reaction of (61) with lithium acetylide in tetrahydrofuran[13], was then treated without isolation with an acid to give the aldehyde (63) (orange crystals, 83% yield). The dimethyl acetal (64), which was obtained from (63) in the usual way, could be converted into the lithium derivative (65) by treatment with butyllithium. The product (66) of

bicyclic glycol (69) (orange yellow crystals) was obtained in 69% yield. A solution of tin(II) chloride in concentrated hydrochloric acid was added to a diluted solution of (69) in dichloromethane/tetrahydrofuran (20:1) at *ca.* −10°C. The tetra-*tert*-butyltrisdehydro[14.14.2][18]annuleno[18]annulene (70)[*] was obtained as sparingly soluble and fairly stable deep-green crystals in 89% yield[19].

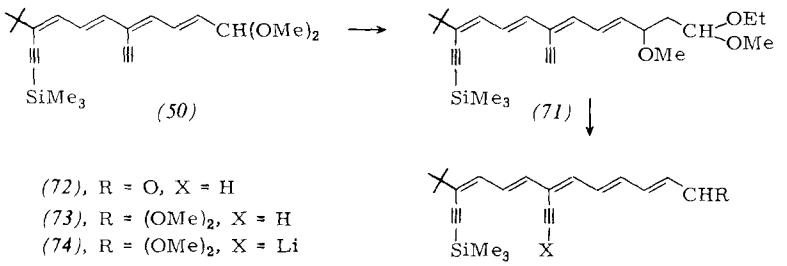
The tetraenedimethyl acetal (50) served as starting material for the synthesis of the trisdehydro[14]annuleno[22]annulene (82). (50) was allowed to react with ethyl vinyl ether in the presence of boron trifluoride etherate[20,21]. The resulting



the reaction of the lithium derivative (65) with the trimethylsilyl ketone (61) gave the dialdehyde (67) (orange crystals, 56% overall yield) on treatment without isolation with an

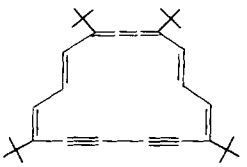
[*] Systematic name of (70): 7,10,22,25-tetra-*tert*-butylbicyclo[14.14.2]dotriaconta-1(31),2,4,6,10,12,14,16(32),17,19,21,25,27,29,31-pentadecaene-8,23-diyne.

methoxy acetal *(71)* was treated with diluted acetic acid containing sodium acetate to give the pentaene aldehyde *(72)*[21], which was converted in the usual way into the dimethyl acetal *(73)*. The lithium derivative *(74)* was obtained on treatment of *(73)* with butyllithium. The aldol condensation of the trimethylsilyltrienyne aldehyde *(75)*[17] with the thiovinyl

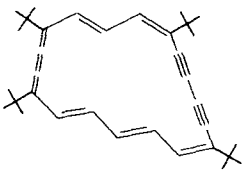


(72), R = O, X = H
(73), R = $(OMe)_2$, X = H
(74), R = $(OMe)_2$, X = Li

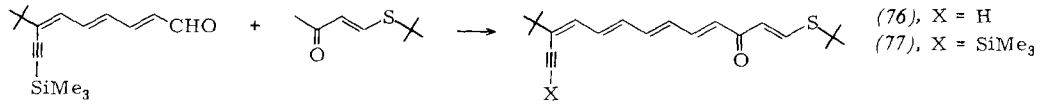
methyl ketone *(34)* gave the pentaenyne ketone *(76)* (yellow crystals), which could be converted into the trimethylsilyl derivative *(77)* (bright yellow crystals) by the previously mentioned method. The lithium derivative *(74)* was allowed to react with the trimethylsilyl pentaene ketone *(77)* and the product *(78)* was treated without isolation with an acid to give the dialdehyde *(79)* (orange-yellow crystals, 78 % yield).



(83)



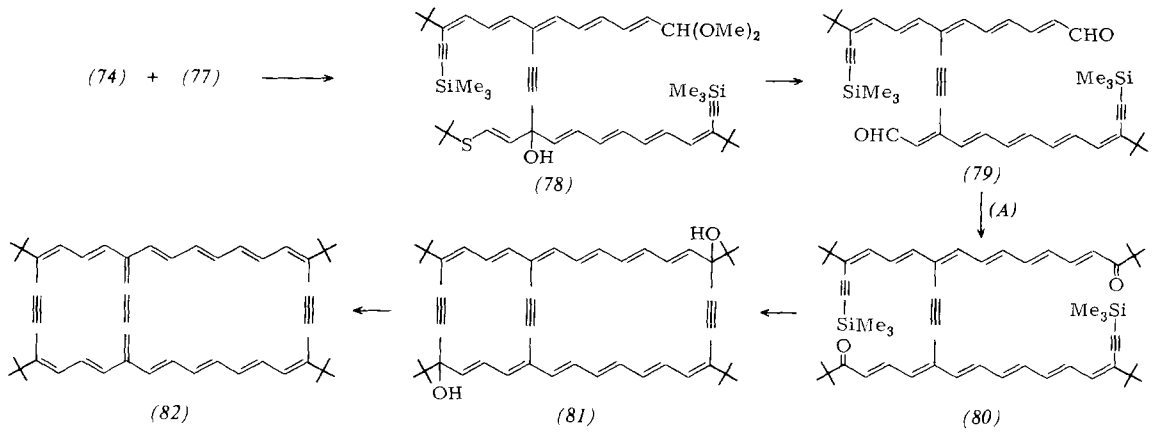
(84)



(76), X = H
(77), X = $SiMe_3$

The bis(trimethylsilyl) diketone *(80)* (red crystals) was obtained in 63 % yield by reaction of *(79)* with the carbanion *(A)*. The bicyclic diol *(81)* (brownish-yellow crystals, 80 % yield) was obtained on treatment of *(80)* with a suspension of potassium hydroxide in liquid ammonia. Reductive dehydroxylation of *(81)* with tin(II) chloride in ether saturated with hydrogen chloride afforded the fairly stable tetra-*tert*-butyltrisdehydro[18.10.2][14]annuleno[22]annulene *(82)*[*] (deep blue-green crystals, 92 %)[22].

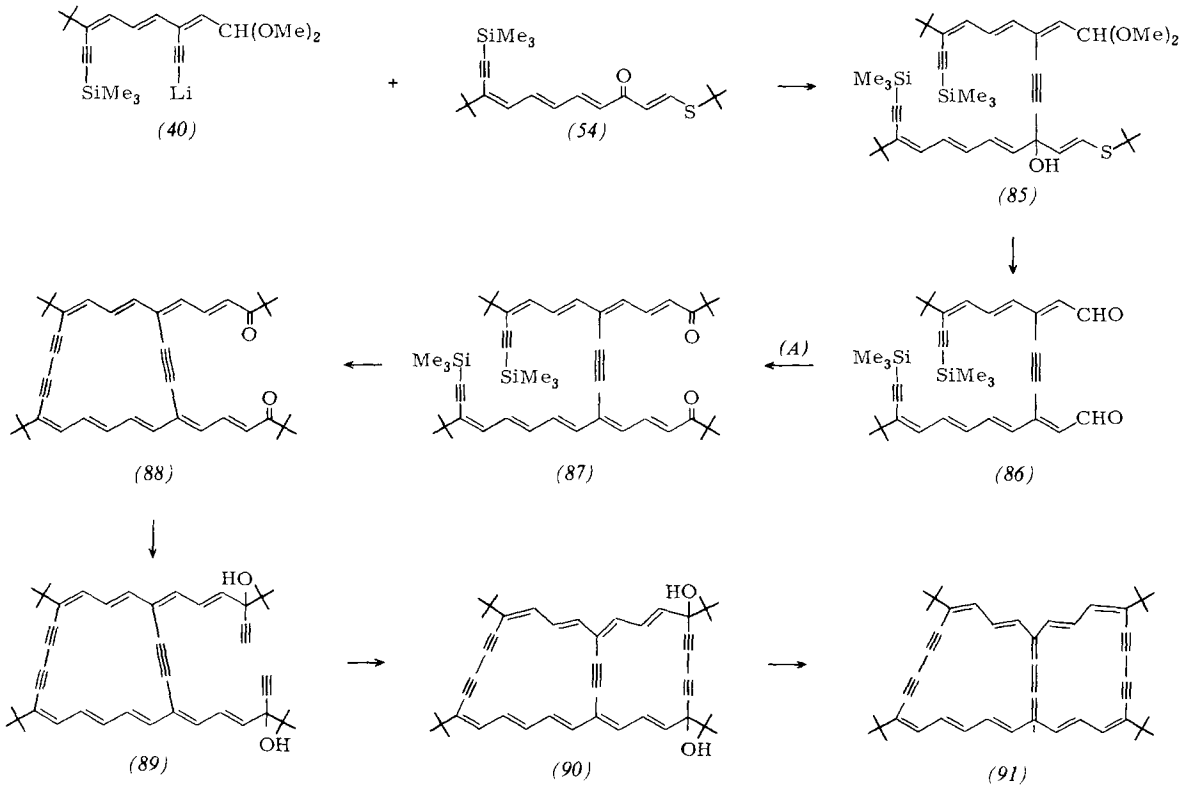
The lithium derivative *(40)* of the triene aldehyde dimethyl acetal *(39)*[15] was allowed to react with the tetraene ketone *(54)*[18] and the product *(85)* was treated with an acid to give the dialdehyde *(86)*. Reaction of *(86)* with the carbanion *(A)* yielded the diketone *(87)* (yellow crystals) in moderate yield. Oxidative coupling of the bis(trimethylsilyl) diketone *(87)* with copper(II) acetate in pyridine at 80—90 °C afforded



the cyclic triyne diketone *(88)* (orange-red crystals, 61 % yield), which could be bisethynylated with lithium acetylide in tetrahydrofuran[13] to give the monocyclic diol *(89)* (yellow liquid,

[*] Systematic name of *(82)*: 9,12,24,27-tetra-*tert*-butylbicyclo[18.10.2]dotriaconta-1(31),2,4,6,8,12,14,16,18,20(32),21,23,27,29,31-pentadecaen-10,25-diyne.

[*] Molecules whose NMR spectra show the effect of a paramagnetic ring current are called *paratropic* [1c].



89 % yield). *(89)* was again oxidized with copper(II) acetate in pyridine to give the bicyclic diol *(90)* (orange brown crystals, 80 % yield). Treatment of the bicyclic glycol *(90)* with tin(II) chloride in ether saturated with hydrogen chloride gave the pentakisdehydro[14.12.2][16]annuleno[18]annulene *(91)*[*] in the form of fairly stable deep-green crystals[25].

3. Properties

3.1. Electronic Spectra

The tetramethyltetrakisdehydroannulenoannulenes *(10)*, *(17)* and *(24)* have been reported to give rather complex electronic spectra; the data are summarized in Table 1[6b]. It has also been pointed out that the location of the strongest absorption maxima of these annulenoannulenes resemble those of the monocyclic dehydroannulenes[26] with the same number of π-electrons. As illustrated in Figure 1, the electronic spectrum of the tetra-*tert*-butylhexakisdehydro-[12.12.4][18]annuleno[18]annulene *(32)* consists of three main absorption bands, clearly showing features characteristic of aromatic [4*n*+2]annulenes; *i.e.*, the spectrum of *(32)* was found to be closely related to that of tetra-*tert*-butylbisdehydro[18]annulene *(98)*[10] except for its showing a bathochromic shift and hyperchromism[7].

Table 1. Absorption maxima in the electronic spectra of *ortho*-annelated tetrakisdehydroannulenoannulenes *(10)*, *(17)* and *(24)* and the strongest absorption maxima of the corresponding monocyclic dehydroannulenes (see [26]); in ether.

Annulenoannulene λ_{max} [nm] (ε)	Dehydroannulene λ_{max} [nm] (ε)
(10), [14][14] 258 (14400), 278 sh (16800), 292 (21100), 387 (45400), 552 sh (1050), 607* (580)	Monodehydro[26] 386 (152000) Trisdehydro[26] 383 (119000)
(17), [14][16] 258 sh (17600), 286 (28100), 350 sh (49100), 380 (61000), 405 sh (44300)	Bisdehydro[28] 373 (177000)
(24), [14][18] 275 (30300), 299 (35900), 395 (80200), 446 sh (25700), 589 sh (2200)	Trisdehydro[30] 397 (114000) Pentakisdehydro[30] 389 (141000)

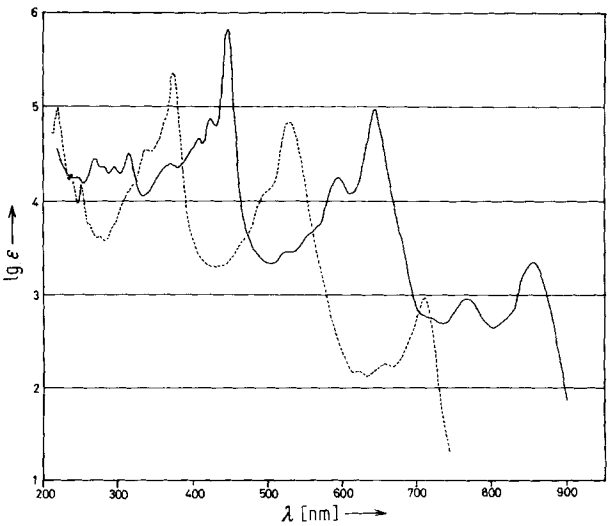


Fig. 1. Electronic spectra of hexakisdehydro[18]annuleno[18]annulene *(32)* (—) and tetrakisdehydro[18]annulene *(98)* (·····) (see Fig. 3) in tetrahydrofuran.

[*] Systematic name of *(91)*: 7,12,20,25-tetra-*tert*-butylbicyclo[14.12.2]-triaconta-1(29),2,4,6,12,14,16(30),17,19,25,27,29-dodecaene-8,10,21,23-tetrayne.

Table 2. Absorption maxima in the electronic spectra of the trisdehydroannulenoannulenes *(44)*, *(59)*, *(70)* and *(82)* and the corresponding monocyclic bisdehydro[4*n*+2]annulenes *(33)*, in tetrahydrofuran.

Annulenoannulene λ_{max} [nm] (ε)	Bisdehydroannulene λ_{max} [nm] (ε)
(44), [14][14] 216 (12300), 244 (15300), 250 (17500), 263 (20400), 274.5 (32700), 322.5 (12600), 371 (37300), 384 (114000), 401 (563000), 468 (4390), 492 sh (6470), 518 (19000), 553 (39900), 637 (480), 676 (1020), 742 (2140)	*(33)*, $n=3$ [22] 221.5 (10400), 248 (11900), 261 sh (8810), 277 sh (9200), 290 (12100), 302.5 (17100), 316.5 sh (9610), 377 sh (7720), 395 (147000), 412.5 (300000), 512 sh (6640), 556 (10400), 591 (11300), 712 sh (83), 757 (72), 782 (77), 853 sh (66), 895 (106)
(59), [14][18] 241.5 (16400), 250.5 (16100), 266.5 sh (22900), 274.5 (27300), 290.5 (33600), 323 sh (7890), 337 sh (12000), 346.5 (15900), 401.5 sh (59300), 417 (158000), 433.5 (219000), 501 sh (4800), 532 sh (6630), 564.5 (17400), 609 (26800), 685 (660), 750 sh (920), 760 (950), 845 (1140)	*(33)*, $n=4$ [26] 223.5 (15000), 268 sh (14000), 280 (15000), 285.5 (15000), 316 (24000), 330 (25000), 427 (170000), 442 sh (150000), 584 (9600), 840 sh (64), 930 (41), 975 (43)
(70), [18][18] 225.5 (17500), 265 (25400), 280.5 sh (25200), 289.5 (36200), 300 (30200), 319.5 (30400), 331 sh (15800), 348 (11500), 366 (18100), 384 (25200), 430 (75000), 450 (192000), 470 (752000), 534 (7080), 568 (8750), 608 (25400), 660 (36400), 765 (560), 835 (980), 932 (1520)	*(33)*, $n=5$ [30] 275.5 (18000), 324 sh (43000), 338 (56000), 352 (54000), 401 sh (78000), 451 (190000), 572 (11000), 607 (11000), 660 sh (8300)
(82), [14][22] 267 (23400), 292 sh (33100), 302.5 (39700), 325.5 sh (10400), 368 sh (24300), 427 sh (102000), 446 (203000), 465.5 (391000), 566.5 sh (11200), 603.5 (21300), 653 (21100), 740 (900), 825 (800), 945 (410)	*(33)*, $n=5$ [30] see above

The UV/VIS spectral data of the trisdehydroannulenoannulenes *(44)*, *(59)*, *(70)* and *(82)* are listed in Table 2 together with those of bisdehydro[4*n*+2]annulenes *(33)* corresponding to the periphery of the annulenoannulenes[17,34,35]. It should be noted that the longest wavelength absorption maxima of these 'acetylene-cumulene'-annulenoannulenes show appreciable hypsochromic shift as compared with those of the corresponding bisdehydroannulenes *(33)*. The absorption curves of the trisdehydroannulenoannulenes *(44)*, *(59)*, *(70)* and *(82)* are illustrated in Figure 2.

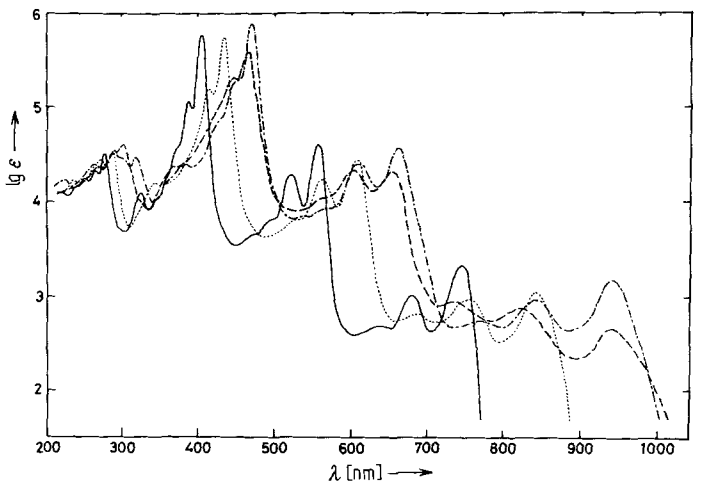
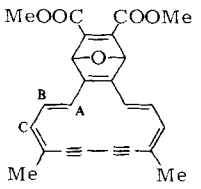


Fig. 2. Electronic spectra of trisdehydroannulenoannulenes [14][14] *(44)* (—), [14][18] *(59)* (·····), [18][18] *(70)* (– – –) and [14][22] *(82)* (-------) in tetrahydrofuran.

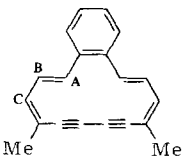
The electronic spectra of the 'acetylene-cumulene'-trisdehydroannulenoannulenes *(44)* and *(59)* exhibit a bathochromic shift and hyperchromism as compared with the spectra of the corresponding *ortho* annelated tetrakisdehydroannulenoannulenes *(10)* and *(24)*, presumably reflecting some difference in the π-electronic structure between the two series.

3.2. NMR Spectra

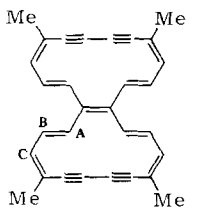
The effect of annelation on the diatropicity of the dimethylbisdehydro[14]annulene moiety in the *ortho*-annelated tetramethyltetrakisdehydroannulenoannulenes *(10)*, *(17)* and *(24)* has already been discussed[6b], comparing the ^{1}H-NMR



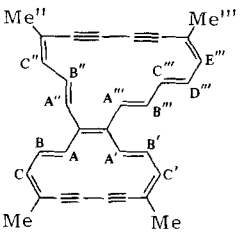
(92)



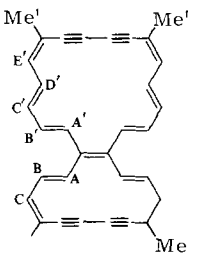
(93)



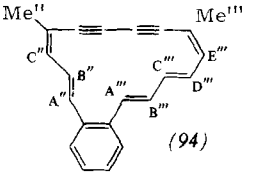
(10)



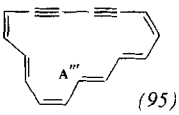
(17)



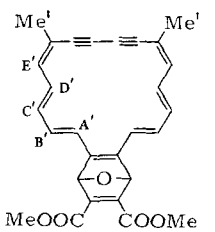
(24)



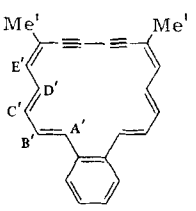
(94)



(95)



(97)



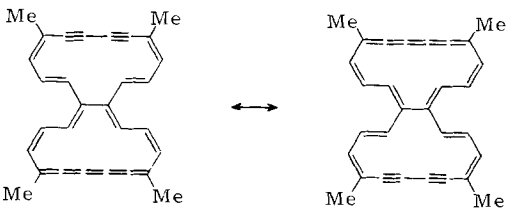
(96)

spectra with those of the reference substances *(92)*[27] and *(93)*[27]. The resonances of H^C, $H^{C'}$ and CH_3, CH_3' were used as a probe for the ring current, because these protons are furthest from the point of annelation, and must be conformationally stable. The ^{1}H-NMR parameters are summarized in Table 3. The fact that the inner protons move to higher field and the outer ones to lower field on going from *(93)* to *(10)* indicates that the diamagnetic ring current in the

Table 3. Some ^{1}H-NMR parameters of dimethylbisdehydro[14]annulenes in $CDCl_3$ at 100 or 220 MHz (τ values; Me_4Si int.).

Compound	H^A, $H^{A'}$	H^B, $H^{B'}$	H^C, $H^{C'}$	CH_3, CH_3'
(92)	12.12	1.22	1.79	7.02
(24) [14][18]	8.22	1.77	2.28	7.28
(17) [14][16]	8.58	2.17	2.46	7.33
	8.68	2.37	2.50	
(10) [14][14]	6.18	2.13	2.69	7.52
(93) [14][6]	5.01	2.56	2.92	7.64

14-membered ring in *(10)* is greater than in *(93)*. It has been suggested that the equivalent Kekulé structures *(10a)* and *(10b)* may be responsible for the enhanced diatropicity of *(10)*[6b]. It is concluded that the diatropicity of the 14-mem-



(10a) *(10b)*

bered ring decreases with decreasing size of the annelated annulene [*(92)* > *(24)* > *(17)* > *(10)* > *(93)*][6b]. (Compound *(92)* is *not* an annulenoannulene.) The fact that the signals of H^A, $H^{A'}$ and H^B, $H^{B'}$ in the [14]annuleno[16]annulene *(17)* are at higher field than would be expected from the H^C, $H^{C'}$ and CH_3, CH_3' resonances is attributed to the shielding effect of the paramagnetic ring current in the 16-membered ring[6b].

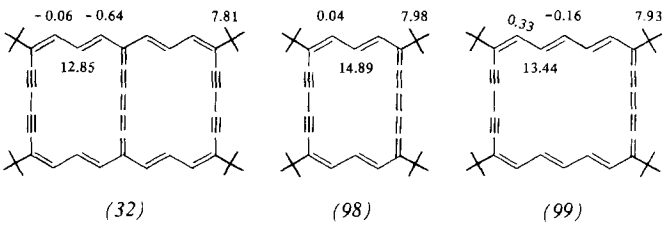
The ^{1}H-NMR spectroscopic data of the bisdehydro[16]annulene moiety in the tetramethyltetrakisdehydro[14]annulene[16]annulene *(17)* and in the dimethylbisdehydrobenzo[16]annulene *(94)*[4e] and the A''' signal of the 1,3-bisdehydro[16]annulene *(95)* are given in Table 4. The 16-membered rings in *(17)* and *(94)* are clearly paratropic, showing the inner proton signals at low field and the outer proton signals at high field. However, marked suppression of paratropicity of the bisdehydro[16]annulene ring on annelation with a [4*n*+2]-membered ring was shown by comparison with the resonance of the A''' proton in the 1,3-bisdehydro[16]annulene *(95)*. The chemical shifts of the outer protons in *(95)* cannot be compared with the corresponding ones in *(17)* and *(94)*, since, in contrast to the conformational stability of *(17)* and *(94)*, *(95)* is conformationally mobile, as evidenced by the temperature dependent NMR spectra[28]. The fact that both of the inner and outer proton signals move to lower field and the magnitude of the low field shift decreases with increasing distance of the protons from the [4*n*+2]-membered rings should be ascribed to the deshielding effect of the diatropic rings. The negligible effect for the furthest removed protons ($H^{D'''}$, $H^{E'''}$, CH_3''' and CH_3'''') showed that the paramagnetic ring currents of the 16-membered rings in *(17)* and *(94)* are essentially the same, regardless of the size of the annelated diatropic rings. This is in contrast to the above-mentioned dependency of diatropicity of 14-membered rings on the size of the annelated rings.

The ^{1}H-NMR resonances of the 18-membered ring protons in the [14]annuleno[18]annulene *(24)*, in the dimethylbisdehydro[18]annulene *(96)*[4e], and in the "model" compound *(97)*[29] are given in Table 5. The high field inner proton signals and the low field outer proton resonances show the 18-membered ring in these compounds to be diatropic, although the diatropicity is clearly greatly reduced by the annelation of the 14- and 6-membered rings.

Table 5. Some ^{1}H-NMR parameters of dimethylbisdehydro[18]annulenes in $CDCl_3$ at 100 or 220 MHz (τ values; Me_4Si int.).

Compound	$H^{A'}$	$H^{B'}$	$H^{C'}$	$H^{D'}$	$H^{E'}$	CH_3'
(97)	10.38	1.98	1.48	11.06	1.30	6.94
(24) [18][14]	4.40	2.79	3.69	4.27	2.93	7.68
(96) [18][6]	4.77	2.76	3.15	5.05	2.83	7.72

The ^{1}H-NMR parameters of the hexakisdehydro[12.12.4]-[18]annuleno[18]annulene *(32)* are shown in Figure 3 together with those of the monocyclic analogues *(98)*[10] and *(99)*[21]. The most remarkable characteristic of the NMR spectrum of *(32)* is the downfield shift of both the inner and outer protons as compared with those in *(98)* and *(99)*.



(32) *(98)* *(99)*

Δτ 13.49, 12.91 14.85 13.60, 13.11

Fig. 3. ^{1}H-NMR parameters (τ values) of hexakisdehydro[18]annuleno[18]annulene *(32)* and related tetradehydro[18]- and [22]annulenes *(98)* and *(99)*, resp. Δτ is the difference in chemical shift of the inner and outer protons.

Table 4. Some ^{1}H-NMR parameters of dimethylbisdehydro[16]annulenes in $CDCl_3$ at 100 or 220 MHz (τ values; Me_4Si int.).

Compound	$H^{A''}$	$H^{B''}$	$H^{C''}$	$H^{A'''}$	$H^{B'''}$	$H^{C'''}$	$H^{D'''}$	$H^{E'''}$	CH_3'''', CH_3''''
(17) [14][16]	2.99	−0.04	3.72	0.54	3.42	0.13	4.25	4.01	8.26, 8.32
(94) [16][6]	3.89	0.55	3.93	1.10	3.80	0.58	4.27	4.06	8.30
(95) [16]				−3.05					

The ^{1}H-NMR parameters of the trisdehydro[4*n*+2]annuleno[4*n*+2]annulenes *(44)*, *(59)*, *(70)* and *(82)* are presented

together with those of the related monocyclic bisdehydro-[4n+2]annulenes in Figures 4 to 6.

The difference in chemical shifts between inner and outer protons ($\Delta\tau = \tau_i - \tau_o$) was regarded as an approximate measure of the diamagnetic ring current in the bisdehydro[4n+2]annulenes *(33)*, n=1—5[1g]. The decrease in $\Delta\tau$ could possibly be in agreement with the theoretical prediction of decreasing resonance energy per π-electron or increasing bond-alternation with increasing ring size[30]. It must be noted that the peripheries of the annulenoannulenes *(32)*, *(44)*, *(59)*, *(70)* and *(82)* are Hückel type [4n+2]π-electron systems.

As can be seen from Figure 4, the ^{1}H-NMR characteristics of the hexakisdehydro[18]annuleno[18]annulene *(32)* are also to be found in the spectrum of the trisdehydro[14]annuleno[14]annulene *(44)*: both the outer and the inner protons in *(44)* show a downfield shift as compared with those of the parent tetra-*tert*-butylbisdehydro[14]annulene *(33)*, n=1[1g, 31]. The $\Delta\tau$ values for the annulenoannulene *(44)* were found to be much larger than those for the bisdehydro[22]annulene *(33)*, n=3, which correspond to the periphery of *(44)*. The conformational stability of the bisdehydro-[22]annulene *(33)*, n=3, has been proven by the essentially temperature-independent NMR spectra[21]; the almost planar structure has been revealed by X-ray structure analysis[32]. Hence, the much higher $\Delta\tau$ values found for the annulenoannulene *(44)* cannot be attributed to an enhancement of rigidity of planarity of the molecular periphery of *(33)*, n=3, caused by the introduction of the acetylenic bridge at the central position.

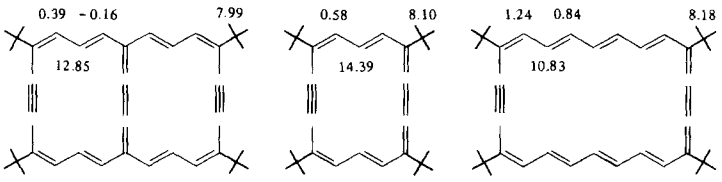


Fig. 4. ^{1}H-NMR parameters (τ values) of the trisdehydro[14]annuleno[14]annulene *(44)*, and the related bisdehydro[14]- and [22]annulenes *(33)*, n=1 and 3, respectively.

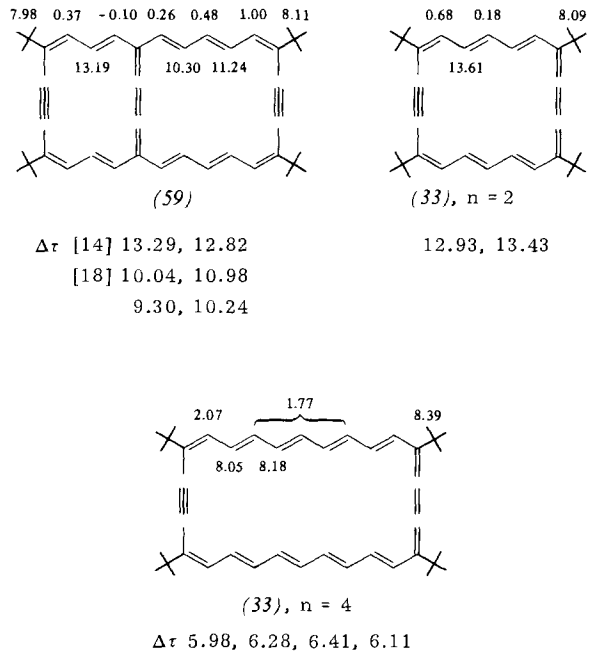


Fig. 5. ^{1}H-NMR parameters (τ values) of the trisdehydro[14]annuleno[18]annulene *(59)*, and the related bisdehydro[18]- and [26]annulenes *(33)*, n=2 and 4, respectively.

n=2 and n=4. The outer proton signals move to higher field as the distance from the bridge is increased. The same trend is observed in the chemical shifts of the inner protons in the 18-membered ring. It should be noted that the $\Delta\tau$ values in the 14-membered ring are much larger than in the 18-membered ring. As shown in Figure 5, the bisdehydro[26]annulene *(33)*, n=4[1g,33], which corresponds to the periphery of the annulenoannulene *(59)*, has much smaller $\Delta\tau$ values than *(59)*.

The ^{1}H-NMR parameters for the [18]annuleno[18]annulene *(70)*[19], the [14]annuleno[22]annulene *(82)*[22] and the bisdehydro[30]annulene *(33)*, n=5[1g, 34], are shown in Figure 6. As in the annulenoannulenes *(44)* and *(59)*, in *(70)* and *(82)* both the signals of the inner and the outer protons shift upfield with increasing distance from the bridge. The signal of an inner proton in the 22-membered ring in *(82)*

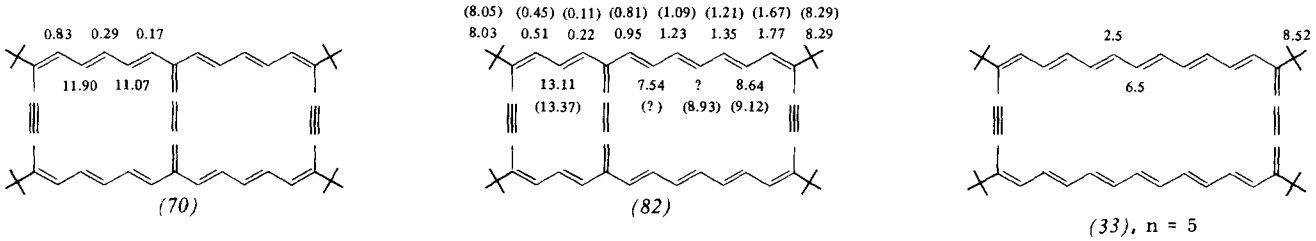


Fig. 6. ^{1}H-NMR parameters (τ values) of the trisdehydro[18]annuleno[18]annulene *(70)*, the trisdehydro[14]annuleno[22]annulene *(82)*, and the related bisdehydro[30]annulene *(33)*, n=5. The data in brackets for *(82)* are the τ values at −60 °C.

The ^{1}H-NMR parameters of the trisdehydro[14]annuleno[18]annulene *(59)*[18] are presented in Figure 5 together with those of the related bisdehydro[4n+2]annulenes *(33)*, is submerged under the tail of strong *tert*-butyl proton signals. As in *(44)* and *(59)* the $\Delta\tau$ values for the annulenoannulenes *(70)* and *(82)* are found to be much larger than that for

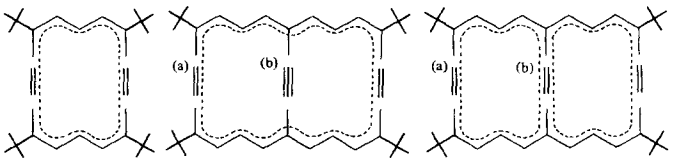
the bisdehydro[30]annulene *(33)*, $n=5$, which corresponds to the periphery of *(70)* and *(82)*. Both of the annulenoannulenes *(70)* and *(82)* were found to be fairly stable compounds, in sharp contrast to the extremely unstable nature of the [30]annulene *(33)*, $n=5$. The ^{1}H-NMR spectral behavior of the trisdehydro[14]annuleno[4n+2]annulenes *(59)*, $n=4$, and *(82)*, $n=5$, can be explained assuming the induction of diamagnetic ring currents of different intensity in each ring. The diamagnetic ring current in the 14-membered ring in *(59)* or *(82)* exerts a deshielding effect on all the protons of the 18- or 22-membered ring, respectively; the increase in the upfield shift of the signals with increasing distance from the 14-membered ring can be reasonably attributed to the diminishing deshielding effect upon remote protons. Similarly all the protons in the 14-membered ring suffer the deshielding effect of the 18- or 22-membered ring, resulting in a downfield shift.

It has been argued that diamagnetic ring currents of different intensity are induced in the neighboring benzene nuclei in polycondensed aromatic hydrocarbons such as anthracene and perylene[35]. The above-mentioned ^{1}H-NMR spectroscopic behavior of the annulenoannulenes *(59)* and *(82)* would seem to afford firm experimental evidence for the theoretical argument on the induction of ring currents of different intensity.

The trisdehydroannulenoannulenes *(32)*, *(44)* and *(70)* consisting of two equally sized dehydroannulenes exhibit quite similar ^{1}H-NMR spectroscopic characteristics to those of the annulenoannulenes *(59)* and *(82)* made up of two differently sized dehydroannulenes. The ring current of naphthalene has been considered to be confined to the 10π periphery, for if two identical ring currents were induced in both rings, the current across the common bond would have to be zero. If a trisdehydro[4n+2]annuleno[4n+2]annulene such as the trisdehydro[14]annuleno[14]annulene *(44)*, *i.e.* a bisdehydro[22]annulene, which is weakly perturbed by the acetylenic bridge, sustains the ring current along the periphery [see *(44a)*], it can be regarded as a resonance hybrid of two canonical forms *(44b)* and *(44c)*. Consequently, the sp-sp bond of the central bridge should have a higher acetylenic character than the other sp-sp linkages in the periphery. On the other hand, if the [14]annuleno[14]annulene *(44)* is an annelated system consisting of two independent diatropic 14π-electron systems [see *(44d)*] and can be regarded as a resonance hybrid of three main canonical forms *(44b)*, *(44c)* and *(44e)*, the mixed acetylene- and cumulene-character in the three sp-sp linkages should almost be the same.

The ^{13}C-NMR spectra of bisdehydro[14]-, bisdehydro[18]- and bisdehydro[22]annulenes *(33)*, $n=1$, 2 and 3, resp., show a single signal of the sp-hybridized carbon atoms, namely at $\delta=116.7$, 115.7 and 116.8, respectively, thus indicating the acetylene-cumulene hybrid nature of the sp-hybridized carbon atoms in the highly delocalized aromatic systems[36]. The observed ^{13}C chemical shifts agree fairly well with the arithmetical average of the chemical shifts of acetylene and cumulene carbon atoms of relevant reference compounds ($\delta=85$ and 153, respectively). The observed and weighted arithmetical mean values of the chemical shifts of sp-hybridized carbon atoms in the bisdehydro[14]annulene *(33)*, $n=1$, and the trisdehydro[14]annuleno[14]annulenes *(44a)* and *(44d)* are listed in Table 6. The good agreement between calculated and observed values for the shifts in *(33)*, $n=1$, would seem to reflect the hybrid acetylenic and cumulenic nature of the sp-hybridized carbon atoms (50:50). The weighted mean values based on the structure *(44d)* were found to be in good agreement with the observed values; however, this was not so in the case of *(44a)*.

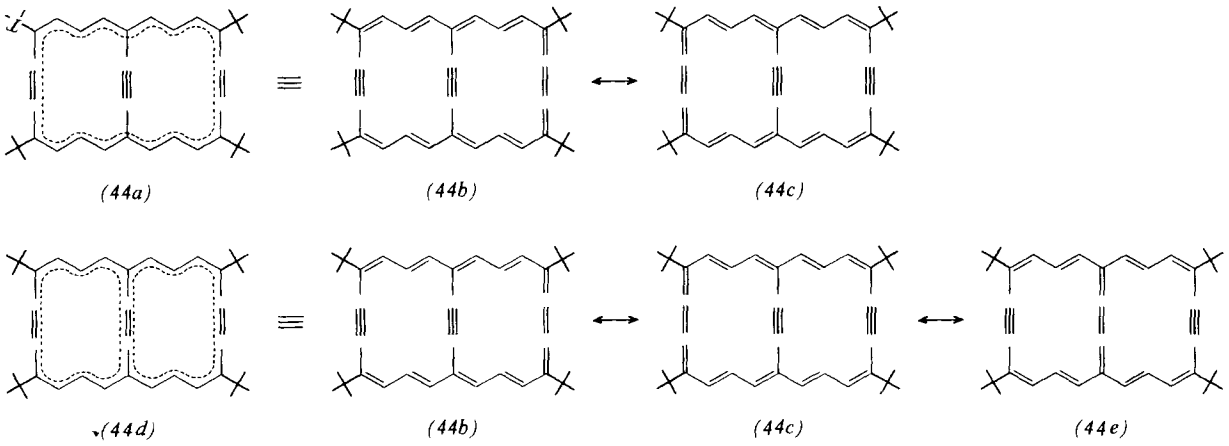
Table 6. ^{13}C-chemical shifts (δ values) of the sp-hybridized carbon atoms in the compounds *(33)*, $n=1$, and *(44a)* and *(44d)* [a].



(33), n = 1 *(44a)* *(44d)*

Cpd.	$\delta_{obs.}$	$\delta_{calc.}$
(33), $n=1$	116.7	(153+85)/2 = 119
(44a)	(a) 107.1	(153+85)/2 = 119
	(b) 102.4	(85+85)/2 = 85
(44d)	(a) 107.1	(153+85+85)/3 = 107.7
	(b) 102.4	(85+85+153)/3 = 107.7

[a] The following chemical shifts were used in the calculations: —C≡C—, $\delta=85$; =C=C=, $\delta=153$.



(44a) *(44b)* *(44c)*

(44d) *(44b)* *(44c)* *(44e)*

The lengths of the three sp-sp bonds in *(44)* have been determined by X-ray structure analysis (Fig. 7)[37]. Consistent with the ^{13}C-NMR spectral properties no appreciable differ-

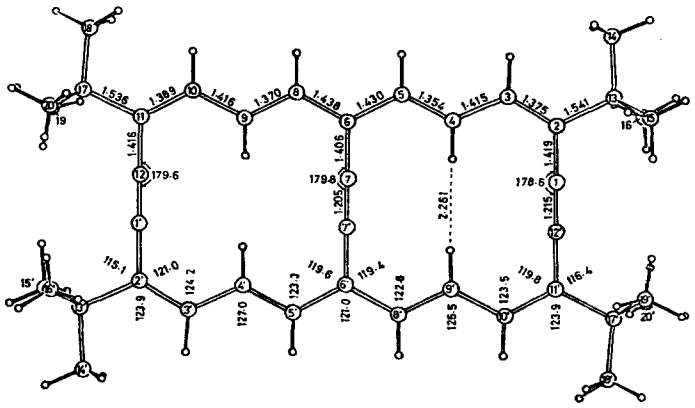


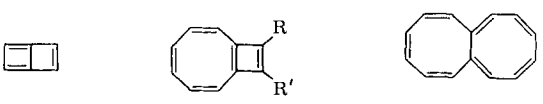
Fig. 7. Bond lengths [Å] and angles [°] in the trisdehydro[14]annuleno[14]annulene *(44)*.

ence between these three sp-sp linkages could be observed. As pointed out previously, it seems to be difficult to explain the ^{1}H-NMR spectra of the annulenoannulenes consisting of two equally sized dehydroannulenes [*(32)*, *(44)* and *(70)*] on the basis of a ring current along the periphery. It would appear that the problem concerning the induction of a diamagnetic ring current in bicyclic systems made up of two annelated diatropic nuclei will have to await a more rigorous theoretical exploration.

The spectroscopic properties of the pentakisdehydro-[14.12.2][16]annuleno[18]annulene *(91)* are presently being studied. The annulene *(91)* sustains fairly strong paramagnetic and diamagnetic ring currents in each ring. However, further discussion would be premature at the moment.

4. [4*n*]Annuleno[4*n*]annulenes

[4*n*]Annuleno[4*n*]annulenes consisting of two annelated antiaromatic [4*n*]annulenes and containing a total of $[4n+2]\pi$-electrons are particularly interesting since they possibly represent a new class of nonbenzenoid aromatic compounds. The question as to whether they have antiaromatic or aromatic character has been the subject of experimental and theoretical studies. The formation and synthesis of lower members of the [4*n*]annuleno[4*n*]annulenes have been reported; *e.g.* generation of [4]annuleno[4]annulene (butalene) *(100)* has been confirmed by a trapping experiment[38], and derivatives of the [4]annuleno[8]annulene *(101)* have been synthesized and proved to have olefinic character[39]. Quite recently, [8]annuleno[8]annulene (octalene) *(102)* could be synthesized and characterized as a conformationally mobile olefinic compound[40].

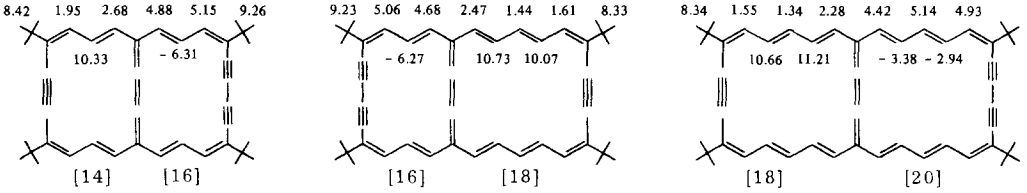


(100) *(101)* *(102)*

A higher planar [4*n*]annuleno[4*n*]annulene is as yet unknown. We have attempted the preparation of a pentakisdehydro[12.12.2][16]annuleno[16]annulene (made up of two trisdehydro[16]annulenes *(83)*) and an analogous pentakisdehydro[16.16.2][20]annuleno[20]annulene. However, the precursors, *i.e.* the corresponding bicyclic diols, were found to persistently resist reductive dehydroxylation, which has been successfully applied in the preparation of $[4n+2]$annulenes, [4*n*]annulenes, $[4n+2]$annuleno$[4n+2]$annulenes and [4*n*]annuleno$[4n+2]$annulenes. However, no conclusions should be be drawn from these negative results.

5. Addendum

Recently the syntheses of a series of trisdehydro[4*n*]-annuleno$[4n+2]$annulenes have been achieved by our group[41]. Unexpectedly, their ^{1}H NMR spectra indicate that



the antiaromatic $4n\pi$ electron systems show a tendency to preserve their inherent paratropicity resulting in a marked suppression of diatropicity of the aromatic moieties (see the chemical shifts—τ-values—in the formulas). The same trend has been observed in the conformationally mobile pentakisdehydro[16]annuleno[18]annulene *(91)*.

Received: January 9, 1978 [A 259 IE]
German version: Angew. Chem. *91*, 215 (1979)

[1] For recent reviews on annulenes, see, a) *F. Sondheimer*, Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 125 (1969); b) Pure Appl. Chem. *28*, 331 (1971); c) Acc. Chem. Res. *5*, 81 (1972); d) Chimia *28*, 163 (1974); e) *T. Nozoe, R. Breslow, K. Hafner, S. Itô* and *I. Murata*: Topics in Nonbenzenoid Aromatic Chemistry. Hirokawa, Tokyo 1973; f) *M. Nakagawa* in [1e], Vol. 1, p. 191; g) Pure Appl. Chem. *44*, 885 (1975).

[2] For recent reviews on bridged annulenes, see, a) *E. Vogel*, Chimia *22*, 21 (1968); b) Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 215 (1969); c) Pure Appl. Chem. *28*, 355 (1971); d) *V. Boekelheide*, Proc. Robert A. Welch Found. Conf. Chem. Res. *12*, 83 (1969); e) in [1e], Vol. 1, p. 47; f) Pure Appl. Chem. *44*, 77 (1975); g) *E. Vogel* in [1e], Vol. 2, p. 243.

[3] *M. Iyoda, M. Morigaki, M. Nakagawa*, Tetrahedron Lett. *1974*, 817, 3677; *A. Yasuhara, T. Satake, M. Iyoda, M. Nakagawa, ibid. 1975*, 895; *M. Morigaki, M. Iyoda, M. Nakagawa, ibid. 1975*, 2311, 2315; *Y. Yasuhara, M. Iyoda, T. Satake, M. Nakagawa, ibid. 1975*, 3931; *M. Iyoda, M. Nakagawa*, Chem. Lett. *1974*, 815.

[4] a) *R. T. Weavers, F. Sondheimer*, Angew. Chem. *86*, 167 (1974); Angew. Chem. Int. Ed. Engl. *13*, 141 (1974); b) *R. H. Wightman, F. Sondheimer*, Tetrahedron Lett. *1975*, 4179; c) *R. R. Jones, J. M. Brown, F. Sondheimer, ibid. 1975*, 4183; d) *R. H. Wightman, T. M. Cresp, F. Sondheimer*, J. Am. Chem. Soc. *98*, 6052 (1976); e) *N. Darby, T. M. Cresp, F. Sondheimer*, J. Org. Chem. *42*, 1960 (1977).

[5] *U. Meissner, B. Meissner, H. A. Staab*, Angew. Chem. *85*, 957 (1973); Angew. Chem. Int. Ed. Engl. *12*, 916 (1973).

[6] a) *T. M. Cresp, F. Sondheimer*, J. Am. Chem. Soc. *97*, 4412 (1975); b) *99*, 194 (1977).

[7] *T. Kashitani, A. Akiyama, M. Iyoda, M. Nakagawa*, J. Am. Chem. Soc. *97*, 4424 (1975).

[8] *P. J. Beeby, R. T. Weavers, F. Sondheimer*, Angew. Chem. *86*, 163 (1974); Angew. Chem. Int. Ed. Engl. *13*, 138 (1974).

[9] *M. Gaudemar*, Ann. Chim. (Paris) *1*, 161 (1956); *G. Prévost, M. Gaudemar, L. M. Miginiac, F. Bardone-Gaudemar, M. Andrac*, Bull. Soc. Chim. Fr. *1959*, 679.

[10] *T. Katakami, S. Tomita, K. Fukui, M. Nakagawa*, Chem. Lett. *1972*, 225; *S. Tomita, M. Nakagawa*, Bull. Chem. Soc. Jpn. *49*, 302 (1976).

[11] D. F. Beumel, Jr., R. F. Harris, J. Org. Chem. 28, 2775 (1963); 29, 1872 (1964).
[12] Cf. K. Bowden, E. A. Braude, E. R. H. Jones, J. Chem. Soc. 1946, 945; E. N. E. N. Prilezhaeva, G. S. Vasil'ev, I. L. Mikhlashvili, V. S. Bogdavov, Zh. Org. Khim. 7 (7), 1349 (1971).
[13] M. M. Midland, J. Org. Chem. 40, 2250 (1973).
[14] G. Sturz, Bull. Soc. Chim. Fr. 1964, 2349.
[15] S. Akiyama, M. Iyoda, M. Nakagawa, J. Am. Chem. Soc. 98, 6410 (1976).
[16] Cf. E. R. H. Jones, J. T. McCombie, J. Chem. Soc. 1942, 733; 1943, 261; K. Bowden, I. M. Heilbron, E. R. H. Jones, B. C. L. Weedon, ibid. 1946, 39; K. Bowden, E. A. Braude, E. R. H. Jones, ibid. 1946, 945.
[17] M. Iyoda, M. Nakagawa, J. Chem. Soc. Chem. Commun. 1972, 1003.
[18] S. Nakatsuji, S. Akiyama, M. Nakagawa, Tetrahedron Lett. 1977, 3723.
[19] M. Osuka, Y. Yoshikawa, S. Akiyama, M. Nakagawa, Tetrahedron Lett. 1977, 3719.
[20] Cf. M. Müller-Cunradi, K. Pieroth, US-Pat. 2165962 (1936); R. Rüegg, M. Montavon, G. Ryser, G. Saucy, U. Schwieter, O. Isler, Helv. Chim. Acta 42, 854 (1959) and preceding papers.
[21] M. Iyoda, H. Miyazaki, M. Nakagawa, J. Chem. Soc. Chem. Commun. 1972, 431; Bull. Chem. Soc. Jpn. 49, 2306 (1976).
[22] S. Nakatsuji, S. Akiyama, M. Nakagawa, unpublished.
[23] S. Nakatsuji, M. Morigaki, S. Akiyama, M. Nakagawa, Tetrahedron Lett. 1975, 1233.
[24] M. Osuka, S. Akiyama, M. Nakagawa, Tetrahedron Lett. 1977, 1649.
[25] S. Nakatsuji, S. Akiyama, M. Nakagawa, unpublished.
[26] P. Garratt, K. Grohmann in Houben-Weyl: Methoden der Organischen Chemie. Vol. V, Part 1d. Thieme, Stuttgart 1972, p. 533.
[27] R. T. Weavers, F. Sondheimer, Angew. Chem. 86, 165 (1974); Angew. Chem. Int. Ed. Engl. 13, 139 (1974).
[28] I. C. Calder, Y. Gaoni, P. J. Garratt, F. Sondheimer, J. Am. Chem. Soc. 90, 4954 (1968).
[29] R. H. Wightman, T. M. Cresp, F. Sondheimer, J. Am. Chem. Soc. 98, 6052 (1976).
[30] H. P. Figeys in D. Lloyd: Topics in Carbocyclic Chemistry. Vol. 1. Logos Press, London 1969, p. 269.
[31] K. Fukui, T. Nomoto, S. Nakatsuji, M. Nakagawa, Tetrahedron Lett. 1972, 3157; K. Fukui, T. Nomoto, S. Nakatsuji, S. Akiyama, M. Nakagawa, Bull. Chem. Soc. Jpn. 50, 2758 (1977).
[32] C. Kabuto, Y. Kitahara, M. Iyoda, M. Nakagawa, Tetrahedron Lett. 1976, 2787.
[33] M. Iyoda, M. Nakagawa, Tetrahedron Lett. 1972, 4253.
[34] M. Iyoda, M. Nakagawa, Tetrahedron Lett. 1973, 4743.
[35] See, e.g. N. Jonathan, S. Gordon, B. P. Dailey, J. Chem. Phys. 36, 2443 (1962); J. D. Memory, ibid. 38, 1341; H. P. Figeys, Tetrahedron Lett. 1966, 4625.
[36] S. Nakatsuji, M. Nakagawa, Tetrahedron Lett. 1975, 3927.
[37] N. Kasai, Y. Kai, N. Yasuda, S. Akiyama, M. Nakagawa, unpublished.
[38] R. Breslow, J. Napierski, T. C. Clarke, J. Am. Chem. Soc. 97, 6275 (1975).
[39] G. Schröder, H. Röttle, Angew. Chem. 80, 665 (1968); Angew. Chem. Int. Ed. Engl. 7, 635 (1968).
[40] E. Vogel, H.-V. Runzheimer, F. Hogrefe, B. Baasner, J. Rex, Angew. Chem. 89, 909 (1977); Angew. Chem. Int. Ed. Engl. 16, 871 (1977); J. F. M. Oth, K. Müllen, H.-V. Runzheimer, P. Mues, E. Vogel, ibid. 89, 910 (1977) bzw. 16, 872 (1977).
[41] M. Nakagawa et al., unpublished.

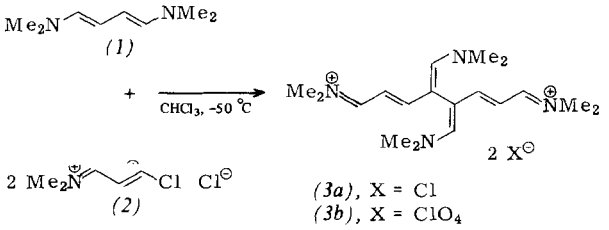
COMMUNICATIONS

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

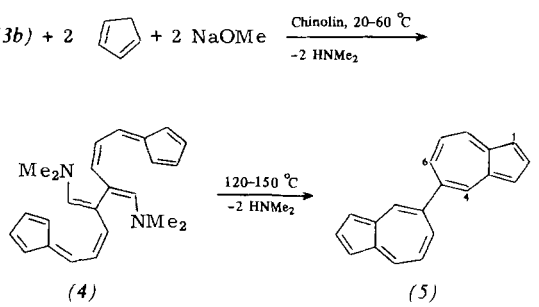
Synthesis of 5,5'-Biazulenyl[**]

By *Manfred Hanke* and *Christian Jutz*[*]

Directed synthesis of the hitherto unknown species 5,5'-biazulenyl *(5)* has been accomplished by the Ziegler-Hafner procedure[1] with the pentamethinium salt *(3b)*. Reaction of *(3b)* with cyclopentadiene and sodium methoxide in quinoline under nitrogen affords the deep-red bisfulvene *(4)* which undergoes *in situ* thermal cyclization to *(5)* with elimination



of dimethylamine[2]. Double electrophilic substitution of 1,4-bis(dimethylamino)-1,3-butadiene *(1)*[3] (which behaves under these circumstances as two non-coupled enamine units) with 3-chloroallylidene(dimethyl)ammonium chloride *(2)* (and subsequently with $HClO_4$) leads to fair yields of *(3b)*. The salt *(2)* was produced in the usual manner by treating 3-dimethylaminopropenal with oxalyl chloride.



[*] Prof. Dr. C. Jutz, Dipl.-Chem. M. Hanke
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

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

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0214 $ 02.50/0

The structure of *(5)* is confirmed by its ^{1}H-NMR spectrum. The pattern of signals closely resembles that of 5-methylazulene[4], the protons 4 (4') and 6 (6') adjacent to the linkage site expectedly appearing $\delta = 0.29$ and 0.21, respectively, downfield from those of 5-methylazulene owing to deshielding. The UV spectrum of *(5)* shows a relatively intense longwave ^1L_b band with vibrational structure and a distinct, remarkably longwave band at 716 nm.

Procedure

Synthesis of *(3b)*: Oxalyl chloride (8.7 ml, 0.10 mol) in chloroform (50 ml) is added dropwise to a stirred solution of 3-dimethylaminopropenal (12 g, 0.12 mol) in chloroform (250 ml) at −30 °C. Evolution of gas ensues (CO, CO_2) and a sludge of *(2)* precipitates; after 15 min, compound *(1)* (7.0 g, 0.05 mol) in chloroform (50 ml) is added dropwise to the cooled (−50 °C) sludge of *(2)*. The resulting dark-red solution is stirred for another 2 h, ultimately without external cooling, and ethanol (10 ml) is added before the mixture is evaporated down *in vacuo* without any heating. On addition of 70 % $HClO_4$ (14.3 g) in ethanol (30 ml) and ether (*ca.* 700 ml) the crude diperchlorate *(3b)* precipitates as a dark viscous oil. After repeated washing with ether and decanting off the ether layer the product is dissolved in a small volume of acetonitrile and ethanol is added until the onset of turbidity. When crystalline *(3b)* begins to precipitate, ether is added very slowly in small portions. Recrystallization of the dark salt (from ethanol in the presence of activated charcoal affords pure *(3b)* (11.3 g, 45 %); yellow needles, m.p. 219—223 °C (dec.); ^{1}H-NMR ([D_6]-DMSO, TMS int.): $\delta = 3.00$ (s, 12H, N—Me), 3.28 (s, 12H, N—Me), 5.33 (dd, $J = 12$ Hz, 2H), 7.40 (d, $J = 12$ Hz, 2H), 7.63 (s, 2H), 7.77 (d, $J = 12$ Hz, 2H); UV (ethanol): λ_{max} ($\log\varepsilon$) = 413 nm (5.00).

Synthesis of *(5)*: A *ca.* 3 N solution of sodium methoxide in methanol (8 mequiv.) is added, after prior addition of cyclopentadiene (0.58 g, 8.8 mmol), to a stirred solution of *(3b)* (2.0 g, 4 mmol) in quinoline (20 ml) under pure nitrogen. The dark-red reaction mixture is stirred at room temperature for 36 h and at 60 °C for 2 h, and heated to 120 °C and 150 °C for 3 h at a time. After stripping off the quinoline at *ca.* 1 torr, the dark residue is dissolved in CH_2Cl_2, filtered, and residual quinoline extracted with 1 N HCl and water. Chromatography, first in CH_2Cl_2 and then in *n*-hexane on Al_2O_3 (neutral, activity II) gives a blue fraction which affords small blue-black crystals (0.21 g, 21 %), m.p. 106 °C; ^{1}H-NMR ($CDCl_3$, TMS int.): $\delta = 6.88$ (dd, $J_{6,7} = J_{7,8} = 10$ Hz, 2H, H-7/7'), 7.27 (d, $J_{1,2} = J_{2,3} = 4$ Hz, 4H, H-1/1', H-3/3'), 7.56 (d, $J_{6,7} = 10$ Hz, 2H, H-6/6'), 7.72 (t, $J_{1,2} = J_{2,3} = 4$ Hz, 2H, H-2/2'), 8.07 (d, $J_{7,8} = 10$ Hz, 2H, H-8/8'), 8.41 (d, $J_{4,6} = 2$ Hz, 2H, H-4/4'); UV (ethanol): λ_{max} ($\log\varepsilon$) = 274 (4.49), 304 (4.78), 382 (4.20), 594 (3.04), 615 (3.03), 645 (3.04), 716 nm (2.74).

Received: November 17, 1978 [Z 150 IE]
German version: Angew. Chem. *91*, 227 (1979)

CAS Registry numbers:
(1), 69309-33-7; *(2)*, 69309-34-8; *(3b)*, 69309-36-0; *(4)*, 69309-37-1; *(5)*, 69309-38-2; 3-dimethylaminopropenal, 927-63-9

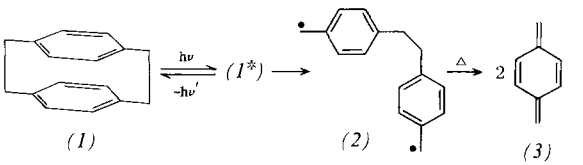
[1] *K. Ziegler, K. Hafner*, Angew. Chem. *67*, 301 (1955); DBP 942326 (1956); *K. Hafner*, Justus Liebigs Ann. Chem. *606*, 79 (1957).
[2] *C. Jutz*, Top. Curr. Chem. *73*, 127 (1978).
[3] *M. F. Fegley, N. M. Bortnick, C. H. McKeever*, J. Am. Chem. Soc. *79*, 4143 (1957).
[4] *D. Meuche, B. B. Molloy, D. H. Reid, E. Heilbronner*, Helv. Chim. Acta *46*, 2483 (1963).

First Spectroscopic Detection of Diradicals in Photocycloreversions[**]

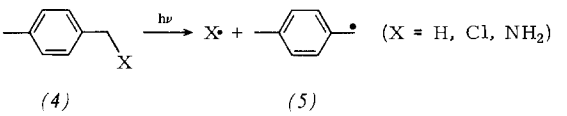
By *Gerd Kaupp, Eberhard Teufel*, and *Henning Hopf*[*]

Short-lived photointermediates can be detected kinetically in "allowed" and "forbidden" cycloadditions (-reversions)[1] and it is of practical utility[2] to call them 1,4-diradicals, as in the case of longer-lived intermediates exhibiting free[2b] or enforced[2c] internal rotations[3]. As the kinetic procedure does not allow any decision whether or not additional excimers or exciplexes will be formed before, after, or parallel to the diradicals[2c, 4], the direct spectroscopic detection of diradicals is of primary importance. For the first time we have now obtained spectroscopic evidence for diradicals in photocycloreversions. Upon appropriate execution of photochemical [6+6]-cycloreversions of [2.2]paracyclophanes[5], the process can be stopped at the 1,4-diradical[3a] stage. The weakly [*(2)*] or strongly [*(7)*] interacting benzyl radicals, which are linked together by an ethano-chain in the *p*-positions, are stable in glassy media at low temperatures and they can be readily recognized by their highly characteristic absorption and fluorescence spectra (see Fig. 1. and 2).

Irradiation of *(1)* (m.p. 285 °C) in a 2-methyltetrahydrofuran (MTHF) glass at 83 K with low pressure mercury lamps ($\lambda = 253.7$ nm) yields *(3)*[5] in competition with excimer fluorescence and phosphorescence. However, at 77 K *(2)* is formed rather than *(3)*. UV/VIS and fluorescence spectra are obtained which are very similar to those of *(5)*, which forms upon



corresponding irradiation of *(4)*[6] at 77 K (see Fig. 1). The spectra of *(2)* are almost as sharply structured as those of *(5)*. Therefore the mutual interaction of the benzyl radicals



in *(2)* must be weak. Its presence follows mainly from the increased UV absorption of *(2)* (but not of *(5)*) below 300 nm. Upon short thawing up to 100—120 K and recooling to 77 K both spectra of *(2)* disappear. If oxygen is carefully excluded[7] one obtains the UV bands of the cleavage product *(3)*[5], which does not fluoresce[8].

The cyclophane *(6)*[9] (intramolecular dimer) yields the intensely yellow species *(7)* in competition with excimer fluorescence upon irradiation at 83 or 77 K in MTHF. *(7)* exhibits sharply structured UV- and fluorescence spectra (see Fig.

[*] Univ.-Doz. Dr. G. Kaupp [+], Dipl.-Chem. E. Teufel
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)
Prof. Dr. H. Hopf
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Work supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Wissenschaftliche Gesellschaft Freiburg, Breisgau.

[+] Author to whom correspondence should be addressed.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0215 $ 02.50/0*

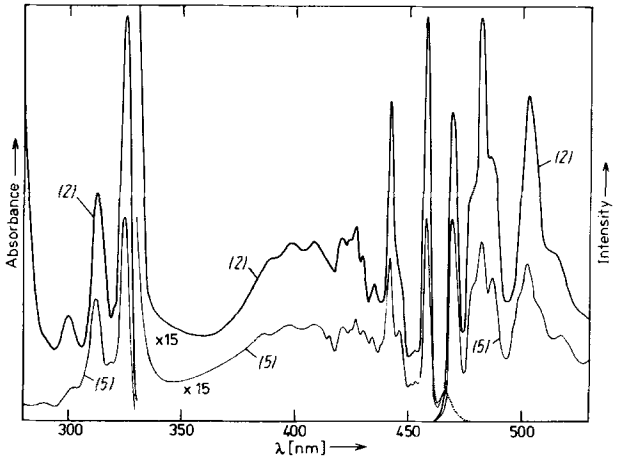


Fig. 1. UV-(excitation) and quantum corrected fluorescence spectrum of *(2)* (—) and *(5)* (—, halved scale) in MTHF at 77 K.

2). Both the absorption and emission of *(7)* are closely related to those of *(2)* and *(5)* but strongly bathochromically shifted. These observations underline the dimer (excimer after light absorption) character of *(7)*, which is enforced by the ethano-bridges.

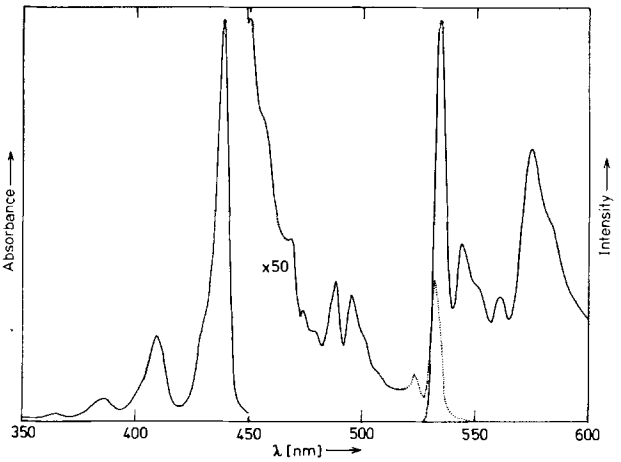


Fig. 2. UV-(excitation) and quantum corrected fluorescence spectrum of *(7)* in MTHF at 77 K.

It is only upon prolonged irradiation of *(7)* (77—83 K, $\lambda = 436$ nm), that one obtains the intramolecular dimers (excimers after light absorption) *(8)* and *(9)*. These exhibit strong or weak interaction, respectively, of the adjacent *p*-quinodimethane chromophores [UV spectra of *(8)*, *(9)*, and *(3)*, see Table 1]. *(9)* is obtained immediately upon short warming of *(7)* to 100—120 K and recooling to 77 K. It does not fluoresce, is photolabile at 77 K, and reacts thermally at 193 K to regenerate *(6)*.

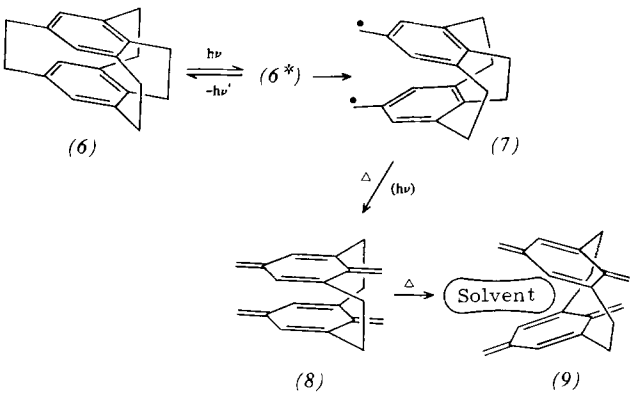


Table 1. UV-, fluorescence, and phosphorescence maxima of the compounds *(1)*, *(3)*, *(6)*, *(8)*, *(9)*.

Cpd.	UV, λ_{max} [nm] MTHF, 77—83 K	Fluorescence (phosphorescence), λ_{max}^{corr} [nm], MTHF, 77 K [a]	Fluorescence, λ_{max}^{corr} [nm] at 298 K [a]
(1)	281, 289, 305	357 (480; $\tau_{Ph} = 4$ s) [b]	355 ($\Phi_{Fl} = 0.0081$) [c]
(3)	283 sh, 287.5, 291 sh, 295 sh, 300.5 [d]	—	—
(6)	287 sh, 308 sh	360	362 [e]
(8)	318, 333, 336, 347 sh, 354	—	—
(9)	280.5, 294, 305 sh, 310	—	—

[a] Quantum correction ($dQ/d\lambda$) with a Perkin-Elmer MPF-3 spectrofluorimeter from 300 to 600 nm; spectral resolution: 1 nm.
[b] In EPA/77 K: 358 (450, 510 sh; $\tau_{Ph} = 5.5$ s) [5].
[c] In cyclohexane [5].
[d] Data in ether/ethanol (1:2) at 83 K: see [5].
[e] In benzene.

The spectroscopic detection of the 1,4-diradicals *(2)* and *(7)*[10] with presumably not-fully-extended as well as cisoid conformations profits from: (i) the relatively high stability of benzyl systems; (ii) the favorable position and intensity of the UV and the fluorescence spectra; and (iii) from barriers opposing geometrical changes, which are apparently high enough to be of significance even in the temperature range of 77—83 K. The sharp structure in the fluorescence spectrum of *(7)* is remarkable. Until now it was considered typical that intra- and intermolecular excimers or electronically excited "sandwich dimers" exhibit broad and structureless emission[11]. Therefore it may be predicted that the spectroscopic distinction between further 1,4-diradicals and dimer or complex (excimer, exciplex) structures (in particular instances perhaps at even lower temperatures) might meet with difficulties. In such cases ESR techniques should be helpful, provided these are not disturbed by radical side products (thus, there is a second fluorescence from the photolysate of *(1)* above 550 nm, which does not belong to *(2)*, but presumably to the [2.2]paracyclophanyl radical [*(1)*—H•]) or by secondary radicals involving solvent participation.

Received: December 12, 1978;
revised: February 2, 1979 [Z 137 IE]
German version: Angew. Chem. *91*, 232 (1979)

CAS Registry numbers:
(1), 1633-22-3; *(3)*, 502-86-3; *(6)*, 61477-04-1

[1] *G. Kaupp*, Angew. Chem. *83*, 361 (1971); Angew. Chem. Int. Ed. Engl. *10*, 340 (1971).
[2] a) *G. Kaupp, M. Stark*, Chem. Ber. *110*, 3084 (1977); references cited therein; b) *e.g. G. Kaupp*, Angew. Chem. *85*, 766 (1973); Angew. Chem. Int. Ed. Engl. *12*, 765 (1973); *J. S. Green, M. Rejtö*, J. Org. Chem. *39*, 3284 (1974); *c) G. Kaupp, M. Stark, H. Fritz*, Chem. Ber. *111*, 3624 (1978).
[3] a) The intermediates of cycloadditions(-reversions) (such as *e.g. (2)* and *(7)*) are most readily classified in terms of 1,4-diradicals. Benzyl radicals have relatively high spin densities in their *p*-positions: see for instance *A. M. Ihrig, P. R. Jones, I. N. Jung, R. V. Lloyd, J. L. Marshall, D. E. Wood*, J. Am. Chem. Soc. *97*, 4477 (1975). b) The postulate of "concerted" and "non-concerted biradicaloid geometries" for "allowed" and "forbidden" reactions, respectively [*J. Michl*, Photochem. Photobiol. *25*, 141 (1977)] cannot predict or reliably interpret all the various kinetic effects caused by real diradical intermediates.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0216 $ 02.50/0*

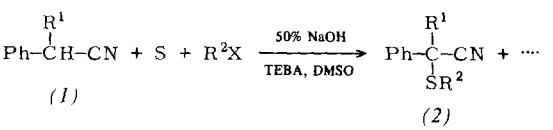
[4] *G. Kaupp*, Justus Liebigs Ann. Chem. *1977*, 254; references cited therein.
[5] *G. Kaupp*, Angew. Chem. *88*, 482 (1976); Angew. Chem. Int. Ed. Engl. *15*, 442 (1976).
[6] *G. Porter, E. Strachan*, Trans. Faraday Soc. *54*, 1595 (1968); numerous further benzyl radicals therein; *S. Leach, A. L. Campillo, R. L. Delgado, M. C. T. Mages*, J. Physique *28*, Suppl. C3—147 (1967).
[7] Photolysis of *(1)* at 83 K (also in EPA or ether/ethanol = 1:2) [5] or at 193 K in triacetin (*G. Kaupp, E. Teufel*, unpublished results) readily yields *(3)* even without exclusion of oxygen in a one-quantum process [5].
[8] We have indications for a similar diradical derived from [2.2](2,5)furano-(1,4)benzocyclophane [*D. J. Cram, C. S. Montgomery, G. H. Know*, J. Am. Chem. Soc. *88*, 515 (1966)] upon irradiation at 77 K in the absorption and fluorescence spectra of its *p*-benzyl part (almost identical to those observed with *(2)* and *(5)*).
[9] *W. Gilb, K. Menke, H. Hopf*, Angew. Chem. *89*, 177 (1977); Angew. Chem. Int. Ed. Engl. *16*, 191 (1977).
[10] Because of the ethano-links between the radicals, *(2)* and *(7)* are completely different from the *m*-quinodimethane or 1,8-naphthoquinodimethane triplets: *J.-F. Muller, D. Muller, H. J. Dewey, J. Michl*, J. Am. Chem. Soc. *100*, 1629 (1978); *M. Gisin, E. Rommel, J. Wirz, M. N. Burnett, R. M. Pagni, ibid*, in press; we thank Dr. *Wirz* for a preprint of this work and Professor *Michl* for a personal communication (Feb. 2, 1979), in which he corrects his singlet postulate of 1978 and now also assigns a triplet structure to the species he obtained.
[11] *J. B. Birks*: Organic Molecular Photophysics. Vol. 2. Wiley-Interscience, New York 1975, pp. 494ff. and further references therein; under our reaction conditions (MTHF, 77 K) the "sandwich dimer" formed from dianthracene [cf. *E. A. Chandross*, J. Chem. Phys. *43*, 4175 (1965)] also emits an unstructured fluorescence spectrum ($\tilde{\nu}_{max}^{corr} = 485$ nm); further examples in Table 1.

Elemental Sulfur/Alkali Metal Hydroxide/Dimethyl Sulfoxide—A New "Reagent" for Preparing Organic Sulfur Compounds[1]

By *Andrzej Jończyk*[*]

Elemental sulfur inserts smoothly into C—M bonds (M = Li, Na, MgX) to generate thiolates C—S^-M^+, which are transformed into thiols, thioethers, or thiol esters by treatment with acids, alkyl halides, or acyl halides, respectively[2]. However, α-alkylthio-substituted derivatives of nitriles, esters, ketones, *etc.* are usually prepared by reaction of the carbanions of these CH acids with disulfides, sulfenamides, sulfenyl halides, or thiocyanates[3]. We therefore examined the possibility of synthesizing these compounds *via* a simple reaction of carbanions with elemental sulfur and alkyl halides in the case of alkylated phenylacetonitriles *(1)*.

Preliminary experiments showed that compound *(1)* does indeed reacts to some extent with elemental sulfur and alkyl halides in the presence of 50% aqueous sodium hydroxide



(1) *(2)*

Table 1. Synthesis of α-(alkylthio)-nitriles *(2)* with the "reagent" S/NaOH/DMSO.

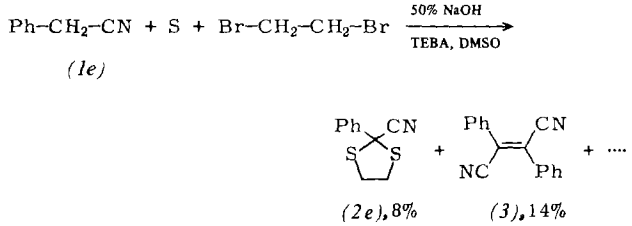
	R^1	R^2X	Yield [%]	B.p. [°C/torr]
a	CH_3	CH_3Br	72	78–80/0.35
b	CH_2=$CHCH_2$	*n*-C_4H_9Cl	71	96–98/0.1
c	*i*-C_3H_7	*n*-C_4H_9Cl	63	100–101/0.1
d	C_6H_5	CH_3Br	49 [a]	125–127/0.1 [b]

[a] Some 21% of $Ph_2C(CN)$—$C(CN)Ph_2$ is also formed, among other by-products. [b] M.p. 52–54 °C (53–54 °C [5c]).

[*] Dr. A. Jończyk
Institute of Organic Chemistry and Technology
Technical University (Politechnika)
Koszykowa 75, PL-00-662 Warszawa (Poland)

solution and benzyl(triethyl)ammonium chloride (TEBA)[4] to give α-alkylthio compounds *(2)*[5]; *e.g.* the yield of *(2b)* was *ca.* 10%. The process becomes of practical value on addition of DMSO [*ca.* 0.7 mol per mol of *(1)*] to the system (Table 1). The yields are about 5% lower without TEBA.

Peculiar transformations take place under these conditions when phenylacetonitrile *(1e)* reacts with sulfur and ethylene dibromide: the desired 2-phenyl-1,3-dithiolanecarbonitrile *(2e)* was accompanied, *inter alia*, by the *trans*-dinitrile *(3)*.



(1e) *(2e)*, 8% *(3)*, 14%

In the reactions between nitriles *(1)*, sulfur, and alkyl halides, polysulfides $R^2S_nR^2$ (mainly $n = 2$) were formed. We therefore treated alkyl halides directly with the S/NaOH/DMSO reagent, and obtained di- and trisulfides *(4)* (Table 2); the structure of the products depends on the reaction conditions and the alkyl halide. The yields of *(4)* were significantly improved by the use of powdered NaOH in DMSO (Table 2), though this variant requires fairly large quantities of DMSO.

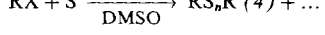


Table 2. Synthesis of oligosulfides *(4)*. All reactions are performed in two steps: I, production of the "reagent" S/NaOH/DMSO; II, its reaction with RX.

RX	Base	Product	Yield [%]
n-C_4H_9Cl	50% NaOH aq	*(4a)*, $n = 1$	28 [a]
		(4a), $n = 3$	34 [a]
n-C_4H_9Cl	NaOH solid	*(4a)*, $n = 2$	56 [b, c]
n-C_4H_9Cl	NaOH solid	*(4a)*, $n = 1$	12 [a, d]
		(4a), $n = 2$	35 [a, d]
i-C_3H_7Cl	NaOH solid	*(4b)*, $n = 2$	43 [b, e]
n-$C_8H_{17}Cl$	NaOH solid	*(4c)*, $n = 2$	66 [b]

[a] By GLC. [b] Isolated. [c] Yield 50% in the presence of solid KOH. [d] Step I carried out at 90—100 °C/1 h. [e] Isopropyl bromide gives trisulfides and possibly higher polysulfides.

Procedure

Synthesis of *(2a)*: Methyl bromide (*ca.* 6 g, 0.067 mol) is bubbled through a stirred mixture of *(1a)* (2.6 g, 0.02 mol), sulfur (1.0 g, 0.031 mol), TEBA (0.1 g), DMSO (1 ml), and 50% aq. NaOH (10 ml) at 45 °C (exothermic reaction). Stirring is continued for 75 min, and the mixture is diluted with water and extracted with benzene. The organic extracts are washed with aq. NaCl, dried ($MgSO_4$), and distilled (yield 2.55 g, 72%).

Synthesis of *(4a)*, $n = 2$: Sulfur (1.6 g, 0.05 mol) is added to a stirred suspension of powdered sodium hydroxide (6.8 g, 0.17 mol) in DMSO (10 ml). Addition results in an exothermic reaction, during which the temperature is kept at 50 °C; after reaction the mixture is cooled to 25 °C. Butyl chloride (6.4 g, 0.069 mol) is added dropwise at 45 °C (cooling necessary). After being stirred for 45 min, the mixture is worked up as

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0303-0217 $ 02.50/0*

described above. Dibutyl disulfide is isolated by vacuum distillation (b.p. 94—97 °C/7 torr, yield 2.5 g = 56 % based on sulfur).

Received: November 23, 1978 [Z 151 IE]
German version: Angew. Chem. 91, 228 (1979)

CAS Registry numbers:
(1a), 1823-91-2; *(1b)*, 5558-87-2; *(1c)*, 5558-29-2; *(1d)*, 86-29-3; *(1e)*, 140-29-4; *(2a)*, 67073-81-8; *(2b)*, 69309-43-9; *(2c)*, 69309-44-0; *(2d)*, 67073-82-9; *(2e)*, 53310-49-9; *(3)*, 2450-55-7; *(4a)* ($n=1$), 544-40-1; *(4a)* ($n=2$), 629-45-8; *(4a)* ($n=3$), 5943-31-7; *(4b)* ($n=2$), 4253-89-8; *(4c)* ($n=2$), 822-27-5; CH_3Br, 74-83-9; n-C_4H_9Cl, 109-69-3; ethylene dibromide, 106-93-4; i-C_3H_7Cl, 75-29-6; n-$C_8H_{17}Cl$, 111-85-3; $Ph_2C(CN)$—$C(CN)Ph_2$, 3122-21-2

[1] Reactions of Organic Anions, Part 93. This work was supported by the Polish Academy of Sciences.—Part 93: *A. Jończyk, A. Kwast, M. Mąkosza*, Tetrahedron Lett., *1979*, 541.

[2] *K. A. Kocheshkov, T. V. Talalaeva:* Mietodi elementoorganicheskoi khimii (litij, natrij, kalcij, rubidij, cezij), Vol. 2. Izdatelstvo Nauka, Moskva 1971, p. 594; *L. Brandsma:* Preparative Acetylenic Chemistry, Elsevier, Amsterdam 1971, p. 83; *K. Nützel* in Houben-Weyl-Müller: Methoden der Organischen Chemie. 4th Ed. Vol. XIII/2a, Thieme, Stuttgart 1973, p. 399.

[3] *D. N. Brattesani, C. H. Heathcock*, Tetrahedron Lett. *1974*, 2279; *P. A. Gassman, D. P. Gilbert, S. M. Cole*, J. Org. Chem. *42*, 3233 (1977); *P. A. Gassman, R. J. Balchunis, ibid. 42*, 3236 (1977), and literature cited therein. Also see ref. [5].

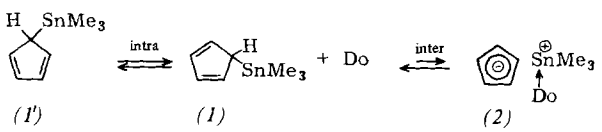
[4] For reviews see, *e.g.*: *M. Mąkosza*, Pure Appl. Chem. *43*, 439 (1975); *E. V. Dehmlow*, Angew. Chem. *86*, 187 (1974); *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974); *16*, 493 (1977).

[5] For synthesis of *(2)*, see a) *S. J. Selikson, D. S. Watt*, Tetrahedron Lett. *1974*, 3029; b) *M. Mąkosza, M. Fedoryński*, Synthesis *1974*, 274; c) *E. Marchand, G. Morel, A. Foucaud, ibid. 1978*, 360.

Intermolecular Exchange of Substituents *via* Ions (Ion Pairs) in Cyclopentadienyl- and Cyclononatetraenyl-trimethylstannane

By *Gernot Boche, Frank Heidenhain*, and *Brigitte Staudigl*[*]

The behavior of η^1-cyclopentadienyl derivatives of main groups IV and V, which is dynamic on the NMR time scale, has generally been recognized as an intramolecular orbital-symmetry controlled process or as one obeying the principle of least motion[1] [*(1')*⇌*(1)*]. We have found that, given suitable solvation, 1,3-cyclopentadienyl- and 1,3,5,7-cyclononatetraenyl-trimethylstannane *(1)* and *(3)*, respectively, can exist as ions (ion pairs) and exhibit intermolecular substituent exchange (Do = donor solvent or LiCl).



(1') *(1)* *(2)*

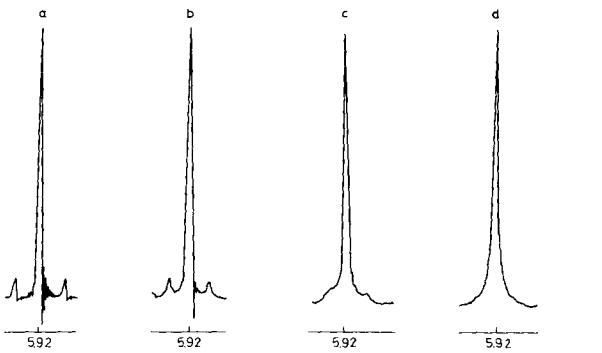


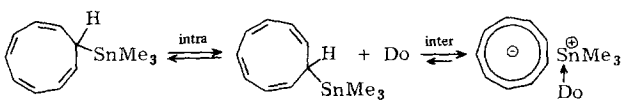
Fig. 1. ^{1}H-NMR spectra (δ values) of cyclopentadienyl-trimethylstannane *(1)* under various conditions (a—d, see Text).

[*] Prof. Dr. G. Boche, Dipl.-Chem. F. Heidenhain, Dipl.-Chem. B. Staudigl
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

Fast intramolecular exchange in the case of *(1)* in tetrahydrofuran (THF) (see Fig. 1a), dimethoxyethane (DME), trichloro-, dichloro-, or dichlorodifluoro-methane between 26 (Fig. 1a) and −70 °C is characterized, *inter alia*, by the sharp satellite bands of the signal of the five cyclopentadienyl protons at $\delta = 5.92$, which are due to ^{117,119}Sn-C-^{1}H coupling ($J = 22$ Hz)[2].

If the THF solution of *(1)* is treated at 26 °C with hexamethylphosphoric triamide (HMPT) (0.85 mol. equiv.), a broadening of the satellite signals is observed (Fig. 1b). Lowering the temperature of this sample leads to further broadening (−48 °C, Fig. 1c) and coalescence (−61 °C, Fig. 1d). A similar sequence of events occurs at constant temperature on increasing the concentration of HMPT, dimethylformamide (DMF), or lithium chloride. A spectrum like that in Figure 1d is obtained, *e.g.* with 0.54 mol. equiv. of LiCl in THF at 26 °C.

It is fully compatible with known ion-pair effects[4], and is adequately confirmed by the results obtained for cyclononatetraenyltrimethylstannane *(3)*, that the disappearance of the satellite signals with increasing concentration of donor solvent[3] or LiCl, and with falling temperature, should be due to an increasing shift of the equilibrium *(1)*⇌*(2)* in favor of the ion pair *(2)* (low concentrations) and thus to an *inter*molecular substituent exchange.



(3') *(3)* *(4)*

While *(3)* likewise exists as an olefinic η^1-compound with fast intramolecular substituent migration *(3')*⇌*(3)*[5] in solvents of low donor strength[3], the solvents DMF, HMPT, and dimethyl sulfoxide (DMSO) lead to a distinct shift of the ring protons from the olefinic region to that of the [9]annulene anion[6] (see Table 1). This is because the equilibrium *(3)*⇌*(4)* lies more on the side of the ion pair than in the case of *(1)*⇌*(2)* because of the easier ionization of the nine-membered ring derivative *(3)*[7]. Accordingly, valence isomerization to dihydroindenes, such as are common for cyclononatetraenes [*e.g. (3)*[5]], no longer occurs. The coupling constants $J(^{117,119}$Sn-C-^{1}H) also increase in parallel with the shift in equilibrium *(3)*⇌*(4)*. This is due to the stronger complexing ability of the above-mentioned donor molecules towards *(4)*[1c,8].

In a mixture of DME : DMF = 2 : 1, roughly the same population of *(3)* and *(4)* is attained, permitting determination of the temperature dependence of the equilibrium. The finding

Table 1. ^{1}H-NMR data of *(3)* in solvents of various donor strengths; δ values relative to TMS at 37 °C.

Solvent	Donor strength [3]	Ring-H (δ value)	$J(^{117,119}$Sn-C-^{1}H) [Hz]
$CDCl_3$	—	5.33	51
THF	20	5.35	51
DME	≈24	5.33	55
DMF	26.6	6.42	62
DMSO	29.8	6.72	65
HMPT	38.8	6.70	71

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0218 $ 02.50/0

that *(3)* is present at room temperature and that *(4)* predominates at $-40\,^{\circ}C$ corresponds to a reaction enthalpy of $\Delta H^{0} = -8.8$ [kcal mol^{-1}] and an entropy of reaction $\Delta S^{0} = -32$ [e. u.] for the transformation *(3)*→*(4)*, with the entropy term in particular confirming the solvation of the ion pair. Since only averaged spectra were recorded throughout the entire temperature range, the equilibrium *(3)*⇌*(4)* must be mobile ($\Delta G^{\neq}_{40\,^{\circ}C} \leq 10$ [kcal mol^{-1}]). Addition of 1 mol. equiv. of LiCl to a 0.4 M solution of *(3)* in THF leads to similar behavior: as the temperature falls the dynamic equilibrium *(3)*⇌*(4)* shifts reversibly to the side of the ion pair *(4)*.

(1) and *(3)* thus demonstrate that covalent trimethylstannyl compounds can be transformed by suitable solvents into ion pairs *(2)* and *(4)* which react differently from *(1)* and *(3)*[9].

Received: December 4, 1978 [Z 152 IE]
German version: Angew. Chem. *91*, 228 (1979)

CAS Registry numbers:
(1), 2726-34-3; *(3)*, 69429-52-3

[1] a) *H. P. Fritz, C. G. Kreiter*, J. Organomet. Chem. *4*, 313 (1965); reviews: b) *F. A. Cotton* in *F. A. Cotton, L. M Jackman:* Dynamic Nuclear Resonance Spectroscopy. Academic Press, New York 1975, p. 377; c) *V. S. Petrosyan*, Prog. NMR Spectrosc. *11*, 115 (1977).

[2] a) Line broadening is observed below $-70\,^{\circ}C$ and at $\approx -105\,^{\circ}C$ the satellites under the signal at $\delta = 5.92$ disappear [2b—d]. At $-150\,^{\circ}C$ splitting to an AA'BB'X spectrum occurs with signals at $\delta = 6.5$ and at $\delta = 4.25$ [2b]; b) *A. V. Kisin, V. A. Korenevsky, N. M. Sergeyev, Y. A. Ustynyuk*, J. Organomet. Chem. *34*, 93 (1972); c) *A. Davison, P. E. Rakita*, J. Am. Chem. Soc. *90*, 4497 (1968); d) *R. B. Larrabee*, J. Organomet. Chem. *74*, 313 (1974).

[3] *V. Gutmann:* Coordination Chemistry in Non-Aqueous Solutions. Springer, Wien 1968.

[4] a) *M. Szwarc:* Ions and Ion Pairs in Organic Reactions. Wiley, New York, Vol. I, 1972, Vol. II, 1974; b) *G. Boche, F. Heidenhain*, Angew. Chem. *90*, 290 (1978); Angew. Chem. Int. Ed. Engl. *17*, 283 (1978); c) J. Am. Chem. Soc. *101*, in press.

[5] *G. Boche, F. Heidenhain*, J. Organomet. Chem. *121*, C 49 (1976).

[6] *T. J. Katz, P. J. Garratt*, J. Am. Chem. Soc. *85*, 2852 (1963); *86*, 5194 (1964); *E. A. Lalancette, R. E. Benson, ibid. 85*, 2853 (1963); *87*, 1941 (1965).

[7] pK_a measurements on cyclopentadiene and cyclononatetraene show the same tendency [6].

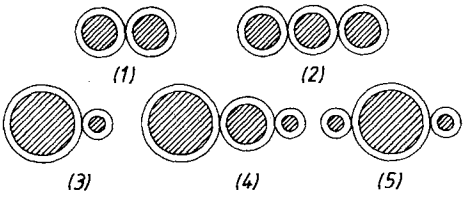
[8] a) *V. S. Petrosyan, N. S. Yashina, V. I. Bakhmutov, A. B. Permin, O. A. Reutov*, J. Organomet. Chem. *72*, 71 (1974); b) *V. S. Petrosyan, O. A. Reutov*, Pure Appl. Chem. *37*, 147 (1974).

[9] See also a) *I. P. Beletskaya, A. N. Kashin, O. A. Reutov*, J. Organomet. Chem. *155*, 31 (1978); b) *I. P. Beletskaya, A. N. Kashin, A. Z. Malhasyan, A. A. Solovyanov, E. U. Behly, O. A. Reutov*, Zh. Org. Khim. *10*, 678 (1974); c) *I. P. Beletskaya, A. N. Kashin, V. A. Khutoryanskii, O. A. Reutov*, Izv. Akad. Nauk SSSR, Ser. Khim. *1976*, 1674.

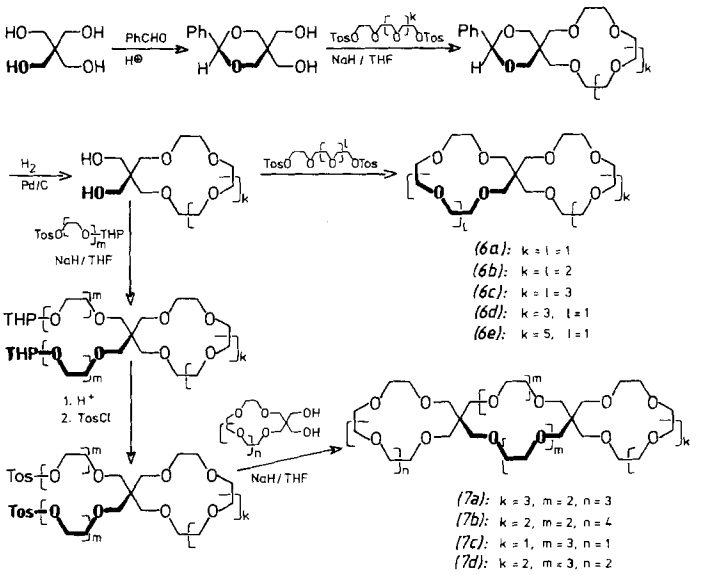
"Multi-Loop Crown Ethers" with Multiple Selectivity[**]

By *Edwin Weber*[*]

While the chemistry of organic neutral ligands has made great advances with regard to the specific recognition of *individual types* of cations/anions and uncharged molecules[1], apparently, very little is known about receptors (host molecules) for the simultaneous selective complexation of several *different types* of alkali metal/alkaline earth metal and heavy metal ions. We report here on the first crown ether combinations "multi-loop crown ethers" of type *(1)*—*(5)*, in which several rings having tailor-made *cavity sizes* and *donor properties* are coupled *via* spiro C-atoms.



Such multi-loop crown ethers should not only be useful for the analysis of mixtures of salts[2] but also attract interest for the enzyme-analogous complexation of polyfunctional organic compounds and polyelectrolytes[3] and as models for cation contact, charge transfer, and energy transport processes[4]. The ligands having topologies *(1)*—*(5)*, *e.g. (6)* and *(7)* were synthesized using pentaerythritol[5] as starting substance (Tos = toluenesulfonyl, THP = tetrahydropyranyl).



The ligands *(6a)*—*(6e)* and *(7a)*—*(7d)* have been shown to be generally useful as hosts for the joint incorporation of *several* cations, and the ratio ionic radius/cavity volume of crown ether (donor number) for each ring can be adjusted at will.

The double-loop crown ether *(6b)* (colorless viscous oil)[6], for example, readily forms a 1:2 complex with NaSCN or with $Ca(SCN)_2$, *i.e.* each of the two similar "crown-5,5" rings[7] incorporate a metal ion—as in *(1)* (Table 1). The same applies for the bulkier "dicrown-6,6" ligand *(6c)* (colorless

Table 1. Complexes of the multi-loop crown ethers *(6)* and *(7)*.

Ligand No.	Ligand Type	Complex Stoichiometry Ligand:Salt	Complex Salt	M.p. [°C]
(6a)	"4,4"	1:2 (2 H_2O)	LiI	>300, dec.
(6b)	"5,5"	1:2	NaSCN	204—206
		1:2	$Ca(SCN)_2$	>300, dec.
		1:1	KSCN	193—195
		3:4	$Ba(SCN)_2$	234 (sinters at 229°C)
(6c)	"6,6"	1:2 (1 H_2O)	BaI_2	>350, dec.
		1:2 (1 H_2O)	$Ba(SCN)_2$	275—276
		1:2 (4 H_2O)	LiI	72—74
(6d)	"4,6"	1:1:1	LiI, BaI_2	280, dec.
		1:2	LiI	196—198
		1:1 (2 H_2O)	BaI_2	225 (sinters at 95°C)
(7a)	"6,6,6"	1:3	KSCN	273—275

[*] Dr. E. Weber
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn (Germany)

[**] Thanks are due to Prof. Dr. *F. Vögtle* for valuable discussions and to Ms *E. Wahrburg* for experimental assistance.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0219 $ 02.50/0*

viscous oil) and BaI_2 and for *(6a)* (colorless crystals, m.p. 78—79°C) and LiI. Consistent with this finding, the triple crown ether *(7a)* (colorless viscous oil) incorporates a total of three K^+ ions in the spatially suitable "6,6,6" subunits and thus acts as a *trifunctional* cation receptor.

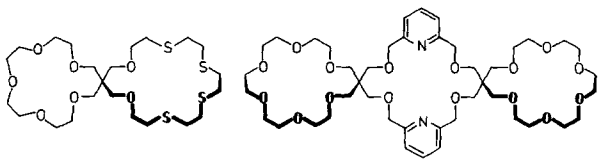
As a rule, with unfavorable cavity size/ionic volume ratios, for example if the cation is too large, no polynuclear complexes are formed: *(6b)* still forms only a 1:1 complex with KSN; in the case of $Ba(SCN)_2$ a stoichiometric 3:4 complex is formed.

Investigations on the separation of cations according to their charge were initiated by the finding that addition of 1:1 mixtures of NaSCN and $Ca(SCN)_2$ to a solution of the "5,5" ligand *(6b)* in acetone/ethyl acetate leads to precipitation of the 1:2 Na^+ complex in almost quantitative yield (see Table 1); in contrast, under the same conditions [15]crown-5 yields the 1:1 complex with $Ca(SCN)_2$. *(6b)* was also added to a solution of KSCN and $Ba(SCN)_2$ (2:1, acetone), whereupon the same Ba^{2+} complex (see Table 1) was formed as in the absence of K^+ ions. *(6c)* and $KSCN/Ba(SCN)_2$ (1:1, in acetone) led to a 1:2 complex with $Ba(SCN)_2$.

The *unsymmetrical* double-loop *(6d)*, *(6e)* [cf. *(3)*] and triple-loop crown ethers *(7b)*—*(7d)* [cf. *(4)*, *(5)*] should be able to incorporate several cations of various sizes: Thus, from a 1:1:1 mixture of *(6d)* (colorless viscous oil), LiI and BaI_2 in acetone/ethyl acetate an analytically pure complex is isolated which contains the components in a 1:1:1 ratio. Remarkably, this has only been achieved up to now with this combination of alkali metal and alkaline earth metal salts.

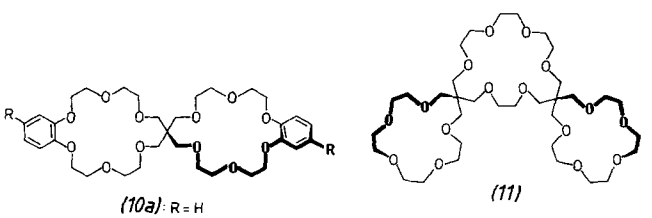
On attempting to exploit the different ring sizes of the "4,6" ligand *(6d)* to prepare mixed polynuclear complexes exclusively with alkali metal ions led—*e.g.* with LiI/KI (1:1, in acetone)—unexpectedly to a 1:2 complex with LiI. Apparently, for unequal occupation of the differently sized rings in *(6d)* differences in charge (or polarizability) as well as large differences in size of the metal ions are necessary.

On reaction of *(6d)* with BaI_2 (1:1) a 1:1 complex containing two H_2O molecules was isolated. It might incorporate the Ba^{2+} in the "6" compartment, while the "4" compartment could possibly take up the H_2O molecules coordinatively. Reaction of *(6c)* and LiI alone leads to a 1:2 complex containing four H_2O molecules. How the Li^+ ions are distributed, however, cannot be determined from the spectroscopic data.



(8) *(9)*

For further gradation of selectivity of the rings in *(6)* and *(7)* also *different* donor atoms were incorporated in the rings[8], as in *(8)* and *(9)*. *(8)* (colorless viscous oil) can provide one cavity for alkali metal/alkaline earth metal cations and one for transition metal ions, while *(9)* (colorless crystals, m.p. 123–125°C) can incorporate alkali metal/alkaline earth metal cations in two of its cavities and a heavy metal in its third cavity. With *(9)*, a mixed 1:2:1 (Ligand: K^+:Co^{2+}) $KSCN/Co(SCN)_2$ complex (m.p. 106–108°C) could be isolated, which most likely contains the Co^{2+} ion in the central ring.



(10a): R = H
(10b): R = CH_3

(11)

Further spiroskeleton/heteroatom combinations[8]—*e.g.* *(10a)* (colorless crystals, m.p. 77–78°C), the *chiral* ligand *(10b)* (colorless crystals, m.p. 55–57°C), and the *angularly* coupled *(11)* (colorless viscous oil)—serve to illustrate the synthetic utility of such complexes and the promising novel applications of the concept, *e.g.* in the simultaneous isolation precious metals from seawater.

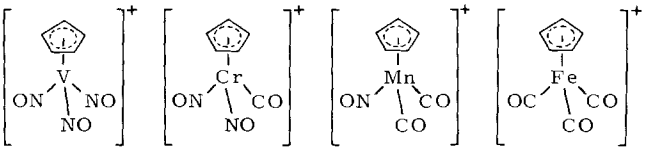
Received: December 21, 1978 [Z 153 IE]
German version: Angew. Chem. *91*, 230 (1979)

[1] *D. J. Cram, J. M. Cram*, Acc. Chem. Res. *11*, 8 (1978); *J.-M. Lehn, ibid. 11*, 49 (1978); *F. Vögtle, E. Weber*, Angew. Chem. and Angew. Chem. Int. Ed. Engl., in press.
[2] Cf. *E. Weber, F. Vögtle*, Kontakte (Merck) *1978*, (2), 16.
[3] *R. C. Hayward*, Nachr. Chem. Tech. Lab. *25*, 15 (1977); *A. J. Hopfinger*: Intermolecular Interactions and Biomolecular Organization. Wiley, New York 1976.
[4] *A. H. Alberts, R. Annunziate, J.-M. Lehn*, J. Am. Chem. Soc. *99*, 8502 (1977); *J. E. Bulkowski, P. L. Burk, M. F. Ludmann, J. A. Osborn*, J. Chem. Soc. Chem. Commun. *1977*, 498.
[5] Cf. *A. C. Coxon, J. F. Stoddart*, J. Chem. Soc. Perkin Trans. 1 *1977*, 767.
[6] Elemental analyses, mass spectra, and other spectra for all the ligands and complexes are consistent with the given structures; the melting points are uncorrected.
[7] This notation is based on the number of oxygen atoms contained in the individual rings.
[8] The syntheses are described in detail elsewhere.

η^5-Cyclopentadienyl(trinitrosyl)vanadium Hexafluorophosphate, $[CpV(NO)_3]PF_6$[**]

By *Max Herberhold, Reinhard Klein*, and *Paul D. Smith*[*]

In continuation of our work on highly nitrosylated metal cations[1] we have now synthesized $[CpV(NO)_3]^+$ *(1)*, thus completing the hitherto incomplete series of isosteric half-sandwich complexes of the type $[CpML_3]^+$ (L=CO or NO).



(1) *(2)*

The new complex *(1)* is formed according to proven methods[2] when the labile CO ligand in $CpV(CO)(NO)_2$[3] is replaced by the isoelectronic nitrosyl cation:

$$CpV(CO)(NO)_2 + NOPF_6 \xrightarrow[CH_3NO_2]{-25\,^\circ C} [CpV(NO)_3]PF_6 + CO$$

The composition of the green, diamagnetic salt $[CpV(NO)_3]PF_6$ is confirmed by elemental analysis and the

[*] Prof. Dr. M. Herberhold [+], Dr. R. Klein, Dr. P. D. Smith
Anorganisch-chemisches Institut der Technischen Universität
Lothstrasse 17, D-8000 München 2 (Germany)
[+] Present address: Laboratorium für Anorganische Chemie der Universität, Am Birkengut, D-8580 Bayreuth (Germany).

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

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* 0570-0833/79/0303-0220 $ 02.50/0

field desorption mass spectrum ($m/e = 206$ for $CpV(NO)_3^+$)[4]; in nitromethane solution it behaves as a 1:1 electrolyte. The pronounced electron deficit at the central metal of *(1)* is reflected in the high ν(NO) frequencies in the IR spectrum and in the strong deshielding of the cyclopentadienyl protons in the ^{1}H-NMR spectrum. Table 1 shows the characteristic spectroscopic data of the cations *(1)* and *(2)*[5] and of the corresponding neutral complexes from which they can be obtained by reaction with $NOPF_6$.

Table 1. IR and ^{1}H-NMR data [a].

Complex	IR [b] ν(CO)	IR [b] ν(NO)	^{1}H-NMR [c] δ(Cp)
$CpCr(CO)_2(NO)$	2025, 1948	1693	5.23
$[CpCr(CO)(NO)_2]PF_6$	2142	1875, 1789	6.25
$CpV(CO)(NO)_2$	2064	1723, 1629	5.71
$[CpV(NO)_3]PF_6$	—	1912, 1794	6.55 [d]

[a] All measurements in nitromethane. [b] Perkin-Elmer 297; cm^{-1}. [c] Jeol C-60-HL; δ values rel. TMS int., calibration with TMS/$CHCl_3$. [d] Measurement at −25°C.

In contrast to the now complete series of the isosteric cations $[CpML_3]^+$ (L = CO, NO), the analogous series of the neutral half-sandwich complexes, $CpML_3$, remains incomplete since the end-member $CpTi(NO)_3$ is still unknown.

Experimental[6]

$CpV(CO)(NO)_2$: $CpV(CO)_4$ (1.27 g, 5.6 mmol) is dissolved in tetrahydrofuran and reduced to $Na_2[CpV(CO)_3]$ with 1% sodium amalgam[3b, 7]. The salt is dried in a high vacuum at +70°C, suspended in 50 ml diethyl ether, and nitrosylated with *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide ("diazald") (2.38 g, 11.1 mmol; dissolved in 10 ml ether). The undissolved material is removed by filtration (G3 frit) and the solution evaporated to dryness; the resulting residue is then extracted with 5 × 20 ml pentane. Column chromatographic separation of the pentane solution on silica gel (pentane, 0°C) affords $CpV(CO)_4$ and $CpV(CO)(NO)_2$ in yields of 11% (0.14 g) and 34% (0.39 g), respectively.

$[CpV(NO)_3]PF_6$: A solution of $NOPF_6$ (0.32 g, 1.8 mmol) in 10 ml nitromethane is added dropwise to the orange-brown solution of $CpV(CO)(NO)_2$ (0.37 g, 1.8 mmol) in 50 ml nitromethane at −25°C. The resulting green solution is filtered through a G3 frit, cooled to −25°C, into 200 ml of cooled ether. After 12 h at −30°C, the resulting green crystals are separated from the mother liquor, washed several times with cooled ether and cooled pentane and then dried for 2 h at −70°C in a high vacuum. Yield 0.40 g (63%); decomposition above 160°C in a nitrogen-filled ampoule[8].

Received: December 27, 1978 [Z 154 IE]
German version: Angew. Chem. *91*, 241 (1979)

CAS Registry numbers:
$CpCr(CO)_2(NO)$, 36312-04-6; $[CpCr(CO)(NO)_2]PF_6$, 69439-82-3; $CpV(CO)(NO)_2$, 31811-51-5; $[CpV(NO)_3]PF_6$, 69439-84-5; $CpV(CO)_4$, 12108-04-2; *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide, 80-11-5; $NOPF_6$, 16921-91-8

[1] *M. Herberhold, R. Klein*, Angew. Chem. *90*, 477 (1978); Angew. Chem. Int. Ed. Engl. *17*, 454 (1978).
[2] *M. T. Mocella, M. S. Okamoto, E. K. Barefield*, Synth. React. Inorg. Met.-Org. Chem. *4*, 69 (1974).
[3] a) *E. O. Fischer, R. J. J. Schneider, J. Müller*, J. Organomet. Chem. *14*, P4 (1968); b) *E. O. Fischer, R. J. J. Schneider*, Chem. Ber. *103*, 3684 (1970).
[4] Varian MAT-311A, FD ion source.
[5] *E. O. Fischer, P. Kuzel*, Z. Anorg. Allg. Chem. *317*, 226 (1962).
[6] All operations under purified argon.
[7] *R. J. Kinney, W. D. Jones, R. G. Bergman*, J. Am. Chem. Soc. *100*, 635 (1978).
[8] *Note added in proof*: The salt $[CpV(NO)_3]PF_6$ is obtained directly when a nitromethane solution of $CpV(CO)_4$ is reacted with $NOPF_6$ at −25°C and then allowed to warm up in a stream of NO gas (*ca.* 90% yield).

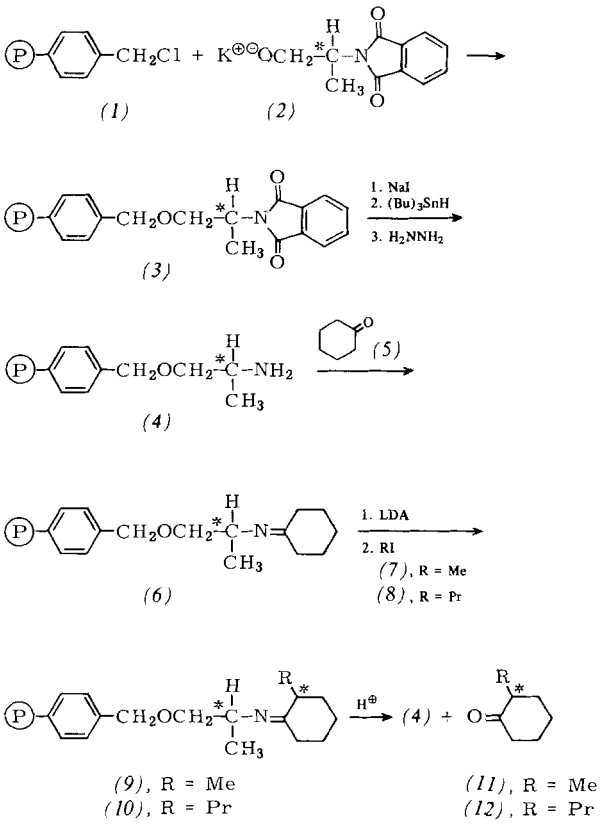
Asymmetric Synthesis of 2-Alkylcyclohexanones on Solid Phases[**]

By *Paul M. Worster, Colin R. McArthur*, and *Clifford C. Leznoff*[*]

Asymmetric syntheses of 2-alkylcyclohexanones[1a] have been recently described in which the optical yields were remarkably high[1b]. The key step is alkylation of an optically active alkoxyiminocyclohexanone.

Insoluble polymer supports have been used in the preparation of enantiomerically pure organic compounds in several ways. Crosslinked polymers containing optically active phosphane ligands have been used as catalysts in asymmetric synthesis[2]. Crosslinked polymers containing chiral cavities have been used for resolving specific organic racemates[3]. In both of these applications the polymer is the reagent and the product remains in solution. In the Merrifield synthesis, however, the reaction product is attached to the polymer and the excess reagents and catalysts are removed by simple filtration. The latter approach was used in the asymmetric synthesis of atrolactic acid on crosslinked polystyrene polymers containing a chiral sugar[4]. The chemical and optical yields were somewhat better than those obtained in solution.

We feel that significant advantages can be gained by performing asymmetric syntheses on insoluble polymer sup-



[*] Dr. P. M. Worster, Dr. C. R. McArthur, and Dr. C. C. Leznoff
York University, Department of Chemistry
Downsview, Toronto, Ontario M3J 1P3 (Canada)

[**] This work was supported by the National Research Council of Canada and York University.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0221 $ 02.50/0*

ports[5]. The expensive chiral reagent can be recovered by simple filtration at the end of the synthesis. In addition, the bulk of the polymer backbone and the reduced mobility of the polymer-bound substrate can mimic enzymatic reactions, giving high optical yields.

We were interested in determing whether the very high chemical and optical yields of the asymmetric synthesis of 2-alkylcyclohexanones[1b] could be achieved on solid phases. Merrifield's commercially available 1 % crosslinked divinylbenzene-styrene copolymer [*(1)*, containing 1.1 mmol of benzyl chloride groups/g of polymer] reacted with the potassium salt of (*S*)-2-phthalamido-1-propanol in benzene containing catalytic amounts of [18]crown-6 to give the polymer-bound phthalamido-blocked chiral amine *(3)*. Treatment of *(3)* with NaI in acetone and subsequent reaction with tri-*n*-butyltin hydride to remove the excess benzyl chloride groups[6] of *(3)*, followed by hydrazinolysis, gave the polymer-bound chiral amine *(4)*. Treatment of *(4)* with cyclohexanone *(5)* in benzene in a Soxhlet extractor [with 3-Å molecular sieves in the thimble] gave polymer-bound chiral alkoxyimine *(6)*. Acid cleavage[7] of *(6)* liberated 0.4 mmol of *(5)*/g of *(6)*. Treatment of *(6)* with lithium diisopropylamide (LDA) at 0 °C followed by the addition of methyl iodide *(7)* or propyl iodide *(8)* at 22 °C yielded the polymer-bound alkylated imines *(9)* or *(10)*, respectively. Mild acid cleavage[7] of *(9)* or *(10)* liberated *(4)* and (*S*)-2-methylcyclohexanone *(11)* ($[\alpha]_D^{26} = +15.5$) in 95% optical yield and 80% chemical yield or (*S*)-2-propylcyclohexanone *(12)* ($[\alpha]_D^{26} = +15.5$) in 60% optical yield and 80% chemical yield. The optical and chemical yields of *(11)* are at least as high as those reported[1b] for reactions performed in solution. The recovered chiral reagent *(4)* loses some of its capacity on recyclization, but the enantiomeric excesses of the product remain unchanged in subsequent cycles. We have thus demonstrated that asymmetric synthesis on solid phases is a practical reality which shows promise of high enantiomeric excesses of product comparable with those obtained in enzymatic systems.

Received: December 27, 1978 [Z 155 IE]
German version: Angew. Chem. *91*, 255 (1979)

[1] a) *M. Kitamoto, K. Hiroi, S. Terashima, S. Yamada*, Chem. Pharm. Bull. *22*, 459 (1974); b) *D. Enders, H. E. Eichenauer*, Angew. Chem. *88*, 579 (1976); Angew. Chem. Int. Ed. Engl. *15*, 549 (1976); *A. I. Meyers, D. R. Williams, M. Druelinger*, J. Am. Chem. Soc. *98*, 3032 (1976); *J. K. Whitesell, M. A. Whitesell*, J. Org. Chem. *42*, 377 (1977).
[2] *W. Dumont, J. C. Poulin, T. P. Dang, H. B. Kagan*, J. Am. Chem. Soc. *95*, 8295 (1973); *N. Takaishi, H. Imai, C. A. Bertelo, J. K. Stille*, *ibid. 100*, 268 (1978).
[3] *G. Wulff, A. Sarhan, K. Zabrocki*, Tetrahedron Lett. *1973*, 4329; *G. Wulff, W. Vesper, R. Grobe-Einsler, A. Sarhan*, Makromol. Chem. *178*, 2799 (1977); *G. Wulff, R. Grobe-Einsler, W. Vesper, A. Sarhan*, *ibid. 178*, 2817 (1977).
[4] *M. Kawana, S. Emoto*, Tetrahedron Lett. *1972*, 4855.
[5] *C. C. Leznoff*, Acc. Chem. Res. *11*, 327 (1978).
[6] *H. G. Kuivila*, Acc. Chem. Res. *1*, *299* (1968).
[7] *G. R. Kieczykowski, R. H. Schlessinger, R. B. Salsky*, Tetrahedron Lett. *1976*, 597.

Novel Glycals as Synthons for Saccharide Syntheses[**]

By *Joachim Thiem, Petra Ossowski,* and *Jens Schwentner*[*]

The sequential construction of long-chain oligodeoxyoligosaccharides and linkage to complex aglycons require readily accessible reactive saccharide precursors and a readily manageable method of coupling. A suitable technique consists in the reaction of glycals with alcohols in the presence of *N*-iodosuccinimide (NIS)[1]. As a potential method for the production of cardenolide oligosaccharides, increasing interest is being focused on a synthesis of D-digitoxal *(3a)*, which proceeds independently of the natural product[2] and of the conventional glycal syntheses[3].

The epoxide ring in methyl 2,3-anhydro-6-deoxy-α-D-allopyranoside *(1)*[4], which is easily accessible in six steps from methyl α-D-glucopyranoside by a standardizable method[5], undergoes smooth nucleophilic cleavage with lithium iodide dihydrate in pyridine with addition of acetic acid. According to the Fürst-Plattner rule[6], the *trans*-diaxial 2,6-dideoxy-2-iodo-α-D-*altro* cleavage product *(2)* predominates (80 % yield, see Table 1 for physical data). In addition, the *trans*-diequatorial 3,6-dideoxy-3-iodo-α-D-*gluco* product (20 %) is also formed.

The reaction of iodohydrin *(2)* with methyllithium in ether[7] has proved to be of considerable advantage. Chromatographic separation of the isomeric iodohydrins formed in the first step is not necessary for the preparation since the stable compound *(3a)*[2] crystallizes directly after reaction of the mixture with methyllithium.

(3a) was acetylated to *(3b)* which could be condensed with the epoxide *(1)* by the *N*-iodosuccinimide method[1]

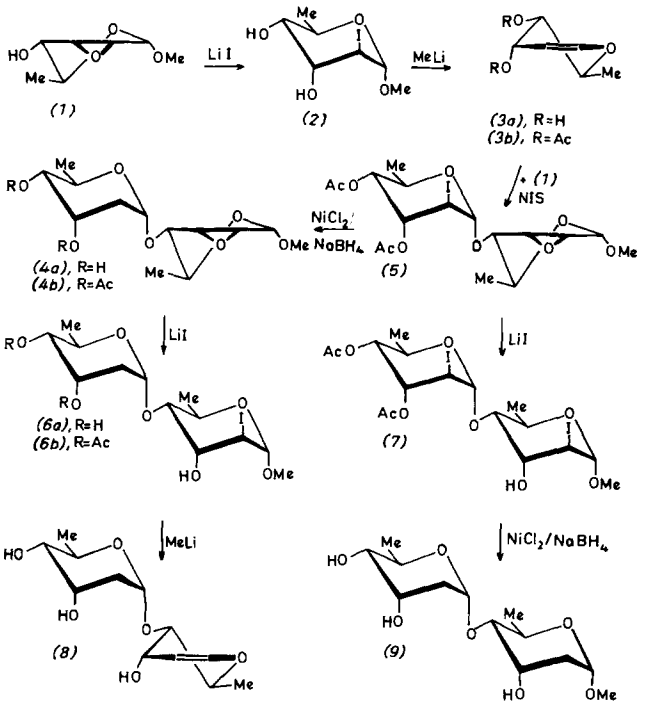


Table 1. Physical data (selection) of the sugar derivatives synthesized. ^{1}H-NMR at 270 MHz (Bruker WH 270) in $CDCl_3$ and CD_3OD.

(2), syrup, $[\alpha]_D^{20} = +44.3°$ ($CHCl_3$)
(3a), m. p. 115 °C, $[\alpha]_D^{20} = +314.2°$ (CH_3OH)
(4b), m. p. 98 °C, $[\alpha]_D^{20} = +256.9°$ ($CHCl_3$)
(5), syrup, $[\alpha]_D^{20} = +153.6°$ ($CHCl_3$); NMR: $\delta = 5.28$ (d, 1'-H), $J_{1',2'} = 2.4$ Hz
(6b), syrup, $[\alpha]_D^{20} = +157.7°$ ($CHCl_3$)
(7), syrup, $[\alpha]_D^{20} = +63.2°$ ($CHCl_3$); NMR: $\delta = 4.93$ (d, 1-H), 4.32 (dd, 2-H), 4.25 (m, 3-H), $J_{1,2} = 1.9$, $J_{2,3} = 4.3$, $J_{3,4} = 2.7$ Hz
(8), syrup, $[\alpha]_D^{20} = +324.1°$ (CH_3OH); NMR: $\delta = 6.31$ (d, 1-H), 4.89 (dd, 2-H), 4.27 (dd, 3-H), 3.64 (dd, 4-H), 4.15 (dq, 5-H), 1.35 (d, 6-CH_3), 5.13 (dd, 1'-H), 1.98 (ddd, 2a'-H), 2.25 (ddd, 2e'-H), 4.02 (ddd, 3'-H), 3.20 (dd, 4'-H), 3.88 (dq, 5'-H), 1.32 (d, 6'-CH_3), $J_{1,2} = 5.9$, $J_{2,3} = 4.9$, $J_{3,4} = 3.8$, $J_{4,5} = 8.5$, $J_{5,6} = 6.4$, $J_{1',2a'} = 3.4$, $J_{1',2e'} = 1.1$, $J_{2a',2e'} = -14.8$, $J_{2a',3'} = 3.5$, $J_{2e',3'} = 3.1$, $J_{3',4'} = 3.1$, $J_{4',5'} = 9.7$, $J_{5',6'} = 6.2$ Hz
(9), m. p. 155–157 °C, $[\alpha]_D^{20} = +284.1°$ (CH_3OH)

[*] Prof. Dr. J. Thiem, Dipl.-Chem. P. Ossowski, Dipl.-Chem. J. Schwentner
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

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

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0220 $ 02.50/0

to give *(5)* (72%). Opening of the epoxide ring of this α,1→4 linked disaccharide derivative with lithium iodide dihydrate gives, in addition to the *gluco-altro* isomer, the bis-*altro* compound *(7)* (56% yield) as the major product.

On reduction with $NiCl_2/NaBH_4$[1,5], compound *(7)* affords methyl 2,6-dideoxy-4-*O*-(2,6-dideoxy-α-D-*ribo*-hexopyranosyl)-α-D-*ribo*-hexopyranoside *(9)*[8], the glycoside of the terminal disaccharide unit of *neo*-digoxin[9]. The synthesis has not yet been optimized and the present yield of 34% should be open to considerable improvement. This synthetic approach provides a convenient entry to other oligodeoxyoligosaccharides.

Reductive removal of the iodine from *(5)* with $NiCl_2/NaBH_4$[1,5] gives the 2'-deoxy derivative *(4b)*. A series of hitherto unelucidated by-products lowers the yield to 32%. Epoxide ring cleavage of *(4b)* affords not only the *gluco-ribo* isomer but mainly the *altro-ribo* configurated derivative *(6b)* (43% yield); the ^{1}H-NMR data for its reducing saccharide ring are comparable with those of *(7)*.

When subjected to elimination reaction with methyllithium in ether[7], *(6b)* smoothly furnishes the disaccharide glycal *(8)*. The derivative *(8)* (45% yield) represents a disaccharide synthon, comparable with the monosaccharide synthon *(3a)*, which permits further synthetic reactions. Addition of methanol to *(8)* in the presence of *N*-iodosuccinimide affords *(6a)*, which was transformed into *(4a)* with sodium methoxide and characterized.

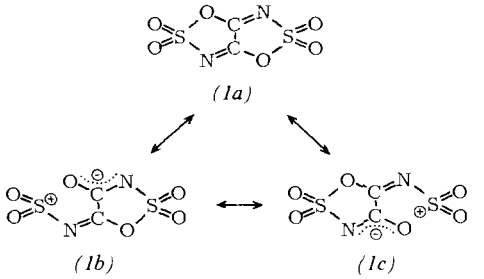
Received: December 20, 1978 [Z 157 IE]
German version: Angew. Chem. *91*, 242 (1979)

[1] *J. Thiem, H. Karl, J. Schwentner*, Synthesis *1978*, 896; *J. Thiem, J. Elvers*, Chem. Ber., in press.
[2] *F. Micheel*, Ber. Dtsch. Chem. Ges. *63*, 347 (1930).
[3] Cf., *e.g., W. Roth, W. Pigman*, Methods Carbohydr. Chem. *2*, 405 (1963).
[4] The 2,3-anhydro derivatives *(1)*, *(4)*, and *(5)* probably prefer the SO_3(D) sofa conformation and are therefore drawn thus; cf. *J. Thiem, J. Schwentner, E. Schüttpelz, J. Kopf*, Chem. Ber., in press.
[5] *H. Paulsen, V. Sinnwell*, Chem. Ber. *111*, 879 (1978).
[6] *A. Fürst, P. A. Plattner*, 12th Int. Congr. Pure Appl. Chem., New York 1951, Abstr. Papers, p. 409.
[7] *M. Sharma, R. K. Brown*, Can. J. Chem. *44*, 2825 (1966).
[8] *J. Thiem, J. Schwentner*, Chem. Ber., in press.
[9] *F. Kaiser, E. Haack, H. Spingler*, Naturwissenschaften *46*, 447 (1959).

Formal Criss-Cross Cycloaddition of Sulfur Trioxide to Cyanogen[**]

By *Herbert W. Roesky, Nurul Amin, Graalf Remmers, Alfred Gieren, Uwe Riemann*, and *Bernhard Dederer*[*]

Cyanogen reacts with sulfur trioxide in the molar ratio 1:2 to give a compound which was formulated[1] as the (bis)adduct of a Lewis acid and a Lewis base. However, its sensitivity towards hydrolysis is incompatible with the properties of the known adducts of SO_3 with Lewis bases[2]. X-ray structure analysis has now shown this compound to be 1,2,3-oxathiazolo[4,5-*d*][1,2,3]oxathiazole 2,2,5,5-tetroxide *(1)*, the product of a formal criss-cross cycloaddition (1,3;2,4 cycloaddition)[3]. However, the reaction mechanism has yet to be elucidated. Neither SO_3 nor $(CN)_2$ has hitherto been found to undergo criss-cross cycloaddition. On bonding of *(1)* the SO_3 component is incorporated regiospecifically. No monoadduct could be isolated, even in the presence of an excess of cyanogen.



(1a)

(1b) *(1c)*

(1) forms monoclinic crystals, space group A2/a with $a=11.928(3)$, $b=6.818(2)$, $c=7.824(2)$ Å, $\gamma=96.37(2)°$, $Z=4$, $\rho_{calc.}=2.228\,g\,cm^{-3}$. Using an automatic single-crystal diffractometer (Siemens AED), 1968 independent reflections were measured with $Mo_{K\alpha}$ radiation ($\theta_{max}=40°$, $\theta/2\theta$ scan, 5-point measurement) of which 219 were regarded as unobserved ($I \leq 2\sigma_I$). After Patterson and Fourier synthesis, refinement (complete matrix) led to $R=0.049$. The molecule is centrosymmetric and in the crystal it deviates only slightly (mainly with regard to the exocyclic oxygen atoms) from the higher 2/m symmetry. The bicyclic skeleton is planar.

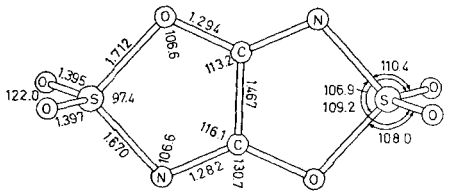


Fig. 1. Molecular structure of 1,2,3-oxathiazolo[4,5-*d*][1,2,3]oxathiazole 2,2,5,5-tetroxide *(1)* in the crystal. Standard deviations 0.002—0.003 Å for bond lengths and 0.1—0.2° for bond angles.

Compound *(1)* exhibits unusual bond lengths: the S—O bond in the ring is extremely long at 1.71 Å, while the exocyclic S=O bonds are shortened to 1.39 Å. This finding suggests a description of the molecule in terms of bond-non bond resonance [*(1a)*↔*(1b)*, *(1c)*], the resonance formulas *(1b)* and *(1c)* also providing some rationalization for the short C—O bond (1.29 Å).

Procedure

Cyanogen (0.1 mol) is passed into ice-cooled sulfur trioxide (0.15 mol) with exclusion of moisture. As soon as the solution has solidified to a gel, the excess of SO_3 is stripped off *in vacuo*. Vacuum sublimation gives colorless crystals of *(1)*; yield 80%. IR: ν(CN) and/or ν(CO) 1690, 1670 cm^{-1}. MS (70 eV): $m/e=106(100\%)M_r/2, 80\,SO_3, 64\,SO_2, 48\,SO, 42\,NCO$.

Received: December 21, 1978;
supplemented: January 4, 1979 [Z 159 IE]
German version: Angew. Chem. *91*, 243 (1979)

[*] Prof. Dr. H. W. Roesky, Dipl.-Chem. N. Amin, Dr. G. Remmers
Anorganisch-chemisches Institut I der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Dr. habil. A. Gieren, U. Riemann, Dr. B. Dederer
Max-Planck-Institut für Biochemie, Abt. Strukturforschung I
Am Klopferspitz, D-8033 Martinsried (Germany)

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

[1] *H. A. Lehmann, L. Riesel, K. Hoehne, E. Maier*, Z. Anorg. Allg. Chem. *310*, 298 (1961).
[2] *A. Gieren, B. Dederer, H. W. Roesky, N. Amin, O. Petersen*, Z. Anorg. Allg. Chem. *440*, 119 (1978).
[3] *K. Burger, W. Thenn, R. Rau, H. Schickaneder, A. Gieren*, Chem. Ber. *108*, 1460 (1975); cf. also *T. Wagner-Jauregg*, Synthesis *1976*, 349.

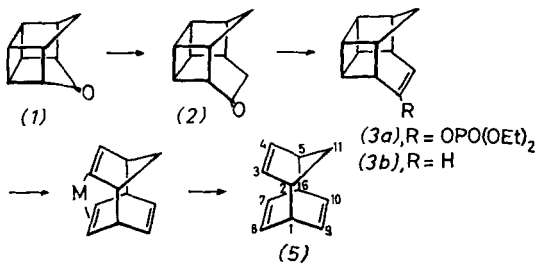
© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0221 $ 02.50/0*

Tricyclo[4.2.2.1^{2,5}]undeca-3,7,9-triene, the [4+4]-Cycloadduct of Benzene and Cyclopentadiene. Reaction Sequence of Its Retro-Cleavage[**]

By *Wolfram Grimme*, *Wolfgang Mauer*, and *Gerd Reinhardt*[*]

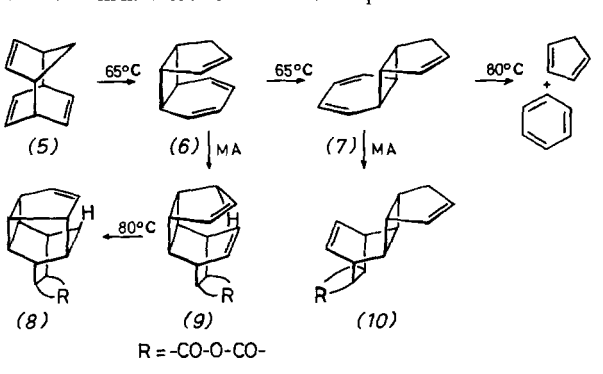
Cycloreversions forming benzene readily proceed both as symmetry allowed [4+2]-[1] and as forbidden [2+2]-processes[2], and their kinetic and thermodynamic data can be determined quite easily. Since very little is known so far about the likewise forbidden [4+4]-cycloreversion[3] we have synthesized the title compound *(5)* and investigated its decomposition to benzene and cyclopentadiene. [2+2]-[2a] and [4+2]-cycloreversions[1a] to the same products are already well known.

The ketone *(1)*[4] is converted by treatment with diazomethane in methanol/ether in the presence of lithium bromide into the homologous compound *(2)* (85% yield; for physical data see Table 1). The enolate of *(2)*, generated by reaction with lithium diisopropylamide in hexane/tetrahydrofuran, is then allowed to react with diethyl chlorophosphate and tetramethylethylenediamine. Reduction of the resulting ester *(3a)* with lithium in liquid ammonia/tetrahydrofuran/*tert*-butanol according to the method of *Ireland*[5] affords, after gas-chromatographic separation, the C_9-homobasketene *(3b)* as volatile crystals (50%).



(4a), M = Rh(F$_3$acac)
(4b), M = Ag$^+$ClO$_4^-$

As expected[6], the tricyclo[4.2.0.0^{2,5}]octane moiety in *(3b)* can be opened by reaction with norbornadiene(trifluoro-2,4-pentanedionato)rhodium in chloroform at 60°C; the isomerization requires one equivalent of the reagent and yields the rhodium complex *(4a)*, which is purified by sublimation (100°C/10^{-2} torr) (87%). In benzene, *(4a)* is stable towards CO (5 atm), and only on addition of silver perchlorate does it split into the silver complex *(4b)* and dicarbonyl(trifluoro-2,4-pentanedionato)rhodium. Treatment of *(4b)* with ammonium nitrate in concentrated aqueous ammonia liberates the title compound *(5)*, which after chromatographic purification (diethylene glycol succinate, 0.5 m, 65°C) is obtained as volatile colorless crystals having a strong odor (26%).



Heating of the [4+4]-cycloadduct *(5)* of benzene and cyclopentadiene to 140°C leads to its complete retrocleavage; however, NMR spectroscopic monitoring of the reaction with stepwise increase in temperature shows that two separate rearrangements precede the decomposition: at 65°C a rapid Cope rearrangement ($t_{1/2}$ = 2 h) leads to the *syn-cis* [2+2]-adduct *(6)*, which can be separated gas chromatographically (diethylene glycol succinate, 0.5 m, 70°C). On prolonged warming at 65°C *(6)* is converted, as a result of reversible opening of the bicyclo[4.2.0]octa-2,4-diene moiety to the eight-membered ring[7], into the *anti-cis* isomer *(7)* (98%, $t_{1/2}$ = *ca.* 24 h). It is *(7)* which subsequently cleaves[2a] at higher temperatures into benzene and cyclopentadiene ($t_{1/2}$ = 35 h at 80°C). The reaction sequence of the retrocleavage of the [4+4]-cycloadduct *(5)* illustrates the energetic advantage of synchronous transition states over a diradical. The latter is obtained only from *(7)* at higher temperature and leads to the decomposition, while it plays no role in the two preceding direct processes.

Table 1. Physical data of the compounds *(2)*, *(3b)*, *(4a)*, *(5)*, *(6)*, *(8)*, *(9)*, and *(10)*. The ^{1}H-NMR spectra were recorded at 90 MHz in $CDCl_3$ [*(4)* and *(6)* in C_6D_6, *(5)* in CCl_4].

(2), m.p. 157°C; ^{1}H-NMR: δ = 6.5—7.3 (m, 8H), 2.17 (AB as doublets, Δ_ν = 24.7 Hz, J = 19.5 Hz, 2H, $COCH_2$), 1.80 (AB, Δ_ν = 16 Hz, J = 13.5 Hz, B-part split, 2H, CH_2); IR (KBr): ν_{CO} = 1700 cm^{-1}

(3b), m.p. 108°C; ^{1}H-NMR: δ = 6.12 (AA'XX' half spectrum, $J+J'$ = 5.4 Hz, J_A = 9.3 Hz, J_X = 0 Hz, 2 olefin-H), 3.1 (m, 4H), 3.0 (m, 2H), 2.6 (m, 2H), 1.48 (AB, Δ_ν = 21.5 Hz, J = 13.2 Hz, B-part as triplets J' = 5.4 Hz, 2H, CH_2); ^{13}C-NMR ($CDCl_3$, 20 MHz): δ = 129.75 (2 olefin-C), 44.83 (2C), 43.80 (2C), 34.70 (2C), 32.75 (1C, CH_2), 32.38 (2C)

(4a), m.p. 142°C; ^{1}H-NMR: δ = 5.97 (AA'XX'-half spectrum, $J+J'$ = 8.1 Hz, J_A = 7.8 Hz, J_X = 0 Hz, H-9,10), 5.57 (s, 1H, F_3acac), 5.17 (AA'XX' half spectrum, $J+J'$ = 8.4 Hz, J_A = 2.4 Hz, J_X = 0, H-7, 8), 4.65 (m, H-3, 4), 3.17 (m, H-1, 6), 2.07 (m, H-2, 5), 1.63 (s, 3H, F_3acac), 1.12 (AB, Δ_ν = 28.5 Hz, J = 11 Hz, A-part as triplets with J' = 4.5 Hz, H-11$_{anti}$, H-11$_{syn}$); MS: m/e = 400 (M^+), 334 ($M^+ - C_5H_6$), 181 ($-F_3$acac), 168 (100%, $RhC_5H_5^+$), 103 (Rh^+), 91 ($C_7H_7^+$)

(5), m.p. 90°C; ^{1}H-NMR: δ = 6.33 (A_2X_2 half spectrum, J = 6 Hz, H-9, 10), 6.20 (A_2X_2 half spectrum, J = 5 Hz, H-7, 8), 5.93 (s, H-3, 4), 2.97 (septet, J = 5 Hz, H-1, 6), 2.4 (m, H-2, 5), 2.09 (AB, Δ_ν = 37.6 Hz, J = 10.5 Hz, B-part as triplets with J' = 4.5 Hz, H-11$_{syn}$, H-11$_{anti}$); ^{13}C-NMR (CCl_4, ext. $CDCl_3$, 20 MHz): δ = 139.51 (2 olefin-C), 137.98 (2 olefin-C), 134.47 (2 olefin-C), 47.90 (C-11), 42.24 (2C), 39.44 (2C)

(6), ^{1}H-NMR: δ = 6.1—5.0 (m, 6 olefin-H), 3.3 (m, 4H), 2.48 (AB, Δ_ν = 47.4 Hz, J = 17.5 Hz, 2H, CH_2)

(8), m.p. 201°C; ^{1}H-NMR: δ = 6.02 (narrow m, 2 olefin-H), 3.5—3.0 (m, 4H), 2.9—2.0 (m, 6H), 1.68 (AB, Δ_ν = 123 Hz, J = 13.5 Hz, B-part as doublets with J' = 8 Hz, 2H, CH_2)

(9), m.p. 213°C; ^{1}H-NMR: δ = 6.07 (AA'XX' half spectrum, 2H), 5.55 (narrow m, 2H), 3.3 (m, 3H), 3.0 (d, J = 1.5 Hz, 2H), 3.1—2.0 (m, 5H)

(10), m.p. 207.5°C; ^{1}H-NMR: δ = 6.42 (AA'XX' half spectrum, 2H), 5.72 (narrow m, 2H), 3.3 (m, 3H), 2.90 (d, J = 1.5 Hz, 2H), 3.0—1.9 (m, 5H)

The *syn-cis* [2+2]-adduct *(6)* had already been postulated by us as an intermediate in the fragmentation of the *as*-homobasketene at *ca.* 180°C[8], since in the presence of an excess of maleic anhydride the addition compound *(8)* was formed. Reaction of the now accessible *(6)* with maleic anhydride confirms our assumption: At room temperature the Diels-Alder product *(9)* is formed (98%), which is converted at 80°C *via* an ene-reaction into *(8)* ($t_{1/2}$ = 15 h). The unusually low activation barrier for the secondary reaction *(9)* → *(8)* is explained in terms of the favorable fixation of the reaction centers in *(9)*. Reaction of *(7)* with maleic anhydride gives the adduct *(10)*.

[*] Dr. W. Grimme, Dr. W. Mauer, Dipl.-Chem. G. Reinhardt
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

[**] This work was supported by the Verein der Freunde und Förderer der Universität Köln and the Fonds der Chemischen Industrie.

Received: December 27, 1978 [Z 156 IE]
German version: Angew. Chem. *91*, 254 (1979)

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0224 $ 02.50/0

[1] a) *A. R. Rye, D. Wege*, Aust. J. Chem. *27*, 1943 (1974); b) *W. G. Dauben, G. T. Rivers, R. T. Twieg, W. T. Zimmerman*, J. Org. Chem. *41*, 887 (1976); c) *W. Grimme, E. Schneider*, Angew. Chem. *89*, 754 (1977); Angew. Chem. Int. Ed. Engl. *16*, 717 (1977).
[2] a) *J. F. Monthony, W. H. Okamura*, Tetrahedron *28*, 4273 (1972); b) *J. C. Berridge, D. Bryce-Smith, A. Gilbert*, J. Chem. Soc. Chem. Commun. *1975*, 611; c) *H. Röttele, W. Martin, J. F. M. Oth, G. Schröder*, Chem. Ber. *102*, 3985 (1965).
[3] *G. Kaupp, R. Dyllick-Brenzinger*, Angew. Chem. *86*, 523 (1974); Angew. Chem. Int. Ed. Engl. *13*, 478 (1974).
[4] *W. G. Dauben, D. L. Whalen*, J. Am. Chem. Soc. *93*, 7244 (1971).
[5] *R. E. Ireland, D. C. Muchmore, U. Hengartner*, J. Am. Chem. Soc. *94*, 5098 (1972).
[6] *P. E. Eaton, D. R. Patterson*, J. Am. Chem. Soc. *100*, 2573 (1978), and references cited therein.
[7] *F. A. Cotton, G. Deganello*, J. Am. Chem. Soc. *95*, 396 (1973), and references cited therein.
[8] *W. Mauer, W. Grimme*, Tetrahedron Lett. *1976*, 1835.

Molecular Structure of Phe²-TRH, an Analogue of Thyrotropin-Releasing Hormone

By *John J. Stezowski, Claus Bürvenich*, and *Wolfgang Voelter*[*]

X-ray analysis of thyrotropin-releasing hormone (TRH) and analogous compounds has hitherto been impossible owing to the lack of suitable crystals. We have found that Phe²-TRH forms crystals suitable for X-ray analysis. Phe²-TRH is an analogue having a relatively high biological activity[1] and antidepressive action[2].

Figure 1 illustrates the methodological strategy for the synthesis of Phe²-TRH. Crystals of Phe²-TRH were obtained by

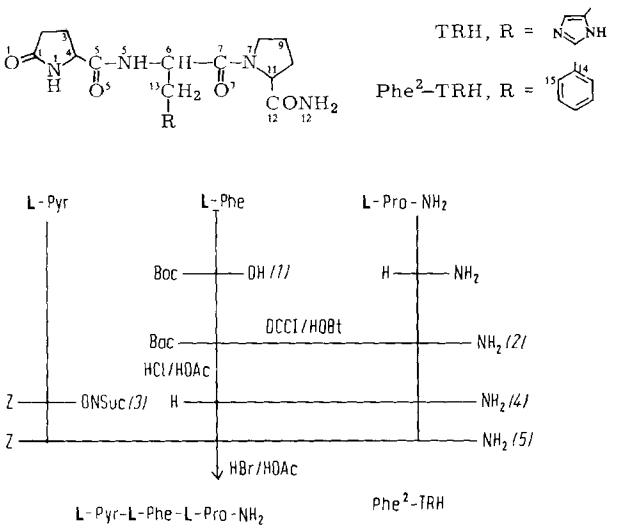


Fig. 1. Schematic diagram of the synthesis of Phe²-TRH. Pyr = pGlu = pyroglutamyl.

slow evaporation of aqueous or 2-propanol solutions; space group $P2_12_12_1$, with 4 Phe²-TRH·H_2O molecules per unit cell, cell constants[3a] at 120 K: $a = 14.831(4)$, $b = 11.440(2)$, $c = 11.448(2)$ Å. The original crystal-structure model[3b] was refined with high-resolution data ($T \approx 120$ K) to $R = 0.044$ (3162 observed reflections).

[*] Dr. J. J. Stezowski
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)
Prof. Dr. W. Voelter, Dipl.-Chem. C. Bürvenich
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

Figure 2 shows the molecular structure of Phe²-TRH. The proline ring is present in two conformations in the crystal.

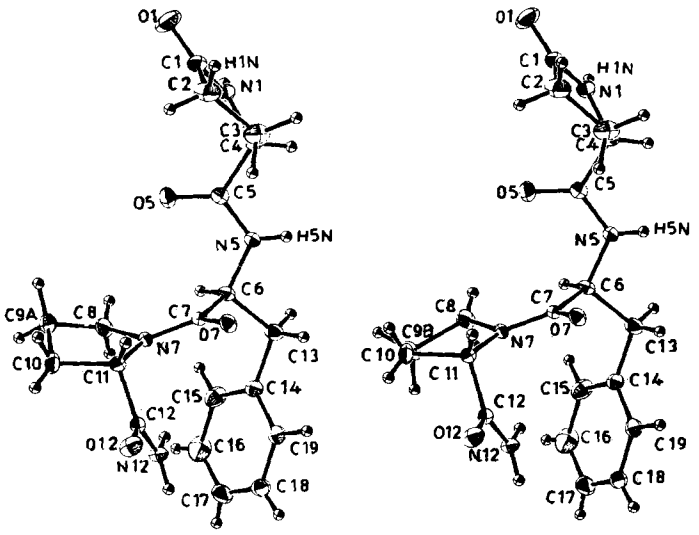


Fig. 2. Molecular structure of Phe²-TRH. The two conformations of the proline ring differ in the disposition of C(9). The rest of the molecule is presented stereoscopically. Dihedral angles: N(1)C(4)C(5)N(5) = 143.8°, N(5)C(6)C(7)N(7) = 132.1°, N(5)C(6)C(13)C(14) = 178.8°, C(6)C(13)C(14)C(15) = 62.5°, N(7)C(11)C(12)N(12) = −24.3°.

The two peptide bonds are *trans*-oriented. The water molecule is bonded *via* one of its protons to O(1) of one Phe²-TRH molecule and *via* its second proton to O(5) of another peptide molecule: its oxygen atom, however, has no acceptor function. H(1N) and H(5N) are bound *via* hydrogen bridges to O(12) of the next molecule. O(7) is coupled *via* a hydrogen bond with H(12N,1); H(12N,2) forms no hydrogen bonds in the crystal.

Experimental

The following amino acids and peptides were synthesized according to methods given in the literature: *(1)* (see Fig. 1)[4], Boc-L-Pro[4], Boc-L-Pro-NH_2[5], L-Pro-NH_2·HCl[6], Z-L-Glu[7a], Z-L-glutamic anhydride[7b], Z-L-Pyr·DCHA[7c], *(3)*[7d].

L-Phe-L-Pro-NH_2 *(4)*: A mixture of *(2)* (30 g) and 1.2 N HCl/HOAc (250 ml) is stirred for 30 min at room temperature. The solvent is then removed in a rotary evaporator and the residue extracted several times with methanol. After removal of the methanol by evaporation *(4)* is crystallized from the remaining oil with methanol/ether; yield 22.08 g (89 %), m. p. 60 °C (decomp.), $[\alpha]_D = -10.95°$ ($c = 1.13$/HOAc).

Z-L-Pyr-L-Phe-L-Pro-NH_2 *(5)*: A mixture of *(3)* (5 g), *(4)*·HCl (4.36 g) and *N*-ethylmorpholine (1.75 ml) is stirred for 24 h at room temperature. The reaction mixture is evaporated to dryness, taken up in ethyl acetate, washed several times with $NaHCO_3$ and water, dried with Na_2SO_4 and crystallized from anhydrous ether; yield 3.41 g (48 %) *(5)*, m. p. 70 °C (decomp.), $[\alpha]_D = -68.88°$ ($c = 1$, MeOH).

Phe²-TRH[8]: A mixture of *(5)* (3 g) and HBr/glacial acetic acid is stirred for 5 min at room temperature; the solvent is then removed and the residue washed several times with methanol. The residue recovered after subsequent evaporation to dryness is taken up in water and treated with ion-exchanger. After filtration the filtrate is concentrated by evaporation and passed through a Sephadex-G10 column and freeze dried.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0225 $ 02.50/0*

Yield 1.78 g (81%) Phe²-TRH, m.p. 180—183 °C, $[\alpha]_D = -43.2°$ ($c = 1$, MeOH).

Received: December 15, 1978 [Z 160 IE]
German version: Angew. Chem. 91, 243 (1979)

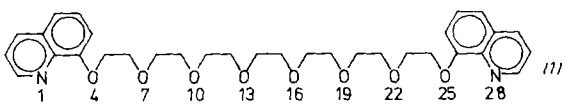
CAS Registry numbers:
(1), 13734-34-4; (2), 69470-09-3; (3), 40291-26-7; (4), 64774-32-9; (5), 69461-91-2; L-prolinamide, 7531-52-4; Phe²-TRH, 34783-35-2

[1] D. Gupta, W. Voelter: Hypothalamic Hormones—Structure, Synthesis and Biological Activity. Verlag Chemie, Weinheim 1975.
[2] W. Voelter, K. Zech, K. Klemm, G. Ludwig, H.-G. Menge, unpublished results.
[3] a) J. M. Stewart, P. A. Machin, C. Dickinson, H. Ammon, H. Heck, H. Flack: The XRAY System, Version of 1976. Tech. Rep. TR-446, Computer Science Center, Univ. of Maryland, College Park, MD; b) P. Main, L. Lessinger, M. M. Woolfson, G. Germain, J. P. Declercq: Multan 77, A Program for the Automatic Solution of Crystal Structures from X-ray Diffraction Data. University of York 1977.
[4] E. Schnabel, Justus Liebigs Ann. Chem. 702, 188 (1967).
[5] K. Zech, Dissertation, Universität Tübingen 1973; S. Fuchs, Dissertation, Universität Tübingen 1975.
[6] R. H. Chambers, F. H. Carpenter, J. Am. Chem. Soc. 77, 1522 (1955); D. Hammer, J. P. Greenstein, J. Biol. Chem. 193, 81 (1951).
[7] a) S. Goldschmidt, C. Jutz, Chem. Ber. 86, 1116 (1953); b) W. J. LeQuesne, G. T. Young, J. Chem. Soc. 1950, 1954, 1959; c) H. Gibian, E. Klieger, Justus Liebigs Ann. Chem. 640, 145 (1961); d) P. Kurath, A. M. Thomas, Helv. Chim. Acta 56, 1656 (1972).
[8] E. Pietrzik, Dissertation, Universität Tübingen 1977.

Spherical Wrapping of a Linear Polyether around a Cation—1,20-Bis(8-quinolyloxy)-3,6,9,12,15,18-hexaoxaeicosane·RbI[**]

By *Gabriela Weber, Wolfram Saenger, Fritz Vögtle*, and *Heinz Sieger*[*]

In addition to crown ethers and three-dimensional cryptands, linear polyethers are being increasingly used for complexing cations[1]. It is remarkable in this context that even 1,2-ethanediol forms crystalline complexes with alkaline earth metal ions[2] and that this property is enhanced by rigid aromatic end groups[1]. Depending upon the chain length of the polyether, various complex structures are obtained in the series of arene-$(OCH_2CH_2)_n$O-arene ligands: ligands with $n = 2$ wrap in a circular fashion around a cation[3], and extension of the ether chain by one or two OCH_2CH_2 units leads to helical structures[4, 5]. Two possible arrangements are conceivable for very long ligands: (i) helical polynuclear complexes could turn out as S-shaped arrangements, with a cation coordinated in each S loop, each cation being bound to an anion for geometrical reasons (see [6]), or (ii) a cation could be spherically wrapped in a long ligand with more than one turn and thus shielded from the anion. The possibility (ii) is actually found in the complex formed from 1,20-bis(8-quinolyloxy)-3,6,9,12,15,18-hexaoxaeicosane *(1)* and RbI.



(1)

Compound *(1)* was obtained by condensation of 8-hydroxyquinoline and heptaethylene glycol in alkaline medium, and the complex with RbI in boiling ethyl acetate/methanol. Synthesis of crystalline complexes with NaSCN, NH_4SCN, KSCN, $Ca(SCN)_2$, and $Ba(SCN)_2$ has so far proved unsuccessful. The ^{1}H-NMR spectrum of *(1)*·RbI does not exhibit any pronounced upfield shift of the α,β-quinoline protons (cf. [7]). Hence it may be deduced that the quinoline rings of *(1)*·RbI are located outside the region of mutual anisotropism.

Slow cooling of *(1)*·RbI in methanol/ethyl acetate yields single crystals (*ca.* $3 \times 1 \times 0.5\ mm^3$), space group C2/c, cell constants $a = 42.17$, $b = 10.80$, $c = 15.95$ Å, $\beta = 100.4°$. The intensities of 4672 independent reflections were measured with a four-circle diffractometer ($Cu_{K\alpha}$). After solving the structure by a combination of direct and Fourier methods, the structural data were refined to $R_w = 9.6\%$ by least-squares methods with anisotropic temperature factors for the heavy atoms and isotropic factors for C, N, O.

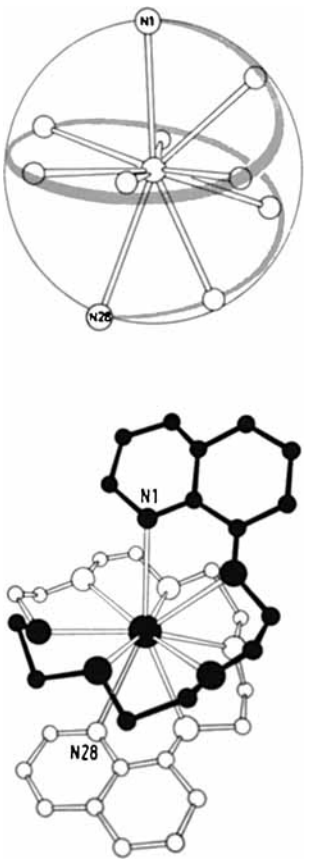


Fig. 1. a) Arrangement of heteroatoms of ligand *(1)* on the coordination sphere of Rb^+; b) structure of complex *(1)*·RbI. Since I^- is not coordinated it has been omitted.
Rb^+...heteroatom distances [Å] for the polar region: N(1), 3.201; N(28), 3.371; O(25), 3.086; for equatorial region: O(4), 2.993; O(7), 3.025; O(10), 3.038; O(13), 2.959; O(16), 2.974; O(19), 3.009; O(22), 3.147 (mean standard deviation ±0.008 Å).

In the complex *(1)*·RbI (Fig. 1), all the heteroatoms lie approximately on the surface of a sphere of radius ≈3 Å. Its poles are occupied by N(1) and N(28), in accord with the results of ^{1}H-NMR studies on the complex in solution. Starting from N(1) the ligand chain runs to the equator of

[*] Prof. Dr. W. Saenger, Dr. G. Weber
Max-Planck-Institut für experimentelle Medizin, Abteilung Chemie
Herman-Rein-Strasse 3, D-3400 Göttingen (Germany)
Prof. Dr. F. Vögtle, Dipl.-Chem. H. Sieger
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

[**] Structures of Polyether Complexes, Part 7.—Part 6: *G. Weber, W. Saenger*, Acta Crystallogr., in press.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0226 $ 02.50/0

the sphere, which it follows, before leaving to reach the other pole at N(28). This description is naturally somewhat idealized. The torsional angles OCCO along the polyether chain lie in the *gauche* region (±60°), whereas the angles CCOC and COCC are *trans*-oriented except for C(3)-O(4)-C(5)-C(6) (126°). +*gauche* and −*gauche* torsional OCCO angles alternate.

The Rb^+ cation is ten-coordinated if the $Rb^+ \cdots N$ and $Rb^+ \cdots O$ contacts of 3.371 and 3.147 Å are included. The ideal van der Waals distances are 2.97 and 2.87 Å, respectively: these values are not attained by any of the Rb...heteroatom contacts. Similar values are known for highly coordinated Rb^+[8], while other $Rb^+ \cdots$polyether complexes with smaller ligands show normal values[3, 4].

Since Rb^+ is completely enclosed by the ligand and thus shielded it cannot interact with I^-. In the unit cell I^- is located in cavities between the "spheres" of *(1)* and Rb^+ and is fixed by weak van der Waals forces only. This is probably the reason for its being twofold disordered.

Procedure

Synthesis of *(1)*: Heptaethylene glycol ditosylate[9] (50 mmol) in benzene/dimethylformamide (1 : 1, 60 ml) is added dropwise to a mixture of 8-hydroxyquinoline (100 mmol) and KOH (100 mmol) in boiling ethanol. After heating for 6 h under reflux, filtration and vacuum distillation of the filtrate, the residual oil is dissolved in $CHCl_3$, extracted several times with dilute caustic soda, washed with H_2O, dried over Na_2SO_4, concentrated to *ca.* 10 ml by distillation in vacuum, and chromatographed on alumina (Woelm, basic, activity I): 15.4 g (53 %) of *(1)*, viscous oil; ^{1}H-NMR ($CDCl_3$): δ = 9.2–9.0 (m, 2H, quinoline), 8.3–8.0 (m, 2H, quinoline), 7.6–7.1 (m, 8H, quinoline), 4.6–4.0 (m, sym, 8H, OCH_2), 3.9—3.6 (m, 20H, OCH_2); MS calc. 580.2785, exp. 580.2790; TLC ($CHCl_3$/ethanol 5 %, silica gel): $R_f = 0.5$.

Synthesis of *(1)*·RbI: *(1)* (0.2 mmol) in ethyl acetate (8 ml) and RbI (0.2 mmol) in methanol (4 ml) are heated together under reflux for ½ h. After cooling, the complex precipitates on addition of light petroleum (50—70 °C) as a viscous oil and is recrystallized from ethyl acetate/methanol: 84 mg (62 %) yellow prisms, m.p. 111—115 °C.

Received: December 27, 1978;
supplemented: February 5, 1979 [Z 161a IE]
German version: Angew. Chem. *91*, 234 (1979)

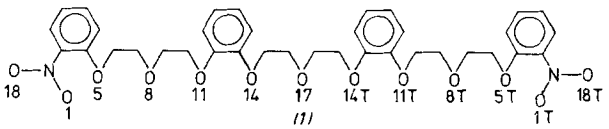
CAS Registry number:
(1)·RbI, 69439-93-6

[1] a) *F. Vögtle, H. Sieger*, Angew. Chem. *89*, 410 (1977); Angew. Chem. Int. Ed. Engl. *16*, 396 (1977); b) *H. Sieger, F. Vögtle, ibid. 90*, 212 (1978) and *17*, 198 (1978); c) *F. Vögtle, H. Sieger, W. M. Müller*, J. Chem. Res. (S) *1978*, 398 (M 4848).
[2] *F. Vögtle, H. Sieger*, Tetrahedron Lett. *1978*, 2709.
[3] *W. Saenger, B. S. Reddy*, Acta Crystallogr., in press.
[4] *W. Saenger, H. Brand, F. Vögtle, E. Weber*, in *B. Pullman, B. Goldblum*: Metal-Ligand Interactions in Organic Chemistry and Biochemistry. Part I. D. Reidel, Dordrecht 1977, p. 363; *G. Weber, W. Saenger*, Acta Crystallogr., in press.
[5] *I.-H. Suh, G. Weber, W. Saenger*, Acta Crystallogr. *B34*, 2752 (1978).
[6] *G. Weber, W. Saenger*, Angew. Chem. *91*, 237 (1979); Angew. Chem. Int. Ed. Engl. *18*, 227 (1979).
[7] *E. Weber, F. Vögtle*, Tetrahedron Lett. *1975*, 2415.
[8] Compare the structure of a bis(tetraglyme)-Rb-biphenylide complex: *J. J. Mooij, A. A. K. Klaassen, E. de Boer, H. M. L. Degans, Th. E. M. van den Hark, J. H. Noordik*, J. Am. Chem. Soc. *98*, 680 (1976).
[9] *J. S. Bradshaw, R. A. Reeder, M. D. Thompson, E. D. Flanders, R. L. Carruth, R. M. Izatt, J. J. Christensen*, J. Org. Chem. *41*, 134 (1976); *J. Dale, P. O. Kristiansen*, Acta Chem. Scand. *26*, 1471 (1972).

S-Shaped Binuclear Cation Complex of a Linear Polyether: 1,5-Bis{2-[5-(2-nitrophenoxy)-3-oxapentyloxy]-phenoxy}-3-oxapentane·2KSCN[**]

By *Gabriela Weber* and *Wolfram Saenger*[*]

Very long linear polyethers can adopt various arrangements on the coordination sphere of a cation. In contrast to the spherical wrapping of a decadentate ligand around Rb^+[1], the polyether *(1)* is S-shaped in the title compound[2] and binds a K^+SCN^- ion pair in each S-loop.



The complex *(2)*·2KSCN crystallizes from ethyl acetate/methanol as thin platelets, space group C2/c, cell constants $a = 23.184$, $b = 9.051$, $c = 22.235$ Å, $\beta = 114.43°$; m.p. 108—109 °[2]. 3438 diffractometer data were measured by $2\theta/\omega$ scanning with $Cu_{K\alpha}$ radiation up to $2\theta = 125°$. The structure was solved by direct methods and refined to a crystallographically weighted value of $R_w = 5.6$ % by least squares methods. In contrast to ref. [2], no water of crystallization could be detected.

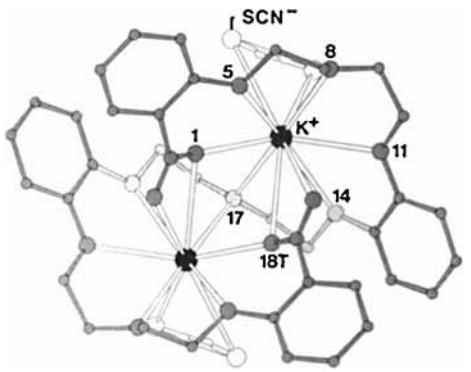


Fig. 1. Structure of the complex *(1)*·2KSCN. The two SCN^- ions are twofold disordered, such that the S and N atoms overlap. Since the C—S and C—N distances are unequal, the SCN^- ion is represented as (N)S—C—C—N(S). $K^+ \cdots$heteroatom distances [Å] for the polar region: O(1T), 3.113; O(18T), 3.180; N, S, 3.387 and 3.256; equatorial region O(5), 3.299; O(8), 2.684; O(11), 2.787; O(14), 2.815; O(17), 2.923.

In the complex *(1)*·2KSCN (Fig. 1) the polyether chain forms one S-loop around each K^+SCN^- ion pair. This arrangement of the ligand *(1)* is stabilized by coordination to K^+; the twofold coordination of O(1) and O(17) is probably the major factor involved. The central atom O(17) lies on a twofold crystallographic axis, *i.e.* the molecule is rotationally symmetric.

The coordination sphere of each K^+ can be divided into equatorial and polar regions. The equator is occupied by the heteroatoms O(1) to O(17) of one S-loop, and the nitro group belonging to the other loop covers one of the poles with O(1T) and O(18T). The other pole is free and can accommodate the SCN^- ion which is disordered for reasons of crystal packing.

[*] Prof. Dr. W. Saenger, Dr. G. Weber
Max-Planck-Institut für experimentelle Medizin
Abteilung Chemie
Hermann-Rein-Strasse 3, D-3400 Göttingen (Germany)

[**] Structures of Polyether Complexes, Part 8. We are grateful to Professor *F. Vögtle*, Bonn, for the title compound.—Part 7: [1].

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0227 $ 02.50/0*

The K^+...O distances in the polar region are generally greater than in the equatorial plane. Nevertheless, the distances to O(1) (2.699 Å) and to O(5) (3.299 Å) deviate considerably from the ideal value of 2.87 Å[3] and reveal the inductive effect of the nitro groups. The fact that the bond to O(8) is shorter than that to O(11) and to O(14) complies with the rule[4] that O atoms of aliphatic ethers are more strongly coordinated by cations, owing to their greater electronegativity, than O atoms of aromatic ethers. The relatively long K^+...O(17) distance can be attributed to the double coordination of the two K^+ entities.

The torsional angles along the polyether chain have the generally preferred values[1, 4]. Only the angle C(7)—O(8)—C(9)—C(10) of 74° lies in the *gauche* instead of the *trans* range, probably in order to facilitate better coordination of O(11).

The nitro group is twisted through −42° relative to the phenoxy ring. Rotation through −13° can be explained due to steric repulsion between an O atom of the nitro group and the *ortho* ether oxygen (cf. [5]). The remaining rotation might possibly be attributable to improved coordination of the two nitro oxygen atoms with K^+.

Formation of a binuclear complex from *(1)* and KSCN probably has purely geometrical reasons. The twofold coordination of the terminal nitro group also appears to favor the binuclear complex. *(1)* and Na^+ and K^+ ions gave only 1:2 complexes. On the other hand, an analogous ligand containing 2,6-dimethoxyphenyl in place of *o*-nitrophenoxy groups gives a 1:1 complex with K^+ but can take up the smaller Na^+ ion in the ratio of 1:2[2].

Received: December 27, 1978 [Z 161b IE]
German version: Angew. Chem. *91*, 237 (1979)

CAS Registry number:
(1)·2KSCN, 69484-09-9

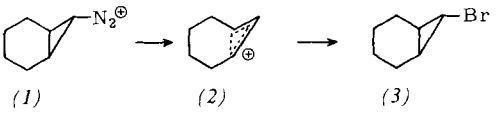
[1] *G. Weber, W. Saenger, F. Vögtle, H. Sieger*, Angew. Chem. *91*, 234 (1979); Angew. Chem. Int. Ed. Engl. *18*, 226 (1979).
[2] Synthesis: *F. Vögtle, U. Heimann*, Chem. Ber. *111*, 2757 (1978).
[3] Handbook of Chemistry and Physics. 57th Edit. CRC Press, Cleveland 1977.
[4] *W. Saenger, H. Brand, F. Vögtle, E. Weber* in *B. Pullman, N. Goldblum:* Metal-Ligand Interactions in Organic Chemistry and Biochemistry. Part I. *D. Reidel*, Dordrecht 1977, p. 363.
[5] *F. Iwasaki, M. Sato, A. Aihora*, Acta Crystallogr. *B 32*, 102 (1976).

Stereochemistry of Nucleophilic Substitution at Cyclopropanediazonium Ions

By *Wolfgang Kirmse* and *Theodor Engbert*[*]

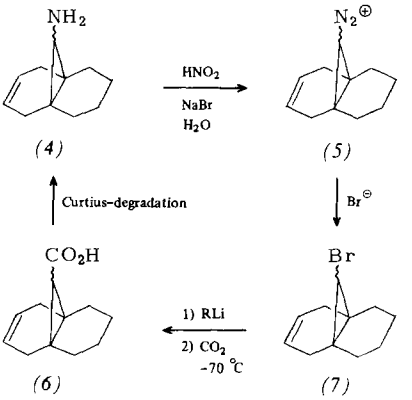
According to MO calculations[11], S_N2-substitution with retention of configuration should be possible at small ring compounds. While inversion has been demonstrated in the case of cyclobutyl tosylates[2], cyclopropyl halides and sulfonates usually undergo ring-cleavage with formation of allyl derivatives[3]. We report here on the behavior of cyclopropanediazonium ions in nucleophilic substitution.

Substitution with retention of configuration: The decomposition of *exo*-7-norcaranediazonium ions *(1)* in the presence of sodium bromide yields *exo*-7-bromonorcarane *(3)* as major product[4]. The complete retention of configuration was explained in terms of formation of a partly opened cyclopropyl



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

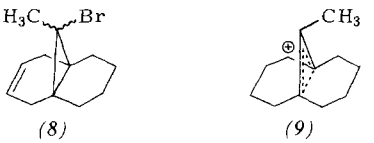
cation *(2)*[3a, 5] as intermediate. It was also conceivable, however, that a "classical" norcarane cation gives only *exo* products for steric reasons, or that an S_N2-substitution with retention of configuration takes place. We therefore investigated a model in which steric discrimination was essentially inapplicable, but where partly opened intermediates are probable.



(4) *(5)* *(6)* *(7)*

(a), syn; (b), anti

The deamination of *syn*- and *anti*-11-aminotricyclo-[4.4.1.$0^{1,6}$]undec-3-ene *(4a, b)* in the presence of sodium bromide gave the bromides in high yields [*(7a)* up to 66%, *(7b)* up to 84%] and with 97—99% retention. As experiments in D_2O have shown, the small amounts (1—3%) of inversion products mainly stem from epimerization of the diazonium ions *(5a, b) via* the diazo compound. (In the inverted bromide, 11-H is replaced up to 85% by D, whereas the bromide formed with retention incorporated only 3—7% D.) The configurations of *(4)* and *(7)* were assigned *via* the carboxylic acids *(6)*. Only *(6a)* forms an iodolactone[6].



(8) *(9)*

The behavior of the diazonium ions *(5a, b)* corresponds to that of the tertiary bromides *(8)*, which on Ag^+-catalyzed methanolysis also react with predominant retention[7]. The cause of retention of configuration is very probably a partly opened cation. The delocalized structure *(9)*, which is nonplanar at C-11, could be identified by NMR spectroscopy in superacids[8].

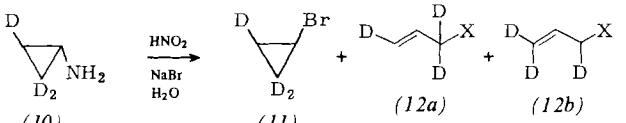
Substitution with inversion of configuration: Cyclopropanediazonium ions, whose ring cleavage can proceed unhindered, give only low yields of cyclopropane derivatives. On deamination of (*E*)-[2,2,3-D_3]cyclopropylamine *(10)*[9] in the presence of sodium bromide we obtained 4% [2,2,3-D_3]cyclopropyl bromide *(11)* with 94±2% inversion. The stereochemistry of *(11)* follows from the D-decoupled ^{1}H-NMR spectrum: The coupling constant of the two protons in (*Z*)-*(11)* is 7.1 Hz, in (*E*)-*(11)* 3.8 Hz[9].

The deamination of *cis*-2-methylcyclopropylamine *(13a)* under analogous conditions gave 1.6—1.7% *trans*-1-bromo-2-methylcyclopropane *(14a)*; *cis*-2-methoxymethylcyclopropyl-

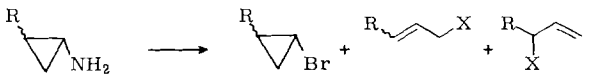
[*] Prof. Dr. W. Kirmse, Dr. Th. Engbert
Abteilung für Chemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0228 $ 02.50/0*

amine *(13b)* afforded 8.5% *trans*-1-bromo-2-methoxymethylcyclopropane *(14b)*.



(10) *(11)* *(12a)* *(12b)*



(13) *(14)* *(15)* *(16)*

(a), R = CH_3; *(b)*, R = CH_2OCH_3

The *trans*-amines *(13a,b)* yielded only traces of cyclopropyl bromides. This finding is consistent with a substitution with inversion, which in the case of the *trans*-diazonium ions is sterically hindered by the 2-substituents, so that it can no longer compete with ring cleavage.—The allyl alcohols *(12)*-OH and *(15)*-(OH) are formed stereospecifically *via* disrotation. The corresponding allyl bromides (X = Br) are not configurationally stable.

Our results refute—at least for nitrogen as leaving group—the concept of a retentive S_N2-substitution at the cyclopropane ring. Retention of configuration is only observed when the disrotatory cyclopropyl-allyl rearrangement is initiated, but cannot be led to completion owing to opposing ring strain; in these cases partly opened cyclopropyl cations are probably involved as intermediates. In the case of unconstrained ring cleavage the competing substitution at cyclopropanediazonium ions proceeds with inversion.

Received: January 4, 1979 [Z 162 IE]
German version: Angew. Chem. *91*, 240 (1979)

[1] *P. D. Gillespie, I. Ugi*, Angew. Chem. *83*, 493 (1971); Angew. Chem. Int. Ed. Engl. *10*, 503 (1971); *W. D. Stohrer, K. R. Schmieder*, Chem. Ber. *109*, 285 (1976).

[2] *C. A. Maryanoff, F. Ogura, K. Mislow*, Tetrahedron Lett. *1975*, 4095; *T. Vergnani, M. Karpf, L. Hoesch, A. S. Dreiding*, Helv. Chim. Acta *58*, 2524 (1975); *T. El Gomati, J. Gasteiger, D. Lenoir, I. Ugi*, Chem. Ber. *109*, 826 (1976).

[3] a) *U. Schöllkopf*, Angew. Chem. *80*, 603 (1968); Angew. Chem. Int. Ed. Engl. *7*, 588 (1968); *P. v. R. Schleyer, W. F. Sliwinski, G. W. Van Dine, U. Schöllkopf, J. Paust, K. Fellenberger*, J. Am. Chem. Soc. *94*, 125 (1972); b) retentive substitution was found for 2,3-benzo-11-bromotricyclo[4.4.1.$0^{1,6}$]undec-2-en-4-one: *H. Yamaguchi, K. Kawada, T. Okamoto, E. Egert, H. J. Lindner, M. Braun, R. Dammann, M. Liesner, H. Neumann, D. Seebach*, Chem. Ber. *109*, 1589 (1976); the reaction probably proceeds, however, according to an elimination-addition mechanism: *R. W. Gray, C. B. Chapleo, T. Vergnani, A. S. Dreiding, M. Liesner, D. Seebach*, Helv. Chim. Acta *59*, 1547 (1976); *H. J. Lindner, B. Kitschke, M. Liesner, D. Seebach, ibid. 60*, 1151 (1977); c) the reaction of *cis*- or *trans*-(2-benzyloxycyclopropyl)trimethylammonium iodide with HI/H_2O gave *trans*-(hydroxycyclopropyl)trimethylammonium iodide: *H. Kunze*, Z. Naturforsch. *B31*, 1676 (1976).

[4] *W. Kirmse, H. Jendralla*, Chem. Ber. *111*, 1857 (1978).

[5] *W. Kutzelnigg*, Tetrahedron Lett. *1967*, 4965; *D. T. Clark, G. Smale*, Tetrahedron *25*, 13 (1969).

[6] *G. L. Thompson, W. E. Heyd, L. A. Paquette*, J. Am. Chem. Soc. *96*, 3177 (1974).

[7] *P. M. Warner, S.-L. Lu, E. Myers, P. W. De Haven, R. A. Jacobson*, J. Am. Chem. Soc. *99*, 5102 (1977).

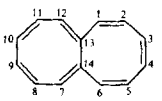
[8] *G. A. Olah, G. Liang, D. B. Ledlie, M. G. Costopoulos*, J. Am. Chem. Soc. *99*, 4196 (1977).

[9] Synthesis of (*E*)-[2,2,3-D_3]-cyclopropanecarboxylic acid: *K. Kobayashi, J. B. Lambert*, J. Org. Chem. *42*, 1254 (1977). This was used for the preparation of *(10)* by Curtius-degradation.

Dianion and Tetraanion of Octalene

By *Klaus Müllen, Jean F. M. Oth, Hans-Wilhelm Engels*, and *Emanuel Vogel*[*]

The ^{13}C- and ^1H-NMR spectra of octalene[1] recorded at −150°C reveal the molecule to show π-bond localization in the ground state and to exist in the double bond configuration depicted in formula *(1)*. Octalene is not planar, does not possess any element of symmetry, and is therefore chiral. Moreover, as temperature-dependent NMR studies (between −150 and +140°C) also show, octalene undergoes fast isodynamic processes: at very low temperatures the cyclooctatriene or/and the cyclooctatetraene ring inverts, and above *ca.* 70°C a π-bond shift occurs[2]. The olefinic nature of this potentially aromatic 14π-electron system is readily explained by the inadequacy of the delocalization energy to overcome the strain of flattening the eight-membered rings[3].



(1)

Mono- and polycyclic π-electron systems are subject to far-reaching changes in their π-bonding and geometry on electrochemically or alkali-metal induced reduction to anions[4]. In the case of octalene, the preparation of anionic derivatives appeared particularly attractive since the construction of this $(4n+2)\pi$-system from two $(4n)\pi$-cyclooctatetraene fragments permits various possible charge distributions in the ionic species and thus also various possible structures.

Measurement of the classical polarograms [dimethylformamide, tetra-*n*-butylammonium perchlorate as supporting electrolyte, calomel electrode (SCE), 1 N KCl as reference] shows that octalene can accept four electrons on reduction. Cyclic voltammetry and potential jump experiments also indicate that the first electron is transferred reversibly at $E_{1/2} = -1.67$ V and the three other electrons in a joint wave at $E_{1/2} = -1.70$ V. This second wave corresponds to chemically reversible processes since no secondary reactions are observed under strictly aprotic conditions; however, the electron transfers themselves are irreversible in that the reoxidation potentials are distinctly shifted towards more positive values relative to the reduction potentials. The electrochemical results[5] suggested that octalene *(1)* should form a radical anion $(1)^{\cdot-}$, a dianion *(2)*, a radical trianion $(2)^{\cdot-}$, and a tetraanion *(3)* on reduction by a metal.

We have therefore exposed octalene (in [D_8]tetrahydrofuran) to the action of lithium for defined periods of time and carefully checked the progress of reduction by recording the ^1H- and ^{13}C-NMR and ESR spectra. After brief contact, a radical anion can be detected in the solution which has turned from pale yellow to red. As shown by the ^1H- and ^{13}C-NMR spectra, the neutral and the radical species present are accompanied by a new diamagnetic compound to be regarded as the dianion *(2)*. The reduction can be interrupted at a stage where this ion is present exclusively. Figure 1 shows the relevant ^1H- and ^{13}C-NMR spectra (see also Table 1). The four signals in the ^{13}C-NMR spectrum of the dianion

[*] Prof. Dr. K. Müllen, Prof. Dr. J. F. M. Oth
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dipl.-Chem. H.-W. Engels, Prof. Dr. E. Vogel
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0229 $ 02.50/0*

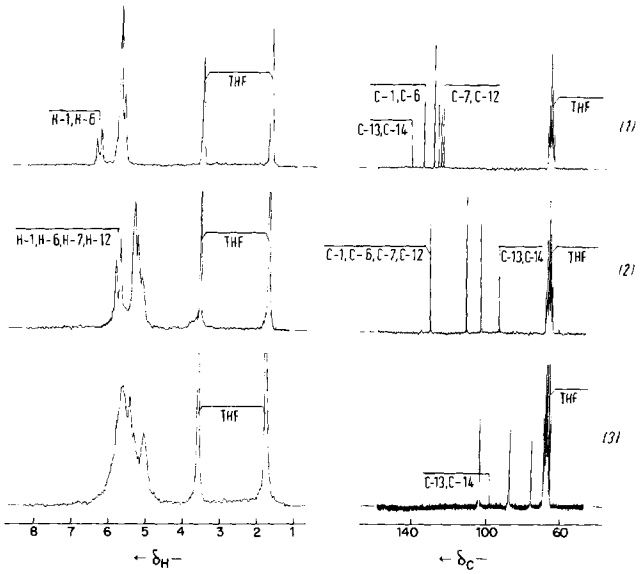


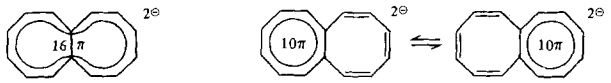
Fig. 1. ^{1}H- and ^{13}C-NMR spectra of octalene *(1)*, its dianion *(2)*, and its tetraanion *(3)* (as lithium salt) ([D$_8$]-THF, −80 °C).

Table 1. ^{1}H- and ^{13}C-NMR chemical shifts of octalene *(1)* [a], its dianion *(2)*, and its tetraanion *(3)* [b] (δ values relative to TMS; in [D$_8$]THF at −80 °C).

(1)	*(2)*	*(3)*
	^{1}H-NMR	
6.39 (H-1, 6)	5.78 (H-1, 6, 7, 12)	5.54
5.78	5.32	
$\langle\delta\rangle = 5.88$	$\langle\delta\rangle = 5.47$	$\langle\delta\rangle = 5.54$
	$\Delta\langle\delta\rangle = 0.41$	$\Delta\langle\delta\rangle = 0.07$
	^{13}C-NMR	
143.15 (C-13, 14)	129.85 (C-1, 6, 7, 12)	100.37
136.94 (C-1, 6)	111.49	86.84
131.89	103.54	75.70
131.79	93.85 (C-13, 14)	89.96 (C-13, 14)
129.45		
127.99		
127.17 (C-7, 12)		
$\langle\delta\rangle = 132.62$	$\langle\delta\rangle = 111.94$	$\langle\delta\rangle = 87.96$
	$\Delta\langle\delta\rangle = 20.68$	$\Delta\langle\delta\rangle = 23.98$

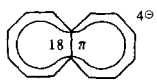
[a] ^{13}C-NMR averaged spectrum [2] owing to fast ring inversion(s) at −80 °C. [b] Owing to the sparing solubility of the tetraanion *(3)* the resonance of the quaternary carbon atoms could only be observed at a low signal-to-noise ratio (2:1) and is therefore unreliable.

suggest D_{2h} molecular symmetry and hence structure *(2a)* with π-bond delocalization. In view of the total number of π-electrons ($14+2=16=4n$), structure *(2b)* containing a cyclooctatetraene dianion fragment would appear more likely. In such a case, the observed ^{13}C-NMR can only be rationalized by assuming a fast charge transfer coupled with a π-bond shift [*(2b)* ⇌ *(2b)*][6].



(2a) *(2b)* *(2b)*

Further reduction transforms the dianion *(2)* into a new diamagnetic anion which, like *(2)*, exhibits four signals in the ^{13}C-NMR spectrum (no ESR signals appear in the case of this reduction) and must therefore also have D_{2h} symmetry. After prolonged contact between the metal and the solution, which has meanwhile become dark brown, only the signals of this species are observed. Thus, it is reasonable to assume that the tetraanion *(3)* with a delocalized 18π-system is present.



(3)

Identification of the diamagnetic ions as dianion and tetraanion of octalene follows from the specific course of the reduction (*i.e.* the appearance and disappearance of the individual species), from the characteristics of the NMR spectra, and also from reoxidation experiments. Oxidation of the partially or completely reduced solution [*(2)* or *(3)*, respectively] with oxygen gave octalene as the sole identifiable product.

On going from *(1)* to *(2)* and *(3)*, the centroid of the ^{13}C-NMR signals underwent an upfield shift as expected from the known correlation of ^{13}C-NMR chemical shifts and π-charge densities[7]. Moreover, the observed sequence of assigned signals can be predicted on the basis of local π-charge densities. In contrast to ^{13}C-NMR chemical shifts, which mainly reflect the charge densities, the ^{1}H-NMR chemical shifts are also affected by field-induced ring currents. The surprisingly small upfield shift of the centroids of the ^{1}H-NMR signals seen on going from *(1)* to *(2)* ($\Delta\langle\delta\rangle = 0.41$) and from *(2)* to *(3)* ($\Delta\langle\delta\rangle = 0.07$) indeed suggests that the charge-induced upfield shift is largely compensated by the effect of a diamagnetic ring current.

In the $(4n+2)\pi$-system *(3)* the existence of a diamagnetic ring current complies with expectation, while this applies to *(2)* only if the anion has structure *(2b)* with a fast charge shift [structure *(2a)* would show a paramagnetic ring current[8]]. Attempts to elucidate this structural problem are currently in progress.

The ^{13}C- and ^{1}H-NMR spectra recorded during the reduction provide information about the relative energies of the octalene anions. When the ESR signals of the radical anion $(1)^{\cdot-}$ has reached maximum intensity, the ^{13}C- and ^{1}H-NMR spectra are each a superposition of the individual spectra of *(1)* and *(2)* (with only minimal line broadening). Hence it follows that the radical anion is extensively disproportionated and that the rate constants of all the bimolecular electron transfer reactions are slow on the NMR time scale. Similar arguments apply to the disproportionation of the radical trianion $(2)^{\cdot-}$ into *(2)* and *(3)*.

The fact that a relatively small molecule like octalene can accept four electrons at low (*i.e.* not very negative) potentials is surprising in view of the Coulomb forces involved[9]. According to the results described, the energy gain from delocalization of charges and π-bonds in the tetraanion *(3)* is so large that it overcompensates both the electrostatic energy and the strain energy associated with flattening of the molecule[2].

The new bicyclic $(4n+2)\pi$-species *(3)*, which is stable for several days at room temperature (in tetrahydrofuran with exclusion of air), can be regarded as an analogue of naphthalene: like the latter, it possesses a perimeter with π-bond delocalization and consists formally of two annelated $(4n+2)\pi$-fragments.

Received: December 28, 1978 [Z 164 IE]
German version: Angew. Chem. *91*, 251 (1979)

[1] *E. Vogel, H.-V. Runzheimer, F. Hogrefe, B. Baasner, J. Lex*, Angew. Chem. *89*, 909 (1977); Angew. Chem. Int. Ed. Engl. *16*, 871 (1977).
[2] *J. F. M. Oth, K. Müllen, H.-V. Runzheimer, P. Mues, E. Vogel*, Angew. Chem. *89*, 910 (1977); Angew. Chem. Int. Ed. Engl. *16*, 872 (1977).

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* 0570-0833/79/0303-0220 $ 02.50/0

[3] *N. L. Allinger, C. Gilardeau*, Tetrahedron *23*, 1569 (1967); *D. H. Lo, M. A. Whitehead*, J. Am. Chem. Soc. *91*, 238 (1969).
[4] *J. F. M. Oth, K. Müllen, H. Königshofen, J. Wassen, E. Vogel*, Helv. Chim. Acta *57*, 2387 (1974); *T. J. Katz*, J. Am. Chem. Soc. *82*, 3784 (1960).
[5] *J. F. M. Oth, K. Müllen*, to be published.
[6] The ^{1}H-NMR data support structure *(2b)*.
[7] *G. A. Olah, G. D. Mateescu*, J. Am. Chem. Soc. *92*, 1430 (1970).
[8] On the basis of the ^{1}H-NMR chemical shifts of cyclooctatetraene and its dianion, an upfield shift of 0.05 would be predicted for the centroid of the signals of *(2)* [as structure *(2b)*] relative to *(1)*.
[9] A similar situation is encountered in the reduction of biscyclooctatetraenyl [*J. F. M. Oth, K. Müllen*, unpublished; see also *L. A. Paquette, G. D. Ewing, S. G. Traynor*, J. Am. Chem. Soc. *98*, 279 (1976)] during the course of which we were able to prepare the dianion and tetraanion (as the lithium salts) and to characterize them by ^{1}H-NMR and ^{13}C-NMR. In this molecule, which is suitable as a reference system for the understanding of the reduction of octalene [5], the Coulomb forces operative on formation of the tetraanion are less serious.

Stable Coordination Compounds of "Thiazyl Fluoride": Structure of $[Co(NSF)_6]^{2+}$ in the Crystal[**]

By *Bruno Buss, Peter G. Jones, Rüdiger Mews, Mathias Noltemeyer*, and *George M. Sheldrick*[*]

The simplest nitrogen-sulfur-fluorine compound, the monomeric "thiazyl fluoride" *(1)* is unstable at room temperature[1]. Stabilization of the molecule can be achieved, however, by incorporation as ligand in transition metal complexes:

$$\underset{(1)}{6\,NSF} + \underset{(2)}{[M(SO_2)_x](AsF_6)_2} \xrightarrow[-SO_2]{} \underset{\substack{(3a),\ M=Co\\(3b),\ M=Ni}}{[M(NSF)_6](AsF_6)_2}$$

The hexakis(thiazyl fluoride) complexes of Co^{II} and Ni^{II} are formed in almost quantitative yield on reaction of the hexafluoroarsenates *(2)* with an excess of NSF in liquid SO_2 below -20 °C. In the crystalline state the salts *(3)* are stable in dry glass vessels at room temperature, whereas in solution ligand-exchange takes place:

$$[M(NSF)_6]^{2+} + x\,SO_2 \rightleftharpoons [M(NSF)_{6-x}(SO_2)_x]^{2+} + x\,NSF$$
(4a), M = Co
(4b), M = Ni

The isolable salts then have a composition with $0 \le x \le 1$ [*(4a)*: $\nu_{as}(SO) = 1326$, $\nu_s(SO) = 1155\ cm^{-1}$; *(4b)*: $\nu_{as}(SO) = 1327$, $\nu_s(SO) = 1161\ cm^{-1}$].

The IR spectra of the complexes *(3a)* and *(3b)* show a strong shift of the SN stretching vibration to higher wave numbers; ν_{SF} also increases:

	ν_{SN} [cm^{-1}]	ν_{SF} [cm^{-1}]	d_{SN} [Å]	d_{SF} [Å]	∢NSF [°]
N≡S—F (Gas)	1361	641	1.446	1.646	116.5 [a]
$[Co(NSF)_6]^{2+}$	1429	655	1.399(12)	1.569(12)	115.0(7) [b]
$[Ni(NSF)_6]^{2+}$	1438	655	—	—	—

[a] Cf. [2]; [b] mean values.

The X-ray structure analysis of *(3a)* also indicates an increase in SN and SF bond strength. The central atom [on the special position (0, 0, 0)] is octahedrally coordinated; the Co—N bond length (mean value 2.093(11) Å) approximates to that in $[Co(NH_3)_6]^{2+}$ (2.114(9) Å)[3]. The NSF angle changes only slightly on formation of the complex; noteworthy is the pronounced shortening of the SF and SN bonds: *(3a)* shows the shortest SN bond so far recorded! The mean CoNS angle is 170.8(10)°. As can be seen from Figure 1, the S- and N-atoms are almost isotropic, although the F-atom vibrates anisotropically. This would indicate that appreciable librational shortening is to be expected only in the SF bond.

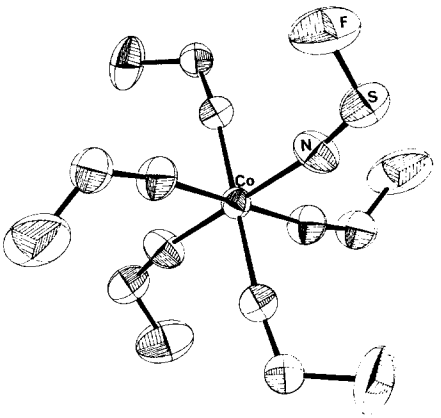


Fig. 1. Structure of the cation $Co(NSF)_6^{2+}$ in the salt *(3a)*, $M_r = 827.17$, monoclinic, $P2_1/n$, $a = 13.105(9)$, $b = 9.201(7)$, $c = 9.366(6)$ Å, $\beta = 90.43(4)°$, $V = 1129$ Å^3, $Z = 2$, $\rho_{calc} = 2.432$ g cm^{-3}, $\mu = 43$ cm^{-1} ($Mo_{K\alpha}$). Structure determination from diffractometer data by direct methods. Refinement, with structure factors of 1102 reflections corrected for absorption [$F > 4\sigma(F)$], to a current R value of 0.083.

Experimental

5 ml of SO_2 and a 10—20 % excess of NSF are condensed into 1—2 g (2—4 mmol) of the corresponding SO_2-complex *(2)*[4] at -196 °C. After stirring for 2—3 hours at -20 °C the reaction mixture is filtered and solvent and excess ligand reagent removed from the filtrate by evaporation. There remain the analytically pure products.

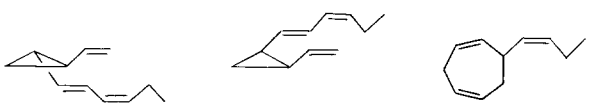
Received: December 14, 1978 [Z 166 IE]
German version: Angew. Chem. *91*, 253 (1979)

[1] *O. Glemser, H. Schröder, E. Wyszomirski*, Z. Anorg. Allg. Chem. *298*, 72 (1959); *O. Glemser, H. Meyer, A. Haas*, Chem. Ber. *97*, 1704 (1964).
[2] *H. Richert, O. Glemser*, Z. Anorg. Allg. Chem. *307*, 328 (1961); *W. H. Kirchhoff, E. B. Wilson jr.*, J. Am. Chem. Soc. *85*, 1726 (1963).
[3] *N. E. Kime, J. A. Ibers*, Acta Crystallogr. *B 25*, 168 (1969).
[4] *C. D. Desjardins, J. Passmore*, J. Fluorine Chem. *6*, 379 (1975); *P. A. W. Dean, ibid. 5*, 499 (1975).

Facile Synthesis of Cyclopropylalkadienes[**]

By *Manfred Schneider* and *Angelika Rau*[*]

In contrast to the synthesis of cyclopropylalkenes there are only few methods known for the preparation of cyclopropylalkadienes. Their synthesis is of interest in connection with



Dictyopterene B Dictyopterene D Dictyopterene D'

[*] Prof. G. M. Sheldrick, Dr. B. Buss, Dr. P. G. Jones, Priv.-Doz. Dr. R. Mews, Dr. M. Noltemeyer
Anorganisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)

[**] This work was supported by the Niedersächsiches Zahlenlotto. We thank Cambridge University for the use of a diffractometer.

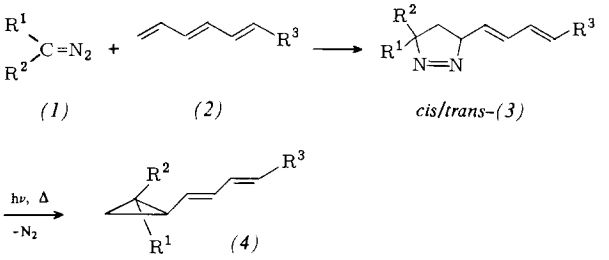
[*] Priv.-Doz. Dr. M. Schneider, A. Rau
Institut für Chemie der Universität Hohenheim
Postfach 106, D-7000 Stuttgart 70 (Germany)

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

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0231 $ 02.50/0

our search for simple routes to constituents of marine brown algae, *e.g.* the dictyopterenes B, D, and D′ (=ectocarpene)[1].

Cyclopropanizations of 1,3,5-trienes are of little synthetic value, since multiple additions and poor regioselectivity lead to mixtures and therefore small yields[2]. According to frontier orbital considerations, however, 1,3-dipolar cycloadditions of diazo compounds *(1)* to 1,3,5-trienes *(2)* should occur regiospecifically at the terminal double bonds of *(2)* with formation of 1-pyrazolines *(3)*. Their thermal or photochemical decomposition would produce the desired cyclopropylalkadienes *(4)* without side reactions.



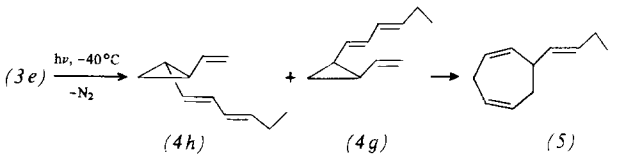
(1) *(2)* *cis/trans-(3)*

(4)

Indeed, the reactions of diazo compounds with (*E*,*E*)-1,3,5-octatriene *(2a)*[3] and the (*Z*)- and (*E*)-1,3,5-hexatrienes *(2b)* and *(2c)*[4] do in fact give the expected 1-pyrazolines *(3)* in satisfactory yields (Table 1). Similarly to other vinyl-substituted 1-pyrazolines[5], decompositions of *(3)* lead exclusively to the desired cyclopropylalkadienes *(4)* in almost quantitative yields (Table 1)[6]. Isolation and purification of the 1-pyrazolines *(3)* is not absolutely necessary; in all cases, photolysis or thermolysis of the crude products suffices. Since both the diazo and the triene components can be synthesized in great variety, the method provides access to a large number of different cyclopropylalkadienes.

Low-temperature photolysis of *(3e)* affords the *cis*- and *trans*-1-(*trans*-1,*trans*-3-hexadienyl)-2-vinylcyclopropanes *(4g)* and *(4h)*, respectively, in almost quantitative yield (isomeric ratio, see Table 1). Whereas *(4h)* is stable at room temperature, *(4g)* rapidly rearranges under these conditions *via* a $[_{\sigma}2_s + _{\pi}2_s + _{\pi}2_s]$ Cope rearrangement into 6-(*trans*-1-butenyl)-1,4-cycloheptadiene *(5)*.

Only *(4h)* and *(5)* are therefore isolated in the thermolysis of *(3e)*, which, similarly to 3,5-divinyl-1-pyrazolines[5], is already detectable at room temperature. *(4h)*, *(4g)*, and *(5)* are identical—apart from the configuration of the double bond in the side-chain—with the dictyopterenes B, D, D′ (=ectocarpene).



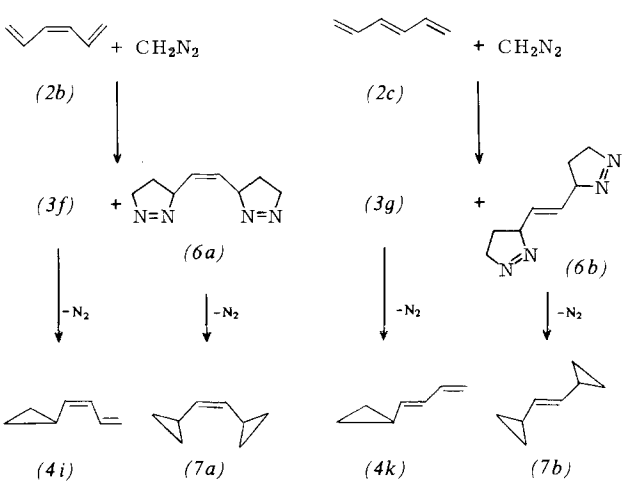
(4h) *(4g)* *(5)*

Two terminal double bonds are available for 1,3-dipolar cycloadditions of diazo compounds to *(2b)* or *(2c)*. However, the reaction of diazomethane with *(2b)* and *(2c)* in a 1:1 molar ratio affords only the isomeric 3-butadienyl-1-pyrazolines *(3f)* and *(3g)*, respectively, which decompose to the (*Z*)- and (*E*)-cyclopropylbutadienes *(4i)* and *(4k)*, respectively. Use of diazomethane and trienes in the molar ratio 2:1 does not only lead to *(3f)* and *(3g)* but also to *ca.* 15% *(6a)* and *(6b)*, respectively, from which the (*Z*)- and (*E*)-1,2-dicyclopropylethenes *(7a)* and *(7b)* are readily obtainable.

Table 1. Cyclopropylalkadienes *(4)* from diazo compounds *(1)* and 1,3,5-trienes *(2)*; intermediates: 1-pyrazoline *(3)*; *(2a)*: (*E*,*E*)-1,3,5-octatriene; *(2b)*: (*Z*)-1,3,5-hexatriene; *(2c)*: (*E*)-1,3,5-hexatriene.

			cis/trans-(3)					*(4)*			
(1)	*(2)*		R^1	R^2	R^3	Yield [%]	Decomposition [a]		R^1	R^2	R^3	*cis*:*trans*
Diazomethane	*(2a)*	*(3a)*,	H	H	Et	60	hν, Δ	*(4a)*,	H	H	Et	—
Diazoethane	*(2a)*	*(3b)*,	H	Me	Et	82	hν	*(4b)*,	Me	H	Et	0.5:1.0
								(4c),	H	Me	Et	
							Δ	*(4b)* + *(4c)*				0.6:1.0
2-Diazopropane	*(2a)*	*(3c)*,	Me	Me	Et	55	hν, Δ	*(4d)*,	Me	Me	Et	—
Phenyl-diazomethane	*(2a)*	*(3d)*,	H	Ph	Et	78	Δ	*(4e)*,	Ph	H	Et	0.1:1.0
								(4f),	H	Ph	Et	
3-Diazo-1-propene	*(2a)*	*(3e)*,	H	Vinyl	Et	20 [b]	hν	*(4g)*,	Vinyl	H	Et	1.0:1.0
								(4h) [d],	H	Vinyl	Et	
							Δ [c]	*(4g)*+*(4h)* [d]				1.5:1.0
Diazomethane	*(2b)*	*(3f)*,	H	H	H [e]	60	hν, Δ	*(4i)*,	H	H	H [e]	—
Diazomethane	*(2c)*	*(3g)*,	H	H	H	60	hν, Δ	*(4k)*,	H	H	H	—

[a] Photolysis in NORMAG photochemical reactor, lamp: Hanau TQ 150 or TQ 718, Pyrex filter, 18°C; static pyrolysis in a sealed ampoule, 140°C. [b] Estimated, an exact determination is not possible due to the side-reaction of 3-diazo-1-propene to give pyrazole. [c] Pyrolysis in *n*-pentane, 30°C. [d] Isolated as *(5)*. [e] 1-*cis*, 3-Butadienyl side chain.



(2b) *(2c)* *(3f)* *(3g)* *(6a)* *(6b)* *(4i)* *(7a)* *(4k)* *(7b)*

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979 0570-0833/79/0303-0232 $ 02.50/0

General Procedure

The 1,3,5-triene *(2)* (25 mmol) is treated with *ca.* 50 mmol of the diazo compound *(1)* (dissolved in a minimum amount of ether, or as neat substance). The so obtained yellow to deep-red mixtures are stored at room temperature (on using 3-diazo-1-propene at +4°C) until completely colorless (8 h to 4 d depending on the reactivity of the diazo compound). The mixture is then taken up in *n*-pentane and the solution washed with water and dried over Na_2SO_4. After removal of solvents in a rotary evaporator at 0°C the remaining crude 1-pyrazolines *(3)* are photolyzed, without further purification, in a NORMAG photochemical reactor (Lamp: Hanau TQ150 or TQ718, pyrex filter, 18°C, 2—3 h) or pyrolyzed in sealed tubes (oil bath, 140°C, ca. 15 h). The products *(4)* are purified by conventional or trap-trap-distillation.

Received: December 29, 1978 [Z 158 IE]
German version: Angew. Chem. *91*, 239 (1979)

[1] *R. E. Moore, J. A. Pettus, Jr., J. Mistysyn*, J. Org. Chem. *39*, 2201 (1974); *L. Jaenicke, D. G. Müller*, Fortschr. Chem. Org. Naturst. *30*, 61 (1973).

[2] *W. v. E. Doering, W. R. Roth*, Tetrahedron *19*, 715 (1963); similar low yields are obtained on solvolysis of homoallyl halides; *M. Hanack, H. Eggensperger*, Justus Liebigs Ann. Chem. *663*, 31 (1963).

[3] Obtainable from (*E,E*)-2,4-heptadienal by Wittig reaction.

[4] *(2b)+(2c)*: Org. Synth. Coll. Vol. V, 608; *(2b)*: by removal of *(2c)* from the mixture with maleic anhydride; *(2c)*: by I_2-catalyzed isomerization of the mixture *(2b)+(2c)*: *J. C. H. Hwa, P. L. de Benneville, H. J. Sims*, J. Am. Chem. Soc. *82*, 2537 (1960).

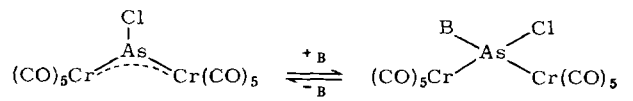
[5] *R. J. Crawford, D. M. Cameron*, Can. J. Chem. *45*, 691 (1967); *R. J. Crawford, M. Ohno, ibid. 52*, 3134 (1974); *M. Schneider*, Angew. Chem. *87*, 717 (1975); Angew. Chem. Int. Ed. Engl. *14*, 707 (1975); *M. Schneider, A. Erben, ibid. 89*, 187 (1977) and *16*, 192 (1977); in contrast, from alkyl-substituted 1-pyrazolines larger amounts of open-chain olefins are always obtained.

[6] All new compounds were characterized spectroscopically and by elemental analysis.

Stabilization of an Arsanediylphosphorane[**]

By *Joachim von Seyerl* and *Gottfried Huttner*[*]

Arsinidene complexes[1] contain a coordinatively unsaturated nitrene-homologous arsanediyl fragment as bridging ligand between two transition metal centers. Though the electron deficit at the trigonal-planar coordinated arsenic atom is largely compensated by back-bonding from the lone pairs of the metal atoms, attack at As by Lewis bases is still possible:

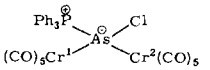


(1) *(2)*, B = PPh_3

UV: 16840 cm^{-1} (ε = 14000) UV: 26180 cm^{-1} (ε = 6300)

B = R_3N, R_3P, R_3As, R_2O, R_2CO

With triphenylphosphane as base (B) the equilibrium of adduct formation is shifted to the right, even at 20°C, while with weak nucleophiles such as esters or ketones the addition to *(1)* is easily reversed and the adduct consequently cannot be isolated at room temperature. In the case of the triphenylphosphane adduct a single-crystal structure determination[2] confirmed the formation of the addition compounds *(2)* and thus provided the first evidence for the existence of an arsanediylphosphorane ligand.



Bond lengths [pm]		Bond angles [°]	
As—Cr^1	246.6(2)	P—As—Cl	89.2(1)
As—Cr^2	249.9(2)	P—As—Cr^1	109.9(1)
As—P	240.1(2)	P—As—Cr^2	113.1(1)
As—Cl	225.6(2)	Cr^1—As—Cr^2	126.9(1)
Cr—C_{ax}	185.5(1)	Cl—As—Cr^1	102.9(1)
Cr—C_{eq}	190.7(1)	Cl—As—Cr^2	107.3(1)
P—C_{Ph}	180.5(1)	C—P—C	105.8—108.7(4)
		C—P—As	108.7—113.3(3)

The bond lengths in *(2)*, B = PPh_3, are consistent with a mesoionic formulation for the complex: The P—As bond length agrees very nearly with the sum of the covalent radii[3a], thus indicating the presence of a highly positive partial charge at the phosphonium center. This is further supported by the short P—C_{Ph} bond lengths and the large CPC angle[3b].

The positive partial charge on the phosphorus is confirmed by the ^{31}P-NMR signal, which, at δ = 11.8 (rel. H_3PO_4 ext.) shows a downfield shift compared to the signal of PPh_3 at δ = −7, as is characteristic for phosphonium salts[4a] and ylides[4b]. The corresponding negative charge appears to be essentially localized on the arsenic atom, since the Cr—C_{CO} bond lengths are only marginally shorter (189.7 pm) than in $Cr(CO)_6$ (190.9 pm)[5]. A small charge transfer is observed only for the axial carbonyl groups, whose Cr—C distances are shorter by about 5 pm than those in the equatorial groups.

The As—Cr bond lengths (mean length 248.2 pm) correspond with those of bonds typically found in carbonylchromium complexes containing arsenide-[6a] or arsane-[6b] ligands. The three-center 4π-system Cr···As···Cr of complexes of type *(1)* ($[Cr(CO)_5]_2AsPh$: As—Cr 238 pm)[1b] is no longer present in the adducts *(2)*; consequently, the characteristic absorption band for this system (*(1)*: 16840 cm^{-1}) is missing in the electron spectrum of *(2)*, whose longest wavelength absorption is observed at 26180 cm^{-1}.

Adduct formation is therefore recognized by a change in color, associated with the disappearance of the long-wave band of the arsinidene complex. We have been able to demonstrate spectroscopically that all the previously described phosphinidene-, arsinidene-, and stibinidene-complexes[1, 7] form analogous adducts according to *(1)*⇌*(2)*, even though in several cases the equilibrium lies well on the side of the starting complex even at −60°C. This reactivity has its parallel in the chemistry of the carbene complexes, where the coordinatively unsaturated carbene carbon atom is capable of ylide formation with phosphanes and amines[8].

Experimental

All operations must be carried out in anhydrous solvents under nitrogen.

A solution of triphenylphosphane (200 mg, 0.76 mmol) in CH_2Cl_2 (10 ml) is added dropwise to a solution of $ClAs[Cr(CO)_5]_2$ (300 mg, 0.6 mmol)[1c] in CH_2Cl_2 (20 ml) until the intense blue color has disappeared. After removal of solvent the residue is taken up in toluene and filtered through 2 cm of silica gel (Merck, particle size 0.063—0.200 mm, column: 0.5 × 10 cm). The eluate is evaporated and the residue recrystallized from dichloromethane in the cold. The orange crystals of *(2)*·CH_2Cl_2 already lose CH_2Cl_2 at 20°C; after drying, 400 mg (83 %) of analytically pure $Ph_3P(Cl)As[Cr(CO)_5]_2$,

[*] Prof. Dr. G. Huttner, Dipl.-Chem. J. von Seyerl
Lehrstuhl für Synthetische Anorganische Chemie der Universität
Postfach 7733, D-7750 Konstanz (Germany)

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

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0233 $ 02.50/0*

m.p. 115—117°C (dec.) is obtained.—The IR spectrum (*n*-hexane) bands at 2073 (m), 2056 (m), 1999 (w), 1990 (w), 1966 (vs), 1962 (m), 1950 (vs) and 1936 (s), shows the presence of rotamers.

Received: December 29, 1978 [Z 163 IE]
German version: Angew. Chem. *91*, 244 (1979)

[1] a) *G. Huttner, H.-G. Schmid*, Angew. Chem. *87*, 454 (1975); Angew. Chem. Int. Ed. Engl. *14*, 433 (1975); b) *G. Huttner, J. v. Seyerl, M. Marsili, H.-G. Schmid, ibid. 87*, 455 (1975) and *14*, 434 (1975); c) *J. v. Seyerl, U. Moering, A. Wagner, A. Frank, G. Huttner, ibid. 90*, 912 (1978) and *17*, 844 (1978).

[2] Syntex P3, graphite monochromator, $\lambda Mo = 71.069$ pm, ω-scan ($1.5 \leq \dot{\omega} \leq 29.3°$ min^{-1}), $T = -80°C$, 2977 independent reflections; $[(CO)_5Cr]_2AsClPPh_3 \cdot CH_2Cl_2$, space group $P\bar{1}$, $Z = 2$; $a = 1021(2)$, $b = 1095(2)$, $c = 1637(2)$ pm, $\alpha = 105.7(2)$, $\beta = 92.3(2)$, $\gamma = 101.8(2)°$; $R_1 = 0.048$.

[3] a) *G. Huttner, H.-G. Schmid, H. Lorenz*, Chem. Ber. *109*, 374 (1976); *G. Huttner, H.-D. Müller, V. Bejenke, O. Orama*, Z. Naturforsch. *B31*, 1166 (1976); b) *J. J. Daly*, Perspect. Struct. Chem. *3*, 165 (1970).

[4] a) *M. M. Crutchfield, C. H. Dungan, J. H. Letcher, V. Mark, J. R. Van Wazer*, Top. Phosphorus Chem. *5*, 1ff. (1967); b) *H. Schmidbaur, J. Eberlein, W. Richter*, Chem. Ber. *110*, 677 (1977).

[5] *A. Withaker, J. W. Jeffery*, Acta Crystallogr. *23*, 977 (1967).

[6] a) *H. Vahrenkamp*, Chem. Ber. *105*, 1486 (1972); b) *F. A. Cotton, T. R. Webb*, Inorg. Chim. Acta *10*, 127 (1974); *F. W. B. Einstein, R. D. G. Jones*, Inorg. Chem. *12*, 1148 (1973).

[7] *J. v. Seyerl, G. Huttner*, Angew. Chem. *90*, 911 (1978); Angew. Chem. Int. Ed. Engl. *17*, 843 (1978); *G. Huttner, H.-D. Müller, A. Frank, H. Lorenz, ibid. 87*, 714 (1975) and *14*, 705 (1975).

[8] *F. R. Kreissl, E. O. Fischer, C. G. Kreiter, H. Fischer*, Chem. Ber. *106*, 1262 (1973); *F. R. Kreissl, P. Stückler, E. W. Meineke, ibid. 110*, 3040 (1977).

Synthesis of a Zeise Salt Derivative with a Phosphorus-Nitrogen Ylide as Chelate Ligand[**]

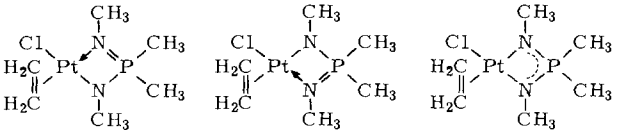
By *Otto J. Scherer* and *Andreas Nahrstedt*[*]

If we imagine a chloride ligand of Zeise's salt $K[PtCl_3(C_2H_4)]$ to be replaced by the aminoiminophosphorane ligand $[(CH_3)_2P(NCH_3)_2]^-$, then ring closure and elimination of KCl should lead to a type of complex in which the chelate ligand system could assume the function of the cation. This structure can indeed by accomplished starting from the lithium amide derivative *(1)*, according to

$$(CH_3)_2P(NCH_3)NCH_3Li \xrightarrow[-\,LiCl,\,-\,KCl]{K[PtCl_3(C_2H_4)]} [Cl(C_2H_4)Pt\{(NCH_3)_2P(CH_3)_2\}]$$

(1) *(2)*

The product *(2)* forms yellow crystals which are insoluble in pentane and hexane, and moderately soluble in ether and benzene. Its structure in solution[1] can be interpreted in terms of the resonance forms *(2a)*—*(2c)*.



(2a) *(2b)* *(2c)*

A mixture of *(2a)* and *(2b)* should be distinguishable by NMR spectroscopy, unless the two forms rapidly interconvert at room temperature, which would lead to structure *(2c)*. DNMR studies in deuterated toluene show only one modification of the original signal pattern down to −80°C. Below −30°C the rotation of the ethylene ligand becomes measurably slow. Worthy of note is the unusually large upfield shift of one CH_3N signal which we tentatively assign, on the basis of J_{PtNCH} reference data[2], to the chelate moiety bonded in the *trans* position relative to C_2H_4 (ligand with lower *trans* influence)[3]. Comparison of *(2)* with the related six-membered ring chelate system $Pt[(NCH_3)P(CH_3)_2NC(C_6H_5)(NCH_3)]_2$[4] shows a distinct downfield shift of $\delta(^{31}P)$ for the former compound; $^2J_{PtP}$ is almost three times as large (*(2)*, 259 Hz; six-membered ring chelate, *ca.* 90 Hz[4]). The slight difference in the coupling constants $^3J_{PH}$ (Table 1)[5] suggests structure *(2c)*.

Procedure

$(CH_3)_2P(NCH_3)NCH_3H$[6] (180 mg, 1.5 mmol), dissolved in benzene (20 ml) (25-ml centrifuge tube, N_2 atmosphere) is metalated at 10°C with an equimolar amount of n-C_4H_9Li/hexane and warmed to 55°C for 2 h. Solid pulverized $K[PtCl_3(C_2H_4)]$ (276 mg, 0.75 mmol) is added at room temperature and the mixture is stirred in the sealed centrifuge tube for 90 min. The suspension is centrifuged, the residue washed twice with benzene (2 × 20 ml), centrifuged once more, and the combined benzene solutions evaporated down in an oil pump vacuum. Yield: 205 mg of crude product which is washed with pentane (15 ml), centrifuged, and recrystallized from ether (20 ml) at −78°C to give 85 mg of *(2)* (30%); decomposes above *ca.* 85°C.

Table 1. NMR data of compound *(2)*.

PCH_3	$\delta(^1H)$, J [Hz] [a] NCH_3		C_2H_4	$\delta(^{31}P)$, J [Hz] [b]
0.62 (d) [c]	1.64 (d) [c]	2.85 (d) [c]	3.72 (s) [c]	94.3 (s) [c]
$^2J_{PH} = 11.8$	$^3J_{PH} = 18.8$	$^3J_{PH} = 17.4$	$J_{PtH} = 58.3$	$^2J_{PtP} = 259$
$^4J_{PtH} = 3.6$	$^3J_{PtH} = 55.7$	$^3J_{PtH} = 45.1$		

[a] 90 MHz; *ca.* 10% solution in benzene, TMS int. [b] *Ca.* 20% solution in benzene, 85% H_3PO_4 ext. A plus sign for δ refers to downfield chemical shift (^1H, ^{31}P). Nothing is said about the sign of J. [c] All signals flanked by a pair of satellites arising from coupling with ^{195}Pt (*ca.* 34%).

Received: December 20, 1978 [Z 165 IE]
German version: Angew. Chem. *91*, 238 (1979)

[*] Prof. Dr. O. J. Scherer, Dipl.-Chem. A. Nahrstedt
Fachbereich Chemie der Universität
Postfach 3049, D-6750 Kaiserslautern (Germany)

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

[1] Neither the mass spectrum [18 eV; $m/e = 378$ (8% M^+)] nor the molecular weight determination [osmometric in benzene; exp. 351, calc. 377.7] evidences a dimer or oligomer.

[2] *T. G. Appleton, J. R. Hall*, Inorg. Chem. *10*, 1717 (1971).

[3] Attempts to substantiate this assignment by displacing C_2H_4 by another ligand have so far been unsuccessful.

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0234 $ 02.50/0*

[4] *O. J. Scherer, A. Nahrstedt*, J. Organomet. Chem. *166*, C1 (1979).
[5] $^3J_{P=NCH_3}$ is considerably greater (*ca.* 25—30 Hz) [6b] in non-coordinated aminoiminophosphoranes.
[6] a) *O. J. Scherer, G. Schnabel*, Inorg. Chim. Acta *19*, L38 (1976); b) *O. J. Scherer, G. Schnabl, Th. Lenhard*, Z. Anorg. Allg. Chem., in press.

Cyclodiaza-λ^6-thianes—Syntheses and Structures[**]

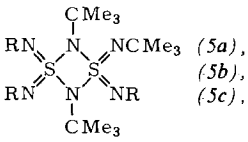
By *Frank-Michael Tesky, Rüdiger Mews*, and *Bernt Krebs*[*]

Iminosulfur compounds of the "Y-triene" type $(RN{=})_3S$, with $R = SiMe_3$ *(1)*[1a] or CMe_3 *(2)*[1b] are stable at room temperature, whereas the derivatives *(3)* prepared from *(2)* by reaction with perfluoroalkyl isocyanates decompose within a short time. Thus *(3a)*—*(3c)* disproportionate, regenerating *(2)* and giving the highly reactive bis(perfluoroalkyl) derivatives *(4)* which cannot be isolated but immediately react with *(3)* present to give the cyclodiaza-λ^6-thianes *(5a)*—*(5c)*. Exceptionally, compound *(3d)* is stable.

$$(Me_3CN{=})_3S + R{-}NCO \longrightarrow RN{=}S(=NCMe_3)_2 + Me_3C{-}NCO$$
(2) *(3a-d)*, R = CF_3, C_2F_5, C_3F_7, i-C_3F_7

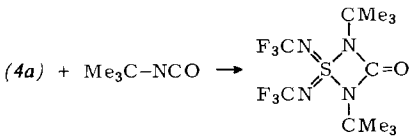
$$2\,(3) \longrightarrow (2) + \{Me_3CN{=}S(=NR)_2\}\ (4)$$

$+(3)\downarrow$



(5a), R = CF_3, m. p. 89 °C
(5b), R = C_2F_5, m. p. 91 °C
(5c), R = C_3F_7, m. p. 105 °C

The intermediate *(4)* can be detected by trapping reactions[2], *e.g.*:



(6), m. p. 77 °C

No structure determinations have hitherto been reported for cyclodiaza-λ^6-thianes[3]. Our studies on *(5b)* show the S_2N_2 skeleton to be nonplanar.

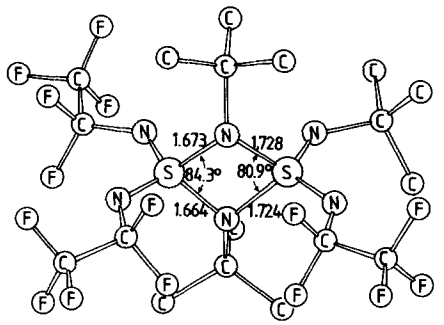


Fig. 1. Molecular structure of cyclodiaza-λ^6-thiane *(5b)* in the crystal with bond lengths and angles in the ring (σ = 0.007 Å and 0.3°).

[*] Priv.-Doz. Dr. R. Mews, Dipl.-Chem. F. M. Tesky
Anorganisch-chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)
Prof. Dr. B. Krebs
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

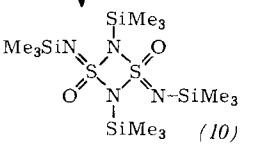
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

Compound *(5b)* forms monoclinic crystals ($P2_1/c$, $a = 10.802(3)$, $b = 16.501(3)$, $c = 18.948(4)$ Å, $\beta = 120.28(4)°$, $Z = 4$). X-Ray structure analysis ($R = 6.5\,\%$) revealed a nonplanar S_2N_2 ring with an SNS angle of 95.7(3)° and transannular S...S and N...N distances of 2.517(3) and 2.240(7) Å. The deviations of the ring S and N atoms from the averaged plane of the ring are +0.10 and −0.10 Å, respectively. Exocyclic bond lengths: 1.469(6)—1.532(7) Å, corresponding SNC angles: 125.4(6)—130.9(6)°.

The geometry of the S_2N_2 ring appears to be strongly dependent upon the nature of the ligand: unlike *(5b)*, the ring in the 1,3-dioxotetrakis(trimethylsilyl) derivative *(10)* is completely planar (cf. Fig. 2). Compound *(10)* is readily accessible from *(1)* and the perfluoroalkyl-*N*-sulfinylamine i-C_3F_7NSO:

$$2\,(1) + 2\,i\text{-}C_3F_7{-}NSO \longrightarrow 2\left\{\begin{array}{l} Me_3SiN{=}S(=O){-}N(SiMe_3){-}S{=}NC_3F_7 \\ \text{(7)} \end{array}\right\}$$

$$\longrightarrow 2\,(Me_3SiN{=})_2S{=}O\ (8) + 2\,Me_3SiN{=}S{=}NC_3F_7\ (9)$$



(10)

Judging by the isolable intermediate and by-product *(8)*[4] and *(9)*, this reaction should proceed *via* the oxadithiazetidine *(7)*.

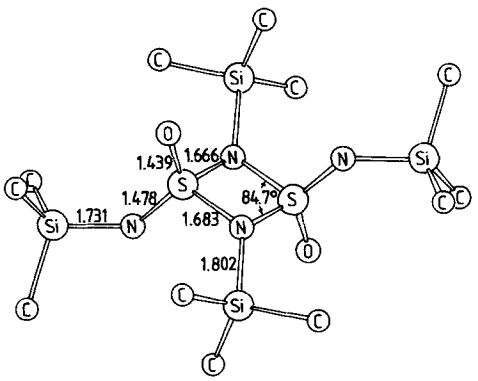


Fig. 2. Molecular structure of cyclodiaza-λ^6-thiane *(10)* in the crystal with bond lengths and angles (σ = 0.002 Å and 0.1°).

In crystalline *(10)* ($I4_1/a$ at −120 °C: $a = 20.231(4)$, $c = 12.199(3)$ Å, $Z = 8$; R factor for the structure determination performed at −120 °C: 3.0 %) the centrosymmetric molecule shows a planar S_2N_2 ring (S...S 2.477(1), N...N 2.257(4) Å. As in *(5b)*, the ring N atoms are pyramidally configurated. Other bond angles: $N_{exocycl.}$—S—O 120.8(1), S—$N_{exocycl.}$—Si 135.2(1)°.

Procedure

2,4-Bis(*tert*-butyl)-1-(*tert*-butylimino)-1,3,3-tris(pentafluoroethylimino)cyclodiaza-λ^6-thiane *(5b)*: Perfluoroethyl iso-

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* *0570-0833/79/0303-0235 $ 02.50/0*

cyanate (1.9 g, 9.0 mmol) is condensed into a solution of *(2)* (1.0 g, 4.1 mmol) in diethyl ether (7 ml) at −196 °C. The temperature is allowed to rise from −50 °C to room temperature within 18 h, stirring is continued for 24 h, and the solvent and volatile products are removed *in vacuo*. The residue is dissolved in dichloromethane; on cooling to 0 °C, compound *(5b)* crystallizes (0.375 g, 27 %). ^{1}H-NMR: $\delta_{=NC(CH_3)_3} = +1.49$ (s), $\delta_{>NC(CH_3)_3} = +1.64$ (s). ^{19}F-NMR: $\delta_{CF_3} = -87.28$, −87.45, −87.67 (1:1:1), $\delta_{CF_2} = -85.86$, −88.33 (1:2).

1,3-Dioxo-2,4-bis(trimethylsilyl)-1,3-bis(trimethylsilylimino)cyclodiaza-λ^6-thiane *(10)*: Reaction of *(1)* (2.93 g, 10 mmol) with *i*-C_3F_7NSO (4.62 g, 20 mmol) in diethyl ether (7 ml) at room temperature gives, after three days' stirring, compound *(9)* (2.6 g, 86 %), b. p. 130 °C, and *(10)* (1.0 g, 23 %), m. p. 86 °C. Compound *(10)* is purified by recrystallization from pentane. ^{1}H-NMR: $\delta_{=NSi(CH_3)_3} = +0.21$, $\delta_{>NSi(CH_3)_3} = +0.415$; MS: $m/e = 444$ (18 %, M^+).

Received: December 11, 1978 [Z 167 IE]
German version: Angew. Chem. *91*, 231 (1979)

[1] a) *O. Glemser, J. Wegener*, Angew. Chem. *82*, 324 (1970); Angew. Chem. Int. Ed. Engl. *9*, 309 (1970); b) *O. Glemser, S. Pohl, F. M. Tesky, R. Mews, ibid. 89*, 829 (1977) and *16*, 789 (1977).
[2] *F. M. Tesky, R. Mews, B. Krebs, M. R. Udupa*, Angew. Chem. *90*, 722 (1978); Angew. Chem. Int. Ed. Engl. *17*, 677 (1978).
[3] *K. D. Schmidt, R. Mews, O. Glemser*, Angew. Chem. *88*, 646 (1976); Angew. Chem. Int. Ed. Engl. *15*, 614 (1976); *H. W. Roesky, M. Aramaki, L. Schönfelder, Z.* Naturforsch. *B33*, 1072 (1978).
[4] Compound *(8)* had already been isolated as a product of the reaction between OSF_4 and $LiN(SiR_3)_2$, but its dimer has not previously been reported: *O. Glemser, M. Feser, S. P. v. Halasz, H. Saran*, Inorg. Nucl. Chem. Lett. *8*, 321 (1972).

BOOK REVIEWS

The Chemistry of Cyclo-octatetraene and Its Derivatives. By *G. I. Fray* and *R. G. Saxton*. Cambridge University Press. Cambridge 1978. x, 492 pp., bound, £ 30.00.

Interest in cyclooctatetraene and its derivatives has been increasing steadily since the discovery and development of a catalytic synthesis by *W. Reppe* and co-workers in 1940. Although a number of reviews on various aspects of COT chemistry exist, there has been a need for a standard reference work to up-date the slim volume by *G. Schröder* which was first published in 1965. This need has now been admirably filled by *Fray* and *Saxton*'s book which certainly belongs in every chemical library. In view of the price it is doubtful, however, whether many individuals will purchase their own private copy.

Two relatively short chapters on the chemistry of cyclooctatetraene and substituted cyclooctatetraenes are followed by a mammoth chapter on "Further reactions of compounds derived from cyclooctatetraenes" in which the authors discuss the chemistry of such directly related species as semibullvalene, cyclooctatriene, 9-oxabicyclo[6.1.0]nona-2,4,6-triene and tricyclo[4.2.2.0^{2,5}]deca-3,6-diene. The book is rounded-off by a 50 page appendix which is referred to both in the text and in the index and which takes the literature coverage up to the end of 1976. The subject matter is well organized and both organometallic as well as organic aspects are discussed in detail. The lay-out makes it easy to find the relevant information while at the same time encouraging the reader to browse through related material.

P. W. Jolly [NB 446 IE]

Atlas of Metal-Liquid Equilibria in Aqueous Solutions. By *J. Kragten*. Ellis Horwood Ltd. and John Wiley & Sons, New York—London—Sydney—Toronto 1978. 1st Edit., 781 pp., numerous illustrations, bound, £ 35.00.

The book is concerned not with complexation equilibria in general but specifically with the heterogeneous equilibria set up when air-(oxygen and carbon dioxide)-saturated suspensions of sparingly soluble hydroxides, oxides, and carbonates of metals are treated with complexing agents in various concentrations. A total of 600 combinations of 45 metal ions and 29 inorganic and organic ligands are considered.

The work consists primarily of graphic representations from which the solubility of the precipitates in solutions of the complexing agent in the pH range 1 to 14 can readily be seen, as can the (reciprocal) amount of the non-coordinated metal ions present in the solutions. Only 25 pages are devoted to essential theoretical explanations. All the curves are computer-plotted with the aid of a suitable program on the basis of complexation constants and solubility products determined from other studies. In view of the general dependence of equilibrium constants on solution partners and that of solubility products on precipitation conditions, the data reported should be regarded merely as orientational aids.

This well produced book will be of interest mainly to readers involved in theoretical analytical chemistry. The more practically biased chemist could consult it if he wishes to prevent precipitation of metals from solutions of their salts.

Fritz Seel [NB 441 IE]

Verordnung über gefährliche Arbeitsstoffe. Vol. 2: Technische Regeln (TRgA) (Regulations on Dangerous Materials. Vol. 2: Technical Rules). By *E. Quellmalz*. Weka-Verlag, Kissing 1977. 1st edit., 309 pp., br., DM 36.00.

The subject of this book, by the fact that the author is experienced in industrial safety, might lead one at first to suppose it to be a reference book. Even a quick skim, however, will show the interested reader that this is not merely a book to be left on the library reference shelves. He will notice the author's absorbing and practical approach to legal rules and regulations, and will certainly make a careful study of the safety measures discussed, which cover the entire field of chemistry. For rapid information on a given Technical Rule for Dangerous Materials (Technische Regel für gefährliche Arbeitsstoffe, or TRgA) the reader will need to consult the contents list, since the publisher has not provided a subject index.

The work covers the TRgA from the introduction (001), the definition of concepts (101), the Technical Standard Concentration (TRK) for vinyl chloride and benzene, and the TRgA for these substances and also for aluminum powder, arsenic, hepatotoxic halogenated hydrocarbons, radiation agents, lead, fluorine, silicogenic dust, magnesium, fluxes, and ammonium nitrate, and also for various technologies. In many places the reviewer would have liked to see literature references to the available data. For example, the determination of the exposure conditions for fluorine by the detection of fluoride

© *Verlag Chemie, GmbH, D-6940 Weinheim, 1979* 0570-0833/79/0303-0236 $ 02.50/0

and the resulations for the investigation in the TRgA could have been even clearer if more references to the occupational hygiene literature, *e.g.* on analytical methods in the biological matrix, could have been quoted.

Part I is organized in a very clear fashion and helps the measures necessary in practice to be clearly recognized and realized. Part II offers an excellent presentation of the problems of characterization, with instructive tables. An impressive statistical proof of the necessity for characterization when dealing with dangerous materials is given. In Part III the working instructions (in accordance with §13, Section 6 of Arb. Stoff. V) are explained with many examples; this section is divided into "Information—actual operating instructions—protection instructions—first aid—unusual incidents—problems of waste".

The book belongs not only in the bookcase of the employer and the chief safety officer; the manager, the "local" safety officer, the works doctor and the responsible persons at universities and research institutes need it as well.

Hans Zorn [NB 458 IE]

Gas Chromatography with Glass Capillary Columns. By *W. Jennings*. Academic Press, New York 1978. 1st Edit., vii, 184 pp., bound, $ 16.50.

The book is intended as an introduction to the topic given in the title, and turns out to be a successful one. The reader senses that a practical chemist has committed his experience to paper. All that the beginner and more advanced user alike need to know about gas chromatography with glass capillary columns will be found in this book, starting from production of columns, drawing and coating, insertion of the column into the instrument, *via* a discussion of inlet system and retention time measurements, to sample preparation. *Jennings* has admirably presented the central problems of glass capillary gas chromatography; he considers possible errors and dangers, and how they can be overcome.

The last part presents selected solutions of problems. This section is somewhat short and the choice of material somewhat arbitrary. Nevertheless, purchase of this clearly written book can be wholeheartedly recommended.

Gerhard Spiteller [NB 443 IE]

Kirk-Othmer: Encyclopedia of Chemical Technology. Vol. 1. A to Alkanolamines. Edited by *H. F. Mark, D. F. Othmer, C. G. Overberger*, and *G. T. Seaborg*. John Wiley & Sons, London 1978. 3rd Edit. xxix, 967 pp., bound, £ 50.00.

This is the first volume of the third, completely revised edition of Kirk-Othmer.

This first taste of the new edition creates a very good impression in several respects. The editors have remained faithful to their principle of producing a tersely written and well arranged reference work serving as an excellent source of information for all manufacturers and users of chemical products. In the individual sections of the new edition, numerous aspects have been included which have attracted increasing interest during the past decade, such as energy considerations and data pertaining to safety engineering and toxicology. Moreover, SI units are now given side by side with British engineering units which will certainly facilitate use of the encyclopedia in many countries.

In the first volume both the sections with an engineering slant (*e.g.* Absorption, Adsorption, Air pollution) and those concerned with substances (*e.g.* Acetaldehyde, Acetic acid, Acetone, Acetylene, Acrylamide, Acrylic acid, Acrylic esters, Acrylic fibers, Acetonitrile, Alcohols) accurately reflect the present state of the art, and could hardly be improved in their clarity and presentation.

Thus the third edition of Kirk-Othmer will doubtless live up to its reputation of being the leading English-language reference work in chemical technology. Let us hope that the subsequent 24 volumes will be published in rapid succession.

R. Steiner [NB 444 IE]

Infrared and Raman Spectroscopy. Part A—C. Edited by *E. G. Brame* and *J. Grasselli*. Marcel Dekker, New York—Basle 1976, 1977. 1st edit., 1039 pp. in all, numerous tables and figures, the whole work SFr. 355.00.

The three parts of this work contain the following chapters: Introduction to Molecular Vibrations (*B. Crawford, D. Swanson*); Inorganic Materials (*R. L. Carter*); Organometallic Compounds (*W. F. Edgell*); Ionic Organometallic Solutions (*W. F. Edgell*); Computer Systems (*R. P. Young*); Organic Materials (*R. A. Nyquist, R. O. Kagel*); Environmental Science (*D. S. Lavery*); Food Industry (*A. Eskamani*); Petroleum (*P. B. Tooke*); Textiles (*G. Celikiz*); Biological Science (*G. J. Thomas, Y. Kyogoku*); Polymers (*S. C. Brown, A. B. Harvey*); Surfaces (*C. D. Craver*). A very broad picture is given of the vibrational spectroscopy of biological (156 pages), inorganic (139 pages), and organic (124 pages) systems. Fibers and textiles (16 pages), petroleum (34 pages), and even polymers (60 pages) come off badly.

I have seldom seen a handbook in which the individual chapters were so variable in quality as in the present work. The opening chapter often acts as a visiting card; were it so in this case, it would bide ill for the book. It is certainly not easy to write an original introduction to vibrational spectroscopy (they can be found in dozens of works). *Crawford* and *Swanson* have managed this—but how! "The nucleons within a nucleus, for example, do not exhibit such nice behavior"; "the practical spectroscopist in the real world"; "We chemists owe our good fortune to the fact that the forces between intramolecular particles ... are of Coulomb nature, and that the natural constants ... have the values they do"; these are just a few examples. Messrs. *Coulomb, Planck, etc.* are not thanked in the accompanying footnote; instead, *D. Dennison* is made responsible for this information. Colloquial nonsense like this makes the chapter no more than a source of amusement; fortunately, the following sections are more serious. (Regrettably, in the discussion of hydrocarbon analysis and group frequencies, no mention is made of the achievements of the Goubeau group.)

The chapter on the vibrational spectra of inorganic substances is competent. A large part is taken up with the section on symmetry and group theory (overlap with the first chapter); it is questionable whether this needs to be repeated in every book on spectroscopy. It is regrettable to find in Table 10 (NO_3^- vibrations) the terms "NO_2 symmetric and asymmetric stretch" (or "... bend") and "NO stretch"; the correct forms would have been found on p. 28. In the bibliography the emphasis is on *Siebert* (and his book); most of the other German-speaking spectroscopists are missing.

The two chapters by *Edgell* are important and interesting, and not only to specialists. In the first of these, $Ni(CO)_4$, $Mn(CO)_4Br$, and $(CH_3)_2SnCl_2$ are discussed in detail; there are also tables metal-hydrogen and metal-metal frequencies and information on vibration calculations. The second chapter gives information on the most important points on the structure of ionic organometallic solutions.

The chapter on computer systems is highly readable and informative, considering the new generation of "computerized grating spectrometers" and the Fourier interferometer. Perhaps the best part of this is the careful (and well explained)

use of "computer Chinese"; the informative illustrations and the extensive bibliography are also praiseworthy. The chapter on organic materials has a series of good spectra, an acceptable discussion, and a not very extensive bibliography (barely half the references by *Nyquist et al.*). The reviewer would have preferred here one of the good books on this topic. The chapter on IR and Raman methods in "Environmental problems" is essentially limited to the description of IR gas cells and their use in gas analysis. A rather wider outlook would have been useful (*e.g.* a comparison of the sensitivity of IR and mass-spectrometric methods). The excessively large calibration curves for some gases are of limited value, since data on the resolution, spectral slit width, and half-width value for the bands in question are missing. "Remote Raman" analysis with a pulsed laser Raman system, the laser IR system, and an IR technique which uses sunlight as a source are all briefly discussed. Analysis of water ranks six pages. The chapter on the application of IR spectroscopy in the food industry is useful. In particular, methods for the determination of water, carbohydrates, lipids, flavoring materials, and vitamins are discussed.

Perhaps the best chapter is the one on the IR and Raman analysis of biological systems. This is based on no fewer than 260 publications (up to 1975) and deals in some detail with proteins (oligopeptides and polypeptides), nucleic acids, lipids, and membranes. The methodology is also thoroughly discussed, including the resonance Raman effect. The illustrations have been carefully chosen; the numerous tables contain a wealth of information.

The physical appearance of the work is somewhat modest, considering its price. The paper is streaked with grey and translucent, and the contributions have been reproduced in manuscript form. The separate volumes appear almost identical in their outward appearance. Author and subject indexes for all three parts are placed at the end of Part C. The series deserves to be continued, though it might be useful if the editors checked the quality of the individual contributions more carefully than in the past.

D. O. Hummel [NB 459 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Aromatic and Heteroaromatic Chemistry, Vol. 6. Senior Reporters: *H. Suschitzky* and *O. Metz-Cohn*. The Chemical Society, London 1978. xii, 326 pp., bound, DM 140.00.—ISBN 0-85186-803-7.—A volume of the series "Specialist Periodical Reports"

Fundamental Research in Homogeneous Catalysis. Vol. 2. Edited by *Y. Ishii* and *M. Tsutsui*. Plenum Press, New York 1978. ix, 305 pp., bound, $ 39.00.—ISBN 0-306-40033-2

Metal β-Diketonates and Allied Derivatives. By *R. C. Mehrotra, R. Bohra*, and *D. P. Gaur*. Academic Press, London 1978. viii, 382 pp., bound, £ 20.50.—ISBN 0-12-488150-5

Biosynthetic Products for Cancer Chemotherapy, Vol. 2. By *G. R. Pettit* and *G. M. Cragg*. Plenum Press, New York 1978. ix, 150 pp., bound, $ 35.00.—ISBN 0-306-37688-1

Nuclear Magnetic Resonance Spectroscopy in Molecular Biology. Edited by *B. Pullman*. D. Reidel, Dordrecht 1978. ix, 537 pp., bound, Dfl. 115.00.—ISBN 90-277-0932-7

Transition Metal Organometallics in Organic Synthesis, Vol. 2. Edited by *H. Alper*. Academic Press, New York 1978. xi, 188 pp., bound, $ 19.00.—ISBN 0-12-053102-X

Physicochemical Applications of Gas Chromatography. By *R. J. Laub* and *R. L. Pecsok*. John Wiley & Sons, New York 1978. xxi, 300 pp., bound, $ 33.00.—ISBN 0-471-51838-7

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstraße 12, D-6940 Weinheim, Germany, Telephone (06201) 14036. Telex 465516 vchwh d.

Editor: *O. Smrekar* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*). Pappelallee 3. P.O. Box 1260/1280, D-6940 Weinheim, Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 4
April 1979
Pages 239–336

Methods of Reactivity Umpolung

By Dieter Seebach[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

The past decade of organic chemistry may be characterized as a period of violent development of new synthetic methods. This was accompanied by a systematization of the analysis of synthetic problems (synthetic strategy). The planning of the synthesis of an organic target molecule is greatly facilitated by distinguishing between reagents $X(C)_n\ldots$ with normal reactivity (acceptor properties at $C^{1,3,5\cdots}$, donor properties at X, $C^{2,4\cdots}$) and with reactivity umpolung (acceptor properties at X, $C^{2,4\cdots}$, donor properties at $C^{1,3,5\cdots}$). In this context, reactivity umpolung turned out to be useful as a heuristic principle, as a classification scheme, and as an aid for locating so-called strategic bonds (synthon, transform, and antithesis according to *E. J. Corey*). There are six principal methods of umpolung: 1,2*n*-oxidation, heteroatom exchange and modification, homologation and its reversal, the cyclopropane "trick", use of acetylenes, and redox reactions; under certain circumstances none of these techniques is necessary in cases where direct umpolung is possible. Throughout the article, normal reactivity is indicated by green print; reactivity umpolung by red print.

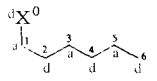
1. Postulates and Nomenclature

Before describing and systematizing the methods of reactivity umpolung, the scope of the discussion, the nomenclature of synthetic methodology and the synthetic problem behind reactivity umpolung must be defined.

1. The reactions most frequently used in organic synthesis are *polar* in nature, *i.e.* nucleophilic or *donor* (**d**) and electrophilic or *acceptor* (**a**) sites are used to make and break bonds (Lewis acid base combinations)[1a, 1b].

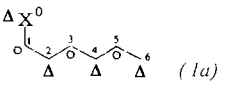
2. The large majority of target molecules of organic synthesis contain the heteroatoms *nitrogen* and *oxygen* as functional groups (amino, imino, hydroxy, ether, carbonyl)[1a].

3. These heteroatoms impose an *alternating acceptor and donor reactivity pattern* (*1*) upon the carbon skeleton, *i.e.* acceptor properties or attack by donors at carbons $C^{1.3.5\cdots}$, and donor properties or attack by acceptors at carbons $C^{2.4.6\cdots}$; the heteroatom X^0 itself is a donor center d^{0}[1a].



(*1*), X = O, N

$a^{1,3,5\cdots}$- and $d^{0,2,4,6\cdots}$-reactivity



(*1a*)

In order to clearly distinguish donor and acceptor reactivity from partial charge separation (⊕ or $\delta^{\oplus}$ and ⊖ or $\delta^{\ominus}$) we use the letters **d** and **a** throughout this article [see (*1*) [1c]]. The signs Δ for **d** and o for **a** [see (*1a*)] may also be employed and avoid additional letters to be written in more complex formulas. Green print indicates normal reactivity, red print reactivity umpolung (see definition 1.8).

4. A consequence and synthetic limitation is the fact that combination of components with reactivity (*1*) leads only

[*] Prof. Dr. D. Seebach
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum
Universitätstrasse 16, CH-8092 Zürich (Switzerland)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0239 $ 02.50/0*

to 1,3-, 1,5- ... 1,(2n+1)-disubstituted products (odd number of carbon atoms between the functional groups) [see *(2)* and *(3)*][1a].

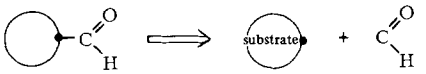


a^3/d^0 or a^1/d^2 a^5/d^0, a^3/d^2 or a^1/d^4

(2) *(3)*

direct or vinylogous Prins-, aldol-, Claisen-, Mannich- and Michael reactions [1a, 2]; X, X' = O, N; double bonds where applicable

5. According to the original proposition, *synthons* are "structural units within a molecule which are related to possible synthetic operations"[3a]. Thus, the molecule *(4)* is related

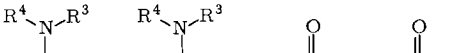


(4) *(5)* *(6)*

with the substrate synthon *(5)* and the formyl synthon *(6)*. This is irrespective of the type of reaction employed (polar, radical[1c], pericyclic, transition-metal mediated, photochemical, electrochemical).

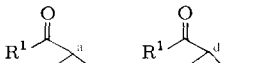
6. An a^n- or d^n-synthon ($n \geq 1$) is, respectively, a synthon with an O- or N-heteroatom at C^1 and an acceptor or donor center at C^n[3b, 4]. Six such synthons are shown in *(7)*–*(9)*. An a^0- or d^0-synthon is an acceptor or donor heteroatom (O or N), respectively.

7. A *reagent* is the compound or intermediate actually used to carry out the synthetic operation. *Synthetically equivalent* reagents or series of reactions perform identical transformations (see Table 1 and definition 1.9)[3c].



a^1 d^1 a^1 d^1

(7a) *(7b)* *(8a)* *(8b)*

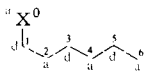


a^2 d^2

(9a) *(9b)*

8. A reagent has normal reactivity if it corresponds to a synthon of general type *(1)*.

Reactivity umpolung is present in a reagent in which **a**- and **d**-centers are reversed as compared to *(1)* [see general representation *(10)*; cf. *(7b)*, *(8b)*, *(9a)*]. Thus, a^{2n+1}- or



$a^{0,2,4,\cdots}$- and $d^{1,3,5,\cdots}$-reactivity

(10), X = O, N

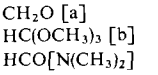
d^{2n}-synthons correspond to reagents of normal reactivity, d^{2n+1}- or a^{2n}-synthons to those with reactivity umpolung (see Table 1).

Umpolung is also present if the alternation of reactivity is violated [see also query 4 in Section 2, and Section 3.5).

Finally umpolung is any *process* by which donor and acceptor reactivity of an atom are interchanged (see Sections 3.2 and 3.6).

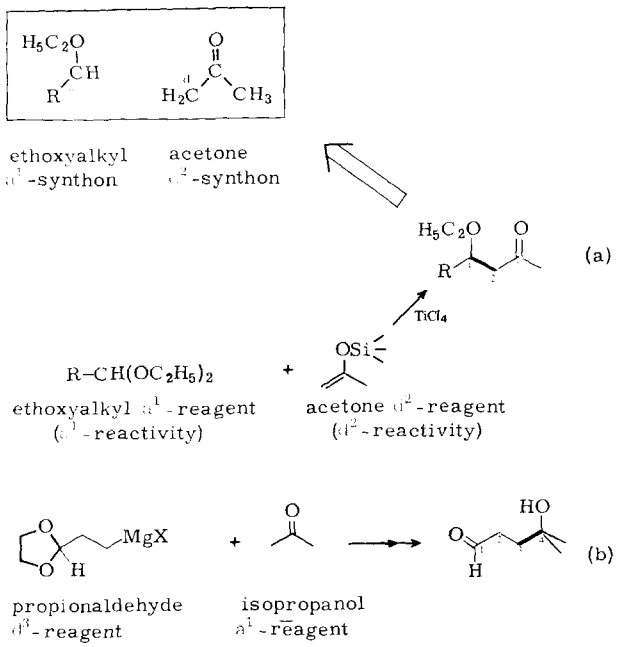
9. When discussing particular transformations, the names of the structural units under consideration are used with the

Table 1. Preparations of an aldehyde R—CH_2—CH_2—CHO (target molecule).

Transformations and synthons leading to target			Reagents			Ref.
R—CH_2—CH_2 **d**	+ a CHO (*the* formyl a^1-synthon)	R—CH_2—CH_2—MgX	+	CH_2O [a]; $HC(OCH_3)_3$ [b]; $HCO[N(CH_3)_2]$; 	*synthetically equivalent reagents* (four of many possible formyl a^1-reagents)	[8]; [4g, 9]
R—CH_2—CH_2 **r**	+ **r** CHO	R—CH=CH_2	+	 [c,b]		[10]
		R—CH_2—CH_2—Br	+	 [b]	*synthetically equivalent reagents* (formyl d^1-reagents)	
R—CH_2—CH_2 **a**	d CHO (d^1)	R—CH_2—CH_2—OTos	+	NaCN [d]		
		R—CH_2—CHO	+	$CH_3OCH=P(C_6H_5)_3$ [b]		
R—CH_2 **a**	+ d CH_2—CHO (d^2)	R—CH_2X	+	 [b];  [d,b]	*synthetically equivalent reagents* (acetaldehyde d^2-reagents)	[11]; [12]
R—CH_2 **d**	+ a CH_2—CHO (a^2)		+	Br—CH_2—$CH(OC_2H_5)_2$ [e, b]	(acetaldehyde a^2-reagent)	
R **a**	+ d CH_2—CH_2—CHO (d^3)	RBr	+	 [f,b]	(propionaldehyde d^3-reagent)	[13]
R **d**	+ a CH_2—CH_2—CHO (a^3)	R_2CuLi	+	 [d]	(propionaldehyde a^3-reagent)	

[a] Oxidation of the product. [b] Hydrolysis of the product. [c] Radical chain initiator. [d] Reduction of the product. [e] Raney-Ni desulfurization. [f] S-methylation of the primary alkylation product.

corresponding reactivity symbols; newly formed bonds are indicated in **bold type** [see eqs (a)[6] and (b)[7] and Table 1[3c, 5]].

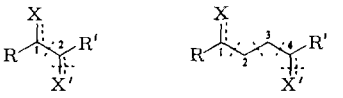


10. A reaction or reagent which differentiates between sites of identical reactivity in a conjugate system of type *(1)* or *(10)* is called *ambidoselective* (see selectivity nomenclature and examples in Table 2).

2. The Synthetic Problem

Four Views of Synthetic Situations Requiring Reactivity Umpolung

1. As stated in Section 1, the normal reactivity *(1)* does not enable us to construct 1,2*n*-disubstituted products (even number of carbon atoms between the functional groups). How are compounds of type *(11)* and *(12)* synthesized?

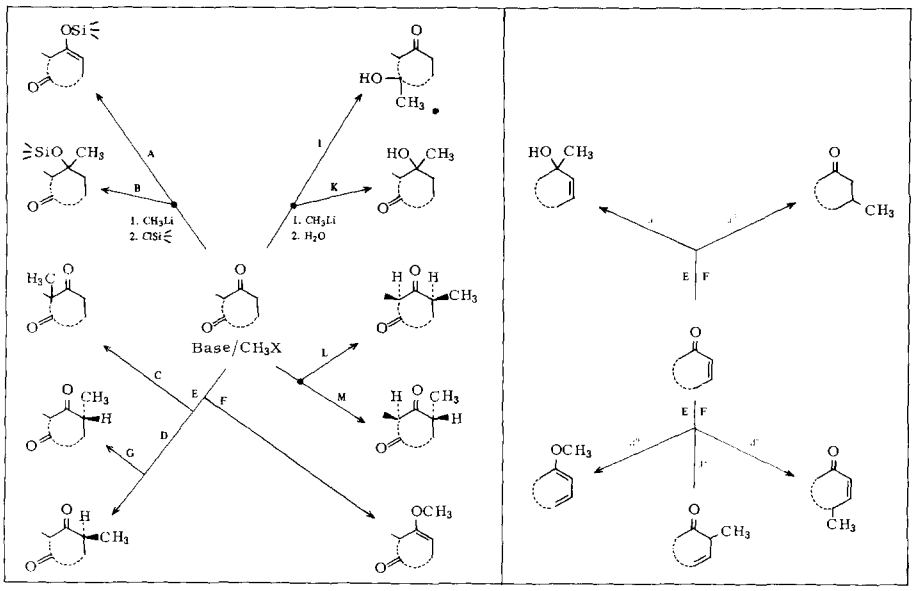


(11) *(12)*

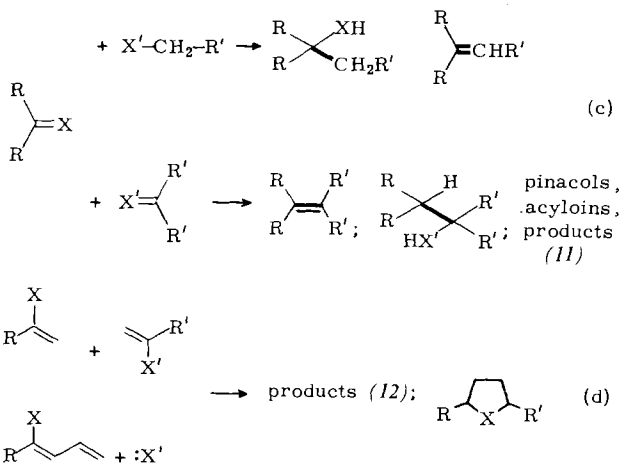
X, X' = NR''_2, OR'', NR'', O

2. We can rephrase this question in the following way: how do we couple two centers of identical polarity or affinity? [see eqs (c) and (d), X/X' = O, N].

Table 2. Structural definition of selectivities.—Three principal selectivities are distinguished [a]: 1. *type* selectivity (*non*-isomeric products, mostly different types of reactions, *i.e.* substitution, addition, elimination, ... A/B); 2. *constitutional* selectivity (same kind of reaction, products are constitutional isomers; C/D, E/F, I/K); 3. *stereo*-selectivity (products are stereoisomers; diastereoselectivity L/M or enantioselectivity G/H [b, c]).—Constitutional selectivity is subdivided into *site* selectivity (differentiates unrelated functional groups in a molecule which can undergo the same type of reaction, I/K), *regio*-selectivity [d] C/D and *ambido*-selectivity E/F (see definition 1.10 [e]).



[a] The term *chemo*selectivity [*B. M. Trost, Th. N. Salzmann, K. Hiroi*, J. Am. Chem. Soc. *98*, 4887 (1976)] is not structurally defined, *stereospecificity* is an often criticized term [*H. E. Zimmermann, L. Singer, B. S. Thyagarajan, ibid. 81*, 108 (1959); *E. Ruch, I. Ugi*, Theoret. Chim. Acta *4*, 287 (1966)]; "specificity" should be dropped altogether. [b] See *Y. Izumi, A. Tai:* Stereodifferentiating Reactions, Academic Press, New York, 1977. [c] Of course, (G) and (H) are only enantioselective routes if the hydrogens of the α-keto CH_2-group are enantiotopic in the starting molecule of the present example; in L/M they must be diastereotopic. [d] See *A. Hassner*, J. Org. Chem. *33*, 2684 (1968). [e] This was part of the original definition of regioselectivity (see [d]). However, the term was rarely used to distinguish between 1,2- *vs.* 1,4-addition to an enone or *O*- *vs.* *C*-alkylation of an enolate [reviews: *J. d'Angelo*, Tetrahedron *32*, 2979 (1976); *R. Gompper, H.-U. Wagner*, Angew. Chem. *88*, 389 (1976); Angew. Chem. Int. Ed. Engl. *15*, 321 (1976); *L. M. Jackman, B. C. Lange*, Tetrahedron *33*, 2737 (1977)]. As evident from the lower part of Table 2, the **a**/**d**-nomenclature is very convenient in this connection.

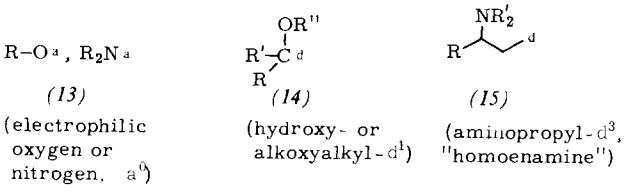


(c)

pinacols, acyloins, products *(11)*

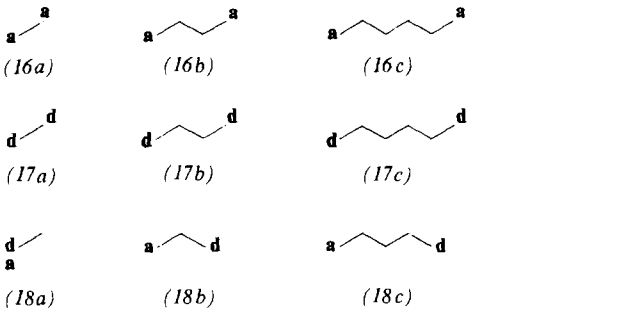
products *(12)*; (d)

3. How can we systematically achieve a reactivity umpolung or construct reagents which correspond to synthons such as *(13)*—*(15)*? [cf. postulates 1.6 and 1.8, *(10)* and Table 1].



R–O^a, R_2N^a		
(13)	*(14)*	*(15)*
(electrophilic oxygen or nitrogen, a^0)	(hydroxy- or alkoxyalkyl-d^1)	(aminopropyl-d^3, "homoenamine")

4. A fourth way of putting the question is: How do we generate equal reactivity in 1,(2*n*)- or opposite reactivity in 1,(2*n* + 1)-positions of a carbon framework? [see *(16)*—*(18)*].



(16a) *(16b)* *(16c)*

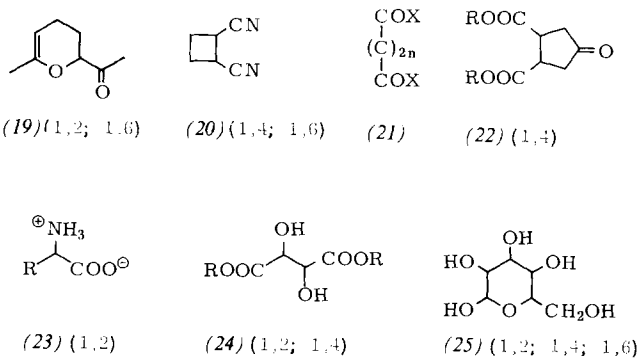
(17a) *(17b)* *(17c)*

(18a) *(18b)* *(18c)*

3. Methods of Reactivity Umpolung

Although the problem has been recognized for a long time[14–16], and although numerous classical solutions are available, an intensive effort has been made in the past decade to answer the four questions in Section 2 in new ways. A confusing variety of apparently independent and unrelated methods has been conceived and demands classification. This is attempted in the following sections.

Prior to doing this, a very important *memo* is appropriate: The preparation of 1,2*n*-bifunctional starting materials such as the [2+4]-dimer *(19)* of methyl vinyl ketone[17] or the head-to-head [2+2]-dimer *(20)* of acrylonitrile[18] is not readily classified in the present context. Also, industrial and biochemical processes furnish readily available and often unusual compounds in large quantities, *e.g.* the dicarboxylic acid derivatives *(21)* (succinic, adipic, fumaric, maleic, phthalic)



(19) (1,2; 1,6) *(20)* (1,4; 1,6) *(21)* *(22)* (1,4)

(23) (1,2) *(24)* (1,2; 1,4) *(25)* (1,2; 1,4; 1,6)

Examples of molecules from the "black magic box".

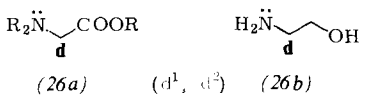
and *(22)* (from fumarate and cyanide[19,20]), furan and its derivatives, amino acids *(23)*, highly functionalized molecules such as tartaric acid *(24)* and carbohydrates *(25)*[21]. These may or may not arise along the lines described below. We might call these sources the "*black magic box*" of the synthetic organic chemist which should never be forgotten when planning the synthesis of a (chiral) molecule with complex functionality[21,22].

3.1. 1,2*n*-Oxidation

A process creating a 1,2*n*-oxygen and/or -nitrogen functionalized carbon skeleton without formation of a C—C bond is an oxidation (conservative conversion, non-connective). Some common transformations of this sort are listed in Table 3. As can be seen, many classical reactions and their recent improvements are among the examples: epoxidation (No. 1, 2), hydroxylation (No. 3, 4, 6, 7), oxygenation (No. 5, 8, 10, 11, 16), amination (No. 4), oximation and imination (No. 9), ozonolysis (No. 18), hydroboration /oxidation (No. 12), the Neber (No. 13), Bayer-Villiger (No. 17), and Criegee-Hock rearrangements (No. 19), the Hofmann-Löffler-Freytag (No. 14), and the Barton reaction (No. 15).

We are dealing with cases in which the heteroatoms oxygen and nitrogen have become acceptor (sextet or septet) sites *(10)* rather than acting as donors *(11)* [umpolung of heteroatom reactivity; a^0-synthons; equal polarity at adjacent heteroatoms R—O—O—R', R_2N—NR'_2, cf. *(17a)*]. Since the methodology of generating and selectively using reagents with electrophilic N or O is rather limited, there are numerous techniques which use other acceptor heteroatoms that are subsequently replaced by oxygen or nitrogen (see Section 3.2).

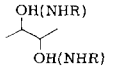
It is evident that all the products in Table 3, like the above mentioned black magic box molecules *(19)*—*(25)*, have a built-in reactivity umpolung: due to the 1,2*n*-functionalization, any of their normal reactions [*(11)*] with respect to one of the functional groups is an umpolung of reactivity [*(10)*] with respect to the other functionality. Thus, the enolate



(26a) (d^1, d^2) *(26b)*

of an amino acid derivative[4d,42] corresponds both to a d^2- *and* a d^1-synthon *(26)* (cf. the use of this type of reagent in the homologative approach, Section 3.3).

Table 3. Some reactions creating 1,2-doubly functionalized carbon skeletons without C—C-formation [23].

No.	Starting material	Reagent [ref.]	Product
1		$R—CO_3H$	
2		*t*-Bu-OOH/Mo V-derivative [24]	
3		OsO_4/R_3NO [25]	
4		OsO_4/chloramine-T [26]	
5		$^1O_2$ [27]	
6		O_2 [28]	
7		MoOPH [29]	
8		$HC(OR)(NR_2)_2/^1O_2$ [30]	
9		$ArN_2^{\oplus}$, $NO^{\oplus}$ [31, 32]	
10		$R—CO_3H$ [6c, 33]	
11		$^1O_2$ [34]	
12		$BH_3(H_2O_2)$ [6c, 35]	
13		NH_2OH/TosCl/base [2]	
		H_2SO_4 [2, 36]	
15		RONO/hv [2, 37]	
16		base/O_2 [38]	
17		H_2O_2 [2, 18, 39]	
18		O_3 or $OsO_4/IO_4^{\ominus}$; $Pb(OAc)_4$ [40]	
19		TosCl [2, 41]	

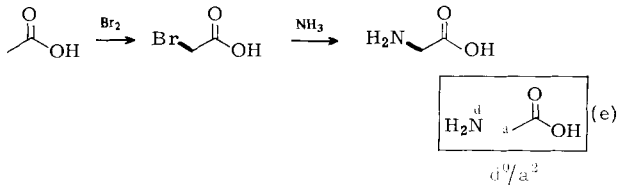
3.2. Exchange and Modification of the Heteroatom

Fortunately, organic chemistry is not restricted to the elements C, H, N, O! We can utilize all the elements of the periodic chart to achieve the goal of synthesizing C, H, N, O-containing products (see postulate 1.2) and to break out of the reactivity pattern *(1)* (see 1.3). The most common and best established systematic way of reactivity umpolung of N- or O-functionalized molecules is the *temporary exchange* of these heteroatoms by others which convey opposite reactivity to the carbon moiety. Thus, we use derivatives of other heteroatoms like a boat to cross a river.

Furthermore, nitrogen, unlike oxygen, has so many oxidation states and occurs in a multitute of bonding situations that it can be "modified" to allow for jumping back and forth between the two reactivity patterns *(1)* and *(10)*.

3.2.1. Heteroatom Exchange

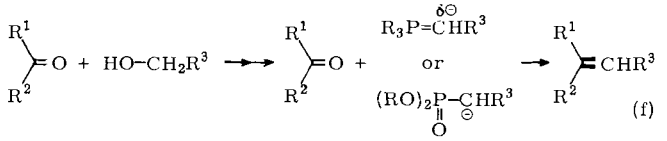
As stated above, there is a lack of methods which cleanly introduce nitrogen and oxygen at donor sites. The use of $Br^{\oplus}$ as an electrophilic substitute heteroatom is a classical solution to this problem [see eq. (e)]. When the desired C—N bond is formed, the nitrogen acts as a nucleophile, the α-car-



(e)

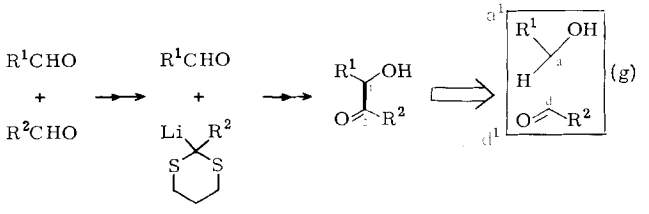
bonyl carbon as an electrophile; therefore the corresponding synthons are d^0 and a^2 (see also the 1,4-oxidation, entry 1 in Table 4). The use of α-chloronitrones (Table 4, entry 2) and of α-heter· ubstituted oximes[43] and hydrazones[44] as ketone a^2-reagents in C—C-bond forming processes has recently been demonstrated. The preparation of Grignard derivatives, the employment of tin-containing intermediates, and the use of certain acyl-metal and acyl-phosphorus compounds for reactivity umpolung are outlined in Table 4 (entries 3—5).

Especially versatile heteroatoms Y for this purpose are phosphorus, sulfur and selenium[4g,45]. They can be readily intro-

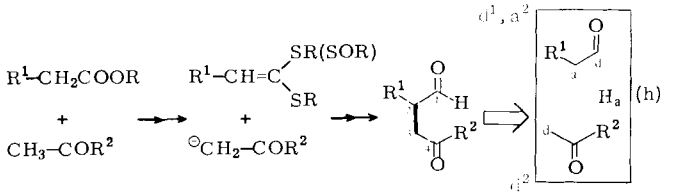


(f)

duced at electrophilic ($+R_nY^{\ominus}$) *and* at nucleophilic sites ($+R_nYX$). Sulfur in particular stabilizes positive *and* negative charges in the α-position, and there are numerous ways of removing all three heteroatoms from a molecule[4g]. Conversions associated with the names of *Wittig*, *Horner*, *Emmons*, *Wadsworth*, *Michaelis* and *Arbuzov*[2] allow the coupling of carbon atoms of the same polarity [cf. eqs. (c) and (f)]; recent improvements and promising developements in this general area are the so called redox condensations with phosphanes[46] and the conversion of NH_2 into the leaving group $N(SO_2R)_2$[47].

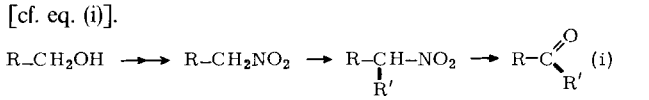


(g)



(h)

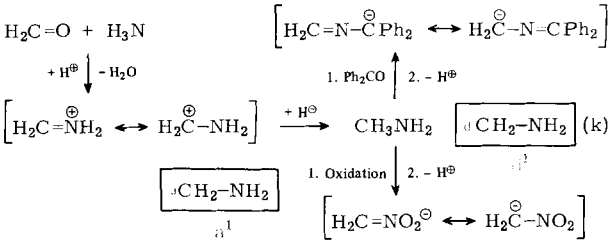
The temporary replacement of the heteroatom oxygen by sulfur for the preparation of 1,2-*n*-functionalized products is described in equations (g) and (h) [cf. eqs. (c) and (d); for further examples see Table 4, entries 6—8, and detailed reviews[4b, 4g, h, 12, 45]]. The interconvertibility of oxygen and nitrogen functions (functional group equivalence[13a]) renders the use of N-containing reagents with reactivity umpolung (see Section 3.2.2) a heteroatom exchange method for oxygen [cf. eq. (i)].



(i)

3.2.2. Heteroatom Modification

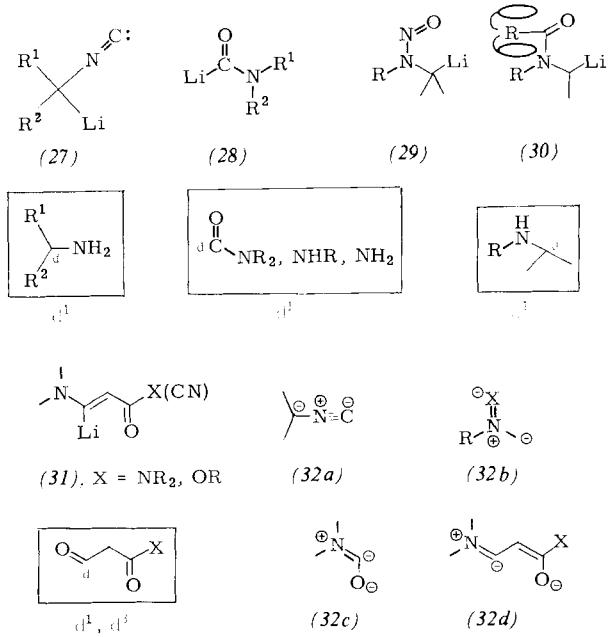
In sharp contrast to oxygen, which can hardly be modified to allow d^1- and a^2-reactivity as in *(10)*[48–50] (see Section 4.1) without the help of heteroatom exchange, nitrogen is a very rich heteroatom in this respect. There are two fundamental reasons for this: nitrogen can 1) make one more bond with carbon and thus be incorporated "in the middle" of conjugated systems, and 2) it has many more oxidation states; it can stabilize α-$C^{\oplus}$ in the lower ones and α-$C^{\ominus}$ in the higher ones. Thus, modification of the nitrogen of methylamine in the Schiff-base with benzophenone allows α-N—CH-deprotonation (cf. umpolung of amine reactivity with pyridoxal in Nature[51]) and converts the normal aminoalkylating a^1-



(k)

reactivity of iminium derivatives[52] into d^1-reactivity[53] [see eq. (k)]. On the other hand, we can convert the amine (oxidation state −3) into the nitronate (oxidation state +5) and use this as an aminomethyl d^1-reagent[41].

We need not go all the way to the nitro or diazo group to achieve α-N—CH acidification and α-N—C-donor properties. Any amine derivative which bears an electron-withdrawing group causing a partial positive charge on nitrogen appears to suffice under appropriate conditions [see the isocyanides *(27)*[54], the carbamoyllithium compounds *(28)*[50,55], the nitrosamines *(29)*[4d,56], the amides *(30)* with sterically pro-



(27) *(28)* *(29)* *(30)*

(31), X = NR_2, OR *(32a)* *(32b)*

(32c) *(32d)*

tected but electronically effective carbonyl groups[48,49,57], and the vinylogous ureas, urethanes, and cyanamides *(31)*[58]. It is not entirely clear yet whether the dipolar anion stabilization indicated in *(32)* is the decisive effect causing the ready

Table 4. Exchange and modification of heteroatoms [23].

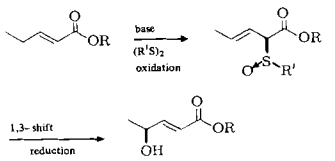
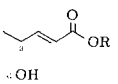
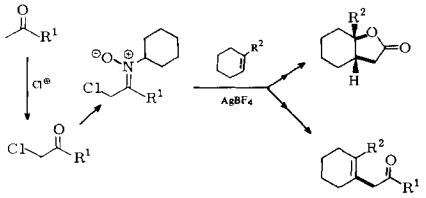
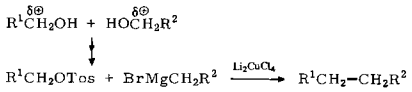
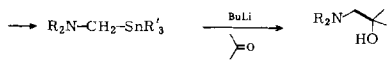
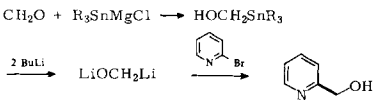
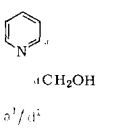
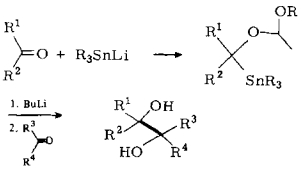
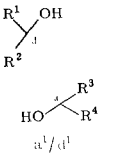
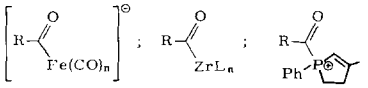
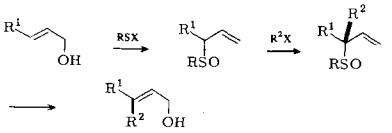
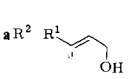
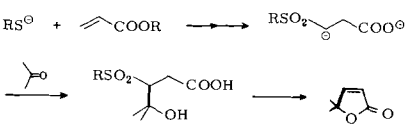
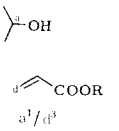
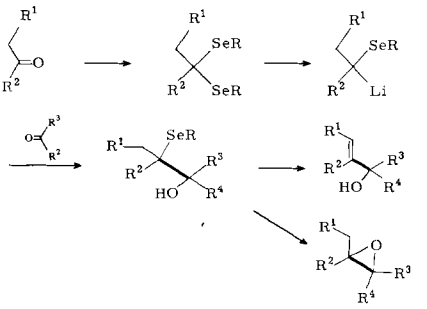
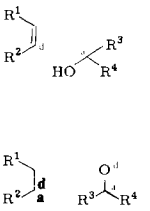
No.	Conversions and Reagents	Synthons	Ref.
1			[61]
2			[62]
3		R^1CH_2 **a** R^2CH_2 **d**	[63]
			[64]
4			[65]
			[66]
5			[67–69]
6			[70]
7			[4g, 71]
8			[45] [72]

Table 4 (continued).

No.	Conversions and Reagents	Synthons	Ref.
9	RCOOH, RCH_2OH, RCHO $\xrightarrow{\ominus CN}$ homologous acid, amide, ketone, aldehyde, alcohol, amine, α-amino acid, α-hydroxyamide, -acid, -ketone, -aldehyde, -amine	d^1COOH $d^1$$CONH_2$ d^1CHO d^1COR $d^1$$CH_2OH$ $d^1$$CH_2NH_2$	[2] [23] [73—76]
10	R^1–COOH + HO–CH_2–CH=CR^2_2 + RCH(NH$_2$)–COOH →	OH or O; $d^1$$CH_2CH=CR^2_2$	[77]
11	NH_2 $\xrightarrow{SOCl_2}$ N=S=O; 1. Base 2. 3. H_2O	NH_2	[78]
12	+ $HN(CH_3)_2$; 1. O 2. Raney-Ni or oxidation or hydrolysis; X = H_2, O	N or HN, OH	[79]
13	NO_2Li; OSi; NH_2, OH	NH_2, OH	[41]

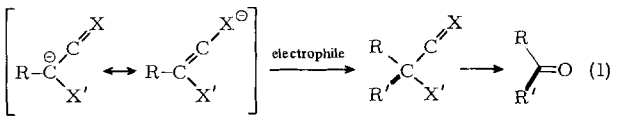
formation and unexpected stability of these systems[4d, 48, 49, 57]. An almost complete list of N-derivatives with nucleophilic α-carbons is found in a previous review (Table 3 in Ref. [4d]). The use of cyanide (Kolbe and Strecker syntheses[2], cyanohydrin formation), a recent example of incorporation of nitrogen into a conjugated system (cf. Section 3.5), and novel derivatives with "dipole stabilization" are listed in Table 4 (entries 9—13).

Examples of simultaneous heteroatom exchange *and* modification for the purpose of reactivity umpolung are the versatile reagent $TosCH_2NC$: (Tosmic[54, 59]) and the thiocarbamoyllithium derivatives $LiCSNR^1R^2$[60].

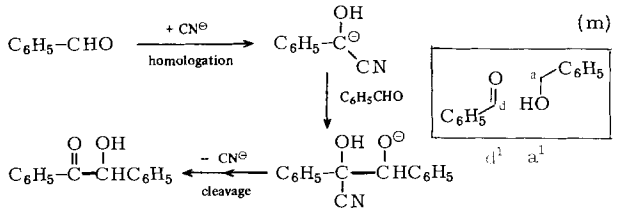
3.3. Homologation and Its Reversal

As stated in Section 3.1, any compound with a 1,2*n*-functionalization has the normal reactivity pattern *(1)* with respect to one of the two functional groups and reactivity umpolung *(10)* of the other one [cf. Section 3.1, *(26)*]. After a reaction with an acceptor at C^2, which in this case is at the same time a d^2- *and* a d^{2n-1}-center, the C—C bond leading to C^1 can be cleaved (reversal of homologation, degradation). This procedure then provides a reagent which corresponds to a d^{2n+1}-synthon. The extra functionalized carbon atom (C^1) can be specifically introduced (homologation) for the purpose of reactivity umpolung.

A d^1-reagent of this type has the general formula *(33)* where X and X′ may be oxygen and/or nitrogen, or other heteroatoms, and must fulfil three conditions: the C=X group is essential for anion stabilization, attack of the electrophile must occur on carbon, and the product must be amenable

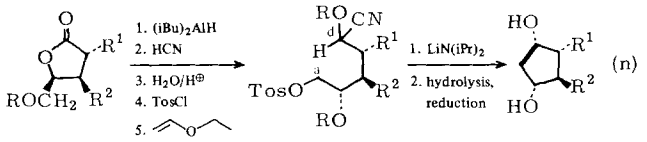


(33)

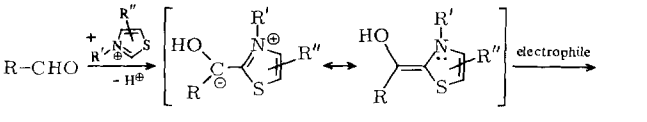


to cleavage to a carbonyl compound [see eq. (l) and Table 5]. Especially attractive are catalytic processes, the best known

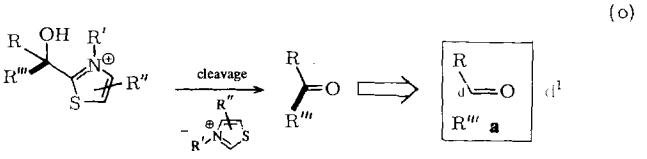
example of which is the benzoin condensation [eq. (m)]. The Stork method[80] is conceived along these lines; it uses lithium derivatives of protected cyanohydrins (see Table 5) and is ingeniously applied to a prostaglandin synthesis as indicated in eq. (n)[81]. The method by which Nature performs nucleophilic acylations again involves a catalytic homologation, with



(n)



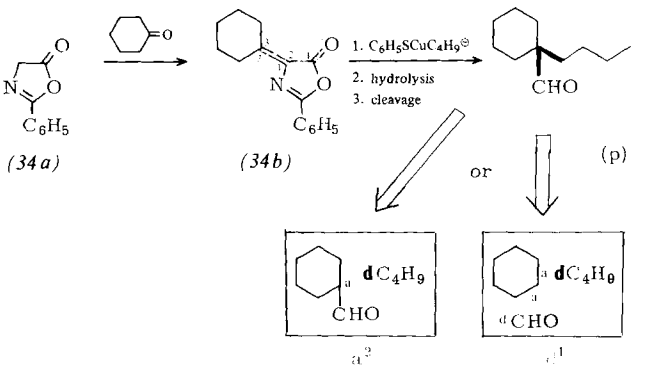
(o)



thiamine pyrophosphate[51,82], and was adopted by *Stetter et al.*[83] for laboratory scale preparations [eq. (o)].

Further examples of devising d^1-reagents by the homologative approach are listed in Table 5.

So far, we have discussed only cases in which d^1-reactions were performed with homologues of the actually required carbon framework. It is equally possible to use this method to supply a^2- and d^3-reagents [see eqs (p)—(r)]. In the first

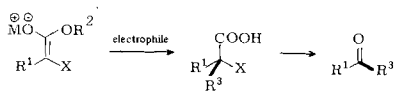
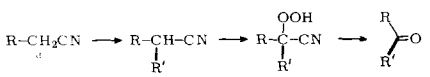
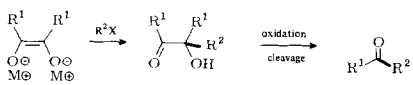
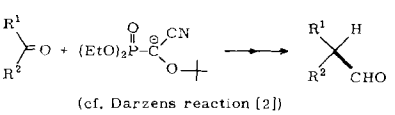
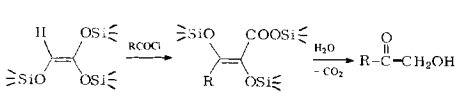


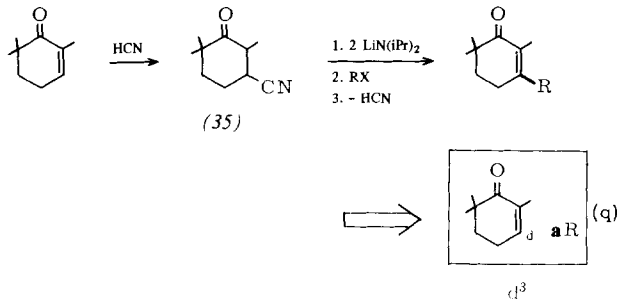
(p)

process a glycine derivative *(34a)* is used as a 1,2-bifunctional molecule[84]. Condensation with cyclohexanone gives a Michael acceptor (a^3) *(34b)*, which also is an enamine derivative (normal reactivity d^2, here a^2); the product obtained from the Gilman reaction[85] is hydrolyzed to the corresponding α-amino acid which is cleaved by lead tetraacetate (retrohomologation; the carbonyl carbon has "done its job"!) to give the final aldehyde product. If we consider the synthesis from cyclohexanone, the oxazolidone *(34a)* is a d^1-reagent (in the Dakin-West reaction[2] it is dCH_2NH_2); comparing *(34b)* with the aldehyde, we see that it is an a^2-reagent.

The reversible homologation of equation (q)[86] is vinylogous to the above mentioned use of cyanide for nucleophilic acylation and brings about a β-alkylation of an enone (cf. entries 7 and 9 of Table 4). The reaction sequence in equation (q) employs a 1,4-bifunctional intermediate *(35)*—like the classical Stobbe condensation[2] (and its many recent modifica-

Table 5. Reactivity umpolung by homologative methods [23]. Reagents (or conversions) corresponding to the d^1-synthons 

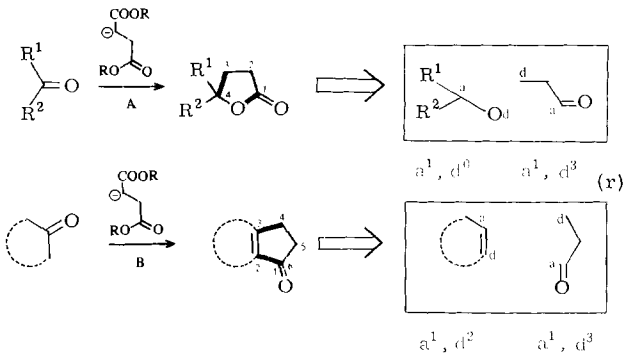
Reagent (or conversion)	Ref.	Reagent (or conversion)	Ref.
 + electrophiles			
X = OCH(CH3)OC2H5	[80, 81]	R^2 = metal or alkyl, X = SR	[98]
O-tetrahydropyranyl	[89]	N=CR	[84, 99]
$OSi(CH_3)_3$	[90]	H(→OOH, see above)	[100]
$OCOC_6H_5$	[91]	COOH	[101]
OCOOR'	[92]	Cl (Darzens reaction)	[2]
$SCSN(CH_3)_2$	[93]		
$NR'COC_6H_5$ (Reissert compounds)	[95]		
NR'_2			
	[96]		[102]
 (cf. Darzens reaction [2])	[97]		[103]



(35)

(q)

tions[87]; see also Section 3.4). As indicated in equation (r), the enolate derived from succinic ester corresponds to a d^3-synthon; the cyclopentenone annelation (route B) is part of a three carbon ring expansion method[88]. Some further

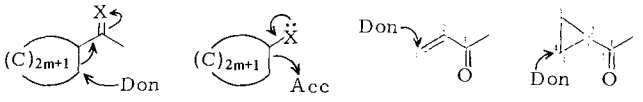


(r)

classical[2] reactions which can be used in homologative reactivity umpolung as defined here are the degradation methods according to *Baeyer-Villiger*, *Beckmann*, *Hofmann-Curtius-Lossen-Schmitt*, *Hunsdiecker* (all RCOR′ or RCOOH→ROH, RNH_2), and *Barbier-Wieland* ($R_2CHCOOH \rightarrow R_2CO$) in which carbon functions as a leaving group and is replaced by a heteroatom (N or O).

3.4. Use of Cyclopropanes

Opening of a cycloalkane with an odd number of carbon atoms and with substituents as indicated in *(36a)* and *(36b)* by donors and acceptors, respectively, constitutes yet another



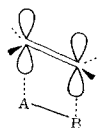
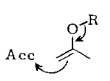
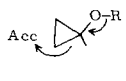
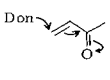
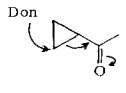
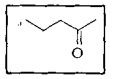
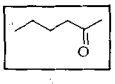
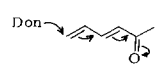
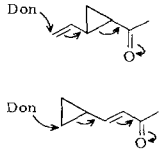
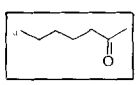
a^{2n}-reactivity d^{2n+1}-reactivity

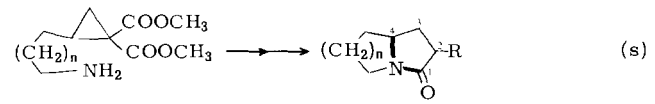
(36a) *(36b)* *(37a)* *(37b)*

principal method of reactivity umpolung. It is related to the homologative method of the previous section by also rendering normal reactivity *(1)* [counting the short distance between the attacked and the functionalized carbon in *(36)*] identical with reactivity umpolung *(10)* [counting around the ring of *(36)*]; the resemblance becomes even closer if we consider that this kind of process is most likely to occur with cyclopropanes (110 kJ/mol strain release), the next higher homologues of "cycloethanes" [see *(37a)* and *(37b)*, and Table 6]. Most of the processes of this scheme were discovered some ten or more years ago[104] (d^3[105a], a^4[105b], a^6[105c]), but only recently have they been exploited systematically for this purpose; improved methodology of cyclopropanation[104,106] was a prerequisite. A fair coverage of the field is not possible in the present article[107]; only a few illustrative examples will be mentioned.

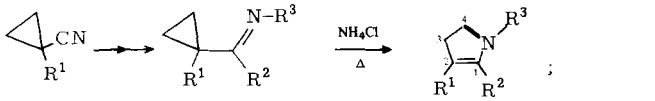
In the field of heterocyclic chemistry and natural product synthesis, the construction of pyrrolines, pyrrolidines, tetrahydrofurans, γ-lactones and γ-lactams is a problem of reactivity umpolung because in all of these five-membered rings, the chain of carbon atoms is 1,4-bifunctionalized. It is therefore not surprising that cyclopropanes have been widely applied in this area. One example each from *Danishefski*'s[108], *Stevens*'[109] and *Wenkert*'s[110] approaches is given in equa-

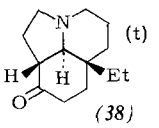
Table 6. Umpolung of carbonyl reactivity with cyclopropanes.

Synthon	Olefin or "cycloethane"	"Homoolefin" or cyclopropane	Synthon
			
			
			
			

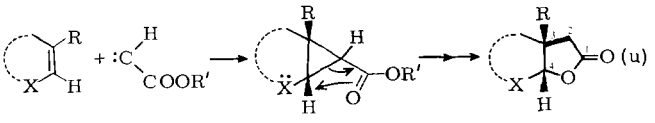


(s)

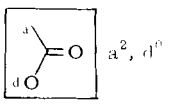




(t)

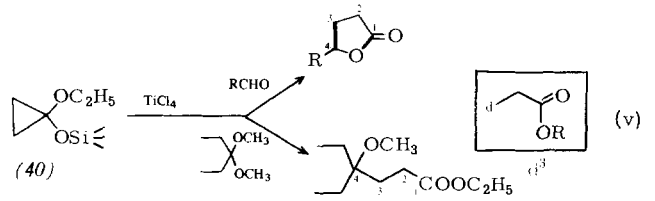


(39)



tions (s)—(u). In reactions of the type (s)[111] the three-membered ring is opened stereoselectively with inversion; they have been termed homoconjugative additions[108]. The general route outlined in equation (t) was followed in a synthesis of aspidospermine *via (38)*[112]; equation (u) outlines the key step of an eburnamonine synthesis[110,113]. Formally, the 1,4-relationships N—C_4—N and O—C_4—O have been established by an a^4-reaction with a nitrogen or oxygen atom donor in all three cases. The ring enlargements in equations (t) and (u) could also be classified as hetero analogues of the pericyclic vinylcyclopropane → cyclopentene rearrangement. The carbene used in equation (u) [cf. *(18a)*] corresponds to the a^2-synthon drawn underneath it; in *(39)* a pushing (or donor) effect of Ẋ is probably also involved [cf. *(36a) and (36b)*].

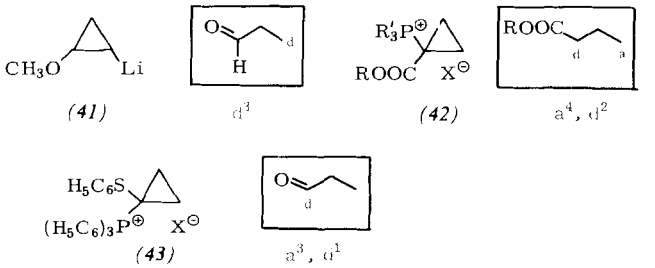
Stobbe-type conversions are possible with the cyclopropanone acetal *(40)*[114] [eq. (v)], a^0-reactivity was observed



(v)



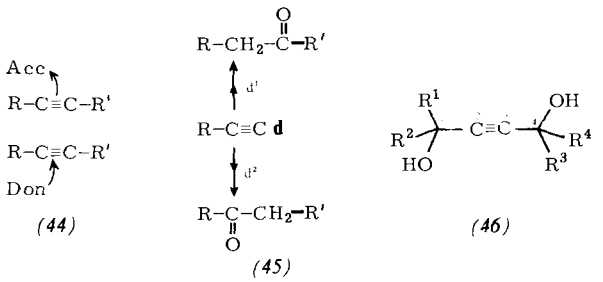
(w)



with the methyl(vinylcyclopropyl) ketone shown in equation (w)[115], methoxycyclopropyllithium *(41)* is a propionaldehyde d^3-reagent[116], and the phosphonium salts *(42)*[117] and *(43)*[118] are used in cyclopentane annelations to 1,3-dicarbonyl derivatives [cf. the synthons with *(18b)*; see also Section 5, *(77)—(82)*, eq. (av) and Table 9].

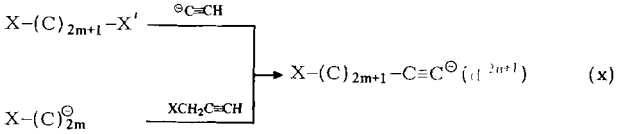
3.5. Acetylenes

Acetylenes are extremely versatile synthetic intermediates[119]. The highly reactive, "strained" triple bond can be attacked by electrophiles or nucleophiles [see *(44)*, and compare *(18a)*], terminal acetylenes are rather strong CH-acids, and the acetylides obtained by deprotonation are very good, non-hindered nucleophiles [*(45)*] (compare *(18a)*, acyl



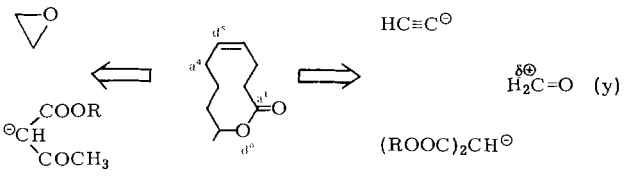
d¹-reagents]. Acetylene itself is therefore a welcome moiety for the synthesis of 1,2*n*-bifunctional systems *(46)* [see *(17a)*]. An advantageous stereochemical aspect is that disubstituted alkynes can be selectively hydrogenated to (*E*) *or* (*Z*)-olefins.

If acetylene is attached to a molecule of normal reactivity (*1*), a carbon framework with reactivity umpolung (*10*) results [eq. (x)]. This principle is used if propiolic acid or propargyl



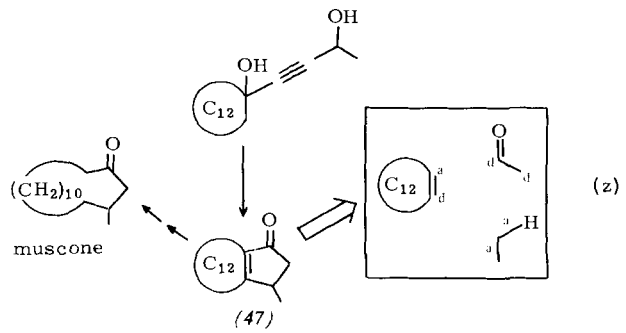
(x)

derivatives (aldehyde, alcohol, bromide) (d^3) or 4-pentynoic acids (d^5) are employed[120]. If one traces back the components of the synthesis of phoracantholide, one finds that the ultimate



(y)

reagents with reactivity umpolung are oxirane (see Section 3.1) and acetylene [see eq. (y)][121]. A recent muscone synthesis

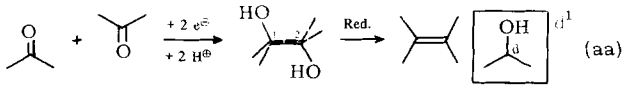


(z)

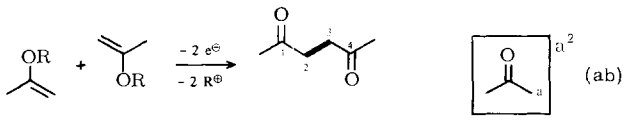
via (47) uses cyclododecanone, acetaldehyde and acetylene as components[122]; these are first joined to a 1,4-diol which is cyclized by sequential Rupe-Meyer-Schuster and Nazarov reactions[2]. Acetylene corresponds to a d^1,d^2-synthon [cf. eq. (z)].

3.6. Redox Reactions

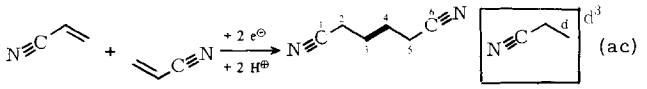
Conceptually, the most simple method of reactivity umpolung is the addition or removal of electrons in a system which is electrophilic or nucleophilic, respectively. This will of course reverse the reactivity of the species (cf. also the formation of a Grignard reagent in Table 4, entry 3). Thus, we can reduce ketones and aldehydes to pinacols [eq. (aa)] and esters to acyloins[123] by electrochemical[124] or photochemical[125] methods or with metals[126]; further reduction leads to olefins which can now be obtained directly from ketones with low-



(aa)

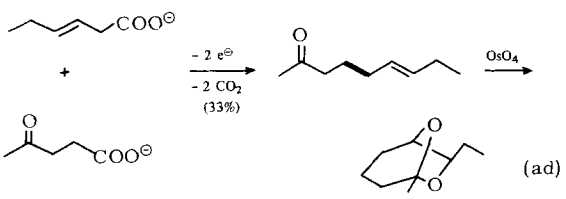


(ab)



(ac)

alkali metal, is readily accomplished[126], while we do not normally cleave pinacols and olefins by such simple methods. The products mentioned—except for the olefin—are 1,2*n*-bifunctional and have been made by joining carbon atoms of the same polarity (cf. queries 1 and 3 in Section 2). We formally obtain these products, if we assume that half of the starting molecules are converted into reagents with reactivity umpolung [see the $d^{1,3}$- and a^2-synthons in eqs (aa)—(ac)] and then couple with the other half of normal reactivity. In reality, of course, radical anion or cation coupling (r-reactivity[1c]) furnishes the products in most cases. Therefore, it is difficult to prepare cross-coupling products in better than statistical amounts, unless we carry out intramolecular reactions[137]. Some exceptions to this statement are listed in Table 7; a confirmation is the still very short and efficient synthesis of the pheromone brevicomin[139,140] [equation (ad) (Kolbe carboxylate electrolysis[2])].

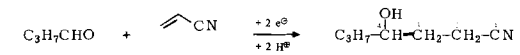
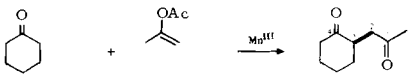
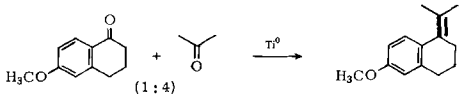
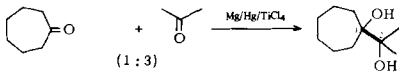
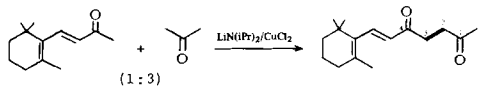


(ad)

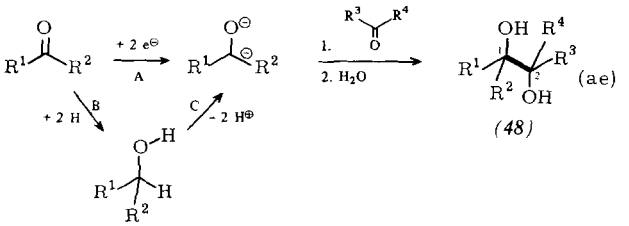
exo-brevicomin

A way out of the problem of "self condensation" or scrambling, when *selective* cross coupling is desired, is being systematically investigated by our group[4f,65,142-148]. The principle

Table 7. Examples for cross-coupling of carbonyl derivatives to olefins, pinacols, and 1,4-dicarbonyl compounds.

Coupling reaction	Yield [%]	Ref.
		[141]
	20—35	[135]
 (1 : 4)	85	[138]
 (1 : 3)	75	[130]
 (1 : 3)	65	[134]

valent titanium[127-131]. Likewise, electrochemical or metal oxidation of enol ethers[132] or enolates[133-135], respectively, furnishes 1,4-dicarbonyl derivatives [eq. (ab)]; electrochemical processes of this type have been called cathodic umpolung[136]. A coupling reaction of industrial importance is the anodic dimerization of acrylonitrile to adiponitrile [eq. (ac)]. The converse of equation (ab), the cleavage of a 1,4-diketone with is described in the accompanying equation (ae). Instead of adding two electrons (A), the π-system is reduced (B) and the resulting dihydro compound is doubly deprotonated (C). The overall result is the same, and no intermediates are involved which could couple with each other. The derivative of the doubly reduced ("LUMO-filled") π-system thus obtained can be added to a different partner to give a "crosslinked

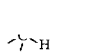
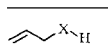
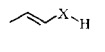
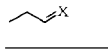
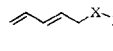
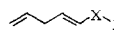
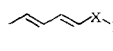
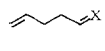
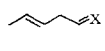
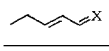
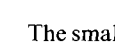


(ae)

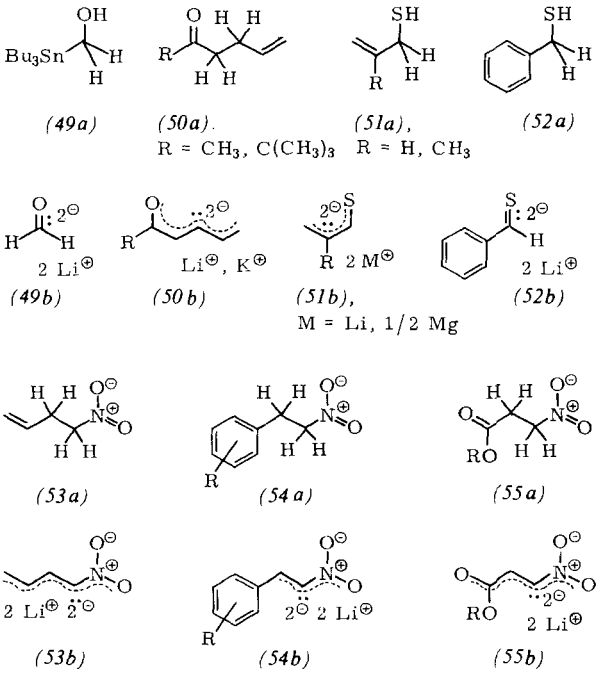
(48)

dimer", for instance *(48)*. Only a one electron transfer during this latter step could prevent a clean cross-coupling and would lead to scrambling. In the conversion *via* route A, the formerly electrophilic carbonyl carbon has become nucleophilic, an umpolung ("polar reversal", "charge reversal") in the literal sense of the word [see also *(18a)*]. With more extended π-systems, there are several possible hydrogenated precursors to the desired dianion (see Table 8).

Table 8. Doubly reduced π-systems from hydrogenated precursors [see eq. (ae)].

Precursors	"LUMO-filled" π-system	
		2 atoms 4 electrons
		
		4 atoms 6 electrons
		
		
		
		
		6 atoms 8 electrons
		
		
		

The smallest system, the formaldehyde dianion *(49b)* could not be generated by double deprotonation of methanol; only tin/lithium exchange in *(49a)* was successful[65] (see also Table 4, entry 4). The other dianion derivatives *(50b)*—*(55b)* are accessible from the "hydrogenated" precursors *(50a)*—*(55a)* and strong base. They preferentially react in the ω-positions with electrophiles. Reagents *(50b)* correspond to d^5-synthons[144b,148]; the lithium compound *(51b)* is attacked at $C^3(d^3)$ by all types of electrophiles[4f,13,142,144], while the magnesium derivative adds to carbonyl compounds with >95 % α-selectivity (d^1); *(52b)* also reacts at the α-S-carbon. The doubly deprotonated nitroalkanes[41] are nitroolefins with reactivity umpolung: while 1-nitro-butadiene is known to accept donors at C^2 or C^4, its dianion *(53b)* (deep-red solution in THF/HMPT, stable at room temperature for a few hours) couples with acceptors (mainly **d^4**-reaction). Similarly, *(54b)* and *(55b)* react with alkyl halides, ketones, and aldehydes at the β-NO_2-position exclusively. It is interesting to note that the nitroolefin dianions *(53b)*—*(55b)* constitute reagents



(49a) *(50a)* *(51a)*, *(52a)*

R = CH_3, $C(CH_3)_3$ R = H, CH_3

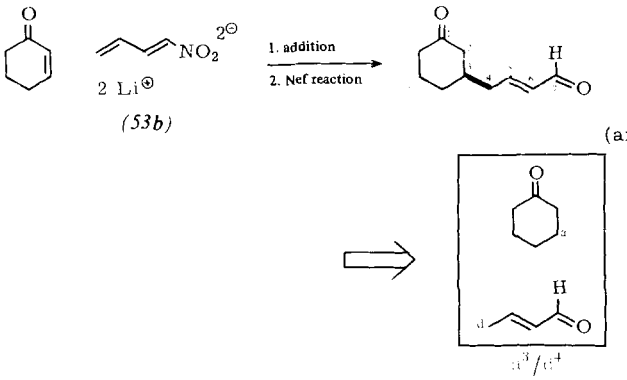
(49b) *(50b)* *(51b)*, *(52b)*

M = Li, 1/2 Mg

(53a) *(54a)* *(55a)*

(53b) *(54b)* *(55b)*

with a double reactivity umpolung if they are used to prepare normal O, N-derivatives (see postulates 1.2—1.4): one is achieved by heteroatom exchange or modification, the other one by the redox method [see eq. (af), cf. eq. (i) and Section 5]. Some amine derivatives with umpolung achieved by going to the doubly reduced state can only be referred to here[149].



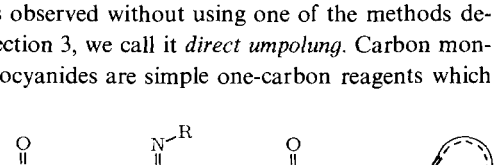
(53b)

(af)

4. Direct Umpolung and Substrate Umpolung

4.1. Direct Umpolung

There are of course exceptions to postulate 1.3. If reactivity umpolung is observed without using one of the methods described in Section 3, we call it *direct umpolung*. Carbon monoxide and isocyanides are simple one-carbon reagents which



a d **a d**

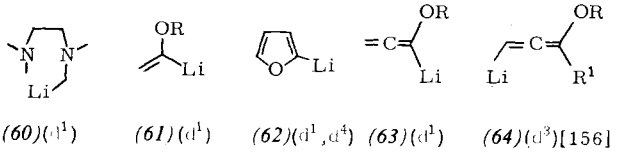
(56) *(57)* *(58)* *(59)*

can be attacked by a donor *and* an acceptor [see *(56)* and *(57)* and compare *(18a)*]. Thus, if carbon monoxide, an olefin and water combine to give a carboxylic acid under strongly

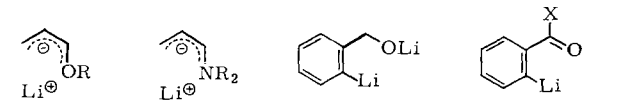
acidic conditions[10b], the CO-carbon atom formally combines with a carbenium ion (**a**/d^1) and $OH^{\ominus}$ (a^1/**d**). Isonitriles are used in the Passerini- and Ugi-reactions (see refs. in [4c]) to prepare α-hydroxy- and α-aminocarboxylic acid derivatives, respectively; given proper substitution in R of *(57)*, Grignard- and lithium-reagents can be added to the carbon atom (a^1) to give an iminoacyl anion derivative; subsequent reaction (d^1) with an electrophile and hydrolysis furnish aldehydes and ketones (Walborsky's method[150]). In the formose reaction[151], formaldehyde *(58)* oligomerizes to give carbohydrates when treated with alkali.

We realize that it is arbitrary to say that CO and CNR are reagents with direct umpolung while we put other, similar compounds [*(27)*—*(31)*, entries 9 and 11—13 of Table 4] into the section on reactivity umpolung by way of heteroatom modification; in *(56)* and *(57)*, not only the carbons but also O and N are in special bonding situations. This is also true of highly conjugated systems such as *(59)*[152]; C^{15} may "not care" whether it is attacked by a nucleophile or an electrophile.

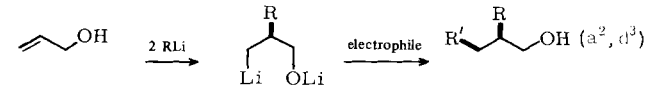
Some unambiguous cases of direct umpolung are the generation of *(60)*—*(68)* directly from the CH-precursors and strong bases, without any of the manipulations described in Section 3. *(60)* is formed by metalation of TMEDA[153] and, like the other α-*O*- and α-*N*-lithium derivatives *(61)*, *(63)*, *(65)* and *(66)*[157], is surprisingly resistant towards Wittig-type rearrangements[154]; *(61)*—*(63)* are also obtained by depro-



(60)(d^1) *(61)*(d^1) *(62)*(d^1,d^4) *(63)*(d^1) *(64)*(d^3)[156]



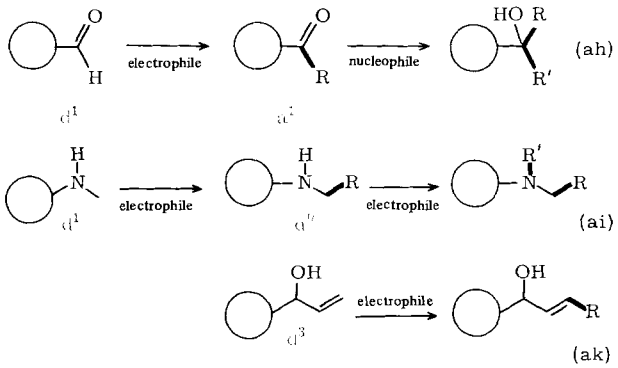
(65)(d^1 or d^3) *(66)*(d^3) *(67)*(d^3) *(68)*(d^3)



tonation[155]; the heterosubstituted allyllithium compounds *(65)* and *(66)* have been discussed in a recent review article[157]. The *ortho*-Li-derivative of benzyl alcohol and a variety of substituted analogues including α-tetralol[158] as well as *(68)*[159] are only two examples of a large number of similar reagents which are formed by direct *ortho*-metalation[160]. Equation (ag) shows a conversion in which allyl alcohol undergoes sequential a^2- and d^3-reactions[161].—It is important to note that in these cases the lithium is bonded to vinylic, arylic (both sp^2), or allylic carbon moieties and/or is internally complexed (chelation).

4.2. Substrate umpolung

By definition, umpolung must be reversible: the final goal is to make O, N-derivatives of normal reactivity. A reversible umpolung is a sequence of operations by which the reactivity of a functional group can be temporarily reversed, and this is not possible with all the methods mentioned in the previous sections. Should we arrive at a certain stage of a synthesis where we need to perform the conversions (ah)—(ak), this would be a task much more difficult than constructing a "small" reagent molecule with reactivity umpolung. We are here concerned with a more complex molecule whose functional groups must be compatible with all operations necessary to achieve the umpolung. Therefore, this may be called a *substrate umpolung*. Of the methods in Section 3 which fulfill this condition, we have to choose the mildest; the ones which require more stringent conditions will be applicable only for reagent umpolung or in the early stages of a synthesis when there is less complexity.

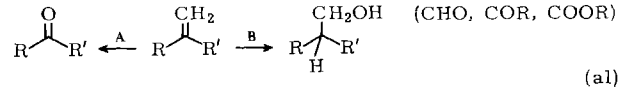


The reversible homologations through cyanohydrins [eq. (n)] and thiazolium derivatives [eq. (o)], and the heteroatom exchange method through thioacetal derivatives[4h] would appear the most promising for the realization of process (ah). The nitrosamine method[4d] [see *(29)*] might be applicable for (ai), and the allyl sulfoxide route[70] (entry 6 in Table 4) for (ak).

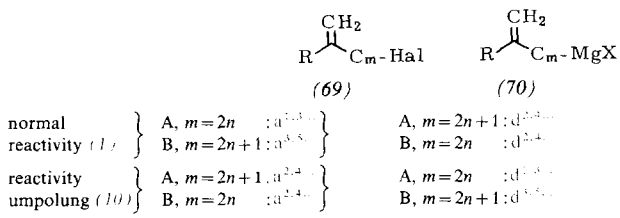
5. Analysis of Some Synthetic Methods

There are many possible combinations of the methods described in Sections 3 and 4.1 by which reactivity umpolung can be achieved. An interesting exercise is the analysis of the numerous ways of preparing 1,4-dicarbonyl compounds *(12)*. This has been a very active field because of the importance of jasmonoid, rethrolonoid, and prostanoid synthesis. Extensive review articles on this subject have appeared[113,162]. In the following discussion some reactions will be analyzed which use the six principal methods given in Section 3 in a more or less 'disguised' way.

One such case is the *use of ω-functionalized terminal olefins* (see *Lednicer*'s article on latent functionality in ref. [5])[163]. This method is based on the oxidative cleavage to a carbonyl



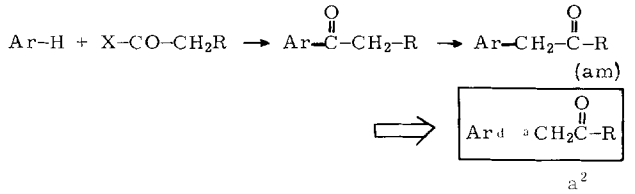
(al)



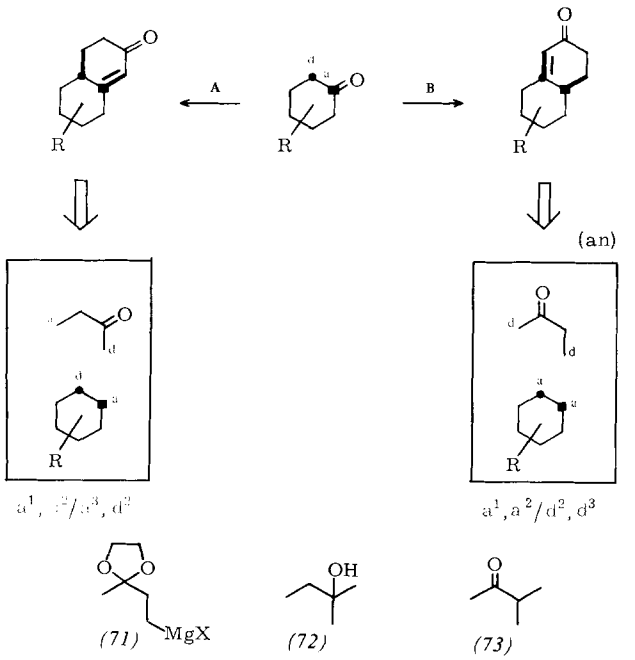
(69) *(70)*

compound, [eq. (al), route A], the anti-Markownikoff hydration [eq. (al), route B] or related reactions of olefinic double bonds, which make the halides *(69)* and the corresponding organometallic compounds *(70)* reagents of normal or reversed reactivity at will. If one also takes the preparation of the halides *(69)* into consideration, one realizes that a combination of heteroatom exchange (Section 3.2), homologation and its reversal (Section 3.3) and 1,2*n*-oxidation (Section 3.1) is at work. The same is true of reagents which contain RO-groups instead of the double bond[164].

Another very useful approach is to combine normal reactivity *(1)* with a *1,2n-functionality transposition*[165] [a 1,(2*n*+1)-transposition will only shift reactivity *within* *(1)* or *(10)*, see below]. A simple example is outlined in equation (am): The 1,2-carbonyl transposition converts the product of the Friedel-Crafts acylation (a^1/d-) into the product of an a^2/d-combination (acylmethylation). All transpositions of this type

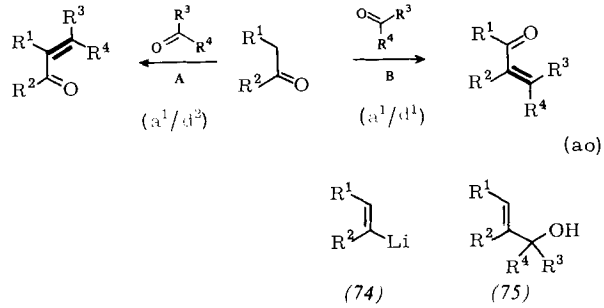


are 1,2*n*-oxidation-reduction processes (see Section 3.1). They either convert the C^1 carbon atom of *(1)* into a donor carbon or they transform d^0 or d^2- into a^0 or a^2-reactivity, respectively (see also Table 3). Two examples are given in equation (an), route B[166], and equation (ao), route B[167a], a "weird" Robinson-annelation [normal: eq. (an), route A][168] and aldol-condensation [normal: eq. (ao) route A][169], respectively. The first sequence of reactions necessitates twofold umpolung. The first one is achieved by heteroatom exchange to *(71)* (Section 3.2), the second one by a 1,2-functionality transposition *(72)* → *(73)* (carried out by dehydration, anti-Markownikoff

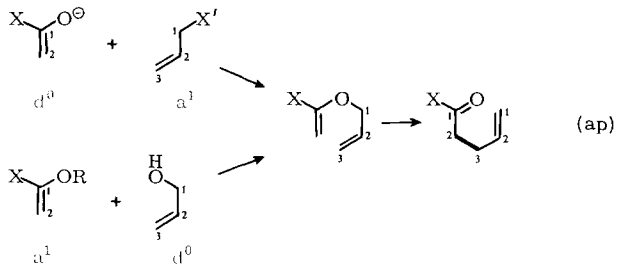


hydration, and oxidation) with an a^0-reagent (BH_3/H_2O_2 corresponds to the HO-a^0 synthon and the H-**d** synthon).

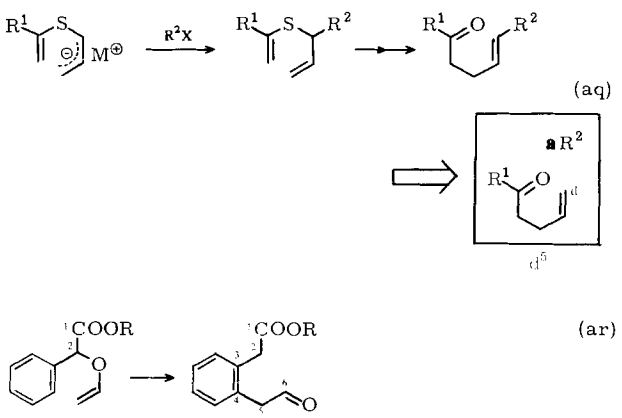
The enone synthesis in equation (ao) uses a reactivity umpolung of the carbonyl carbon [→*(74)*][45,72,167b] with heteroatom exchange methods (Section 3.2) and then a 1,3-transposition of oxygen functionality in *(75)*.



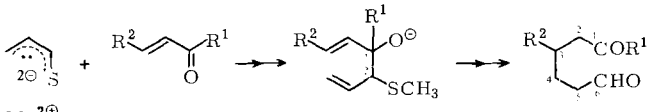
Bond shifts with C—C-formation are another important group of synthetic transformations. A [3,3]-shift does not change the relationship (*i.e.* the number of carbon atoms) between functional groups (whether odd or even). The classical Claisen rearrangement[2,170] converts an a^1/d^0- into an a^3/d^2-product [see eq. (ap)]. If a precursor is synthesized with reactivity umpolung [eq. (aq)][171] or from a compound which contains an even number of carbon atoms between the func-



tional groups [eq. (ar)[172]], the "even relationship" is preserved in the rearrangement product. The first transformation is realized by the heteroatom exchange method and

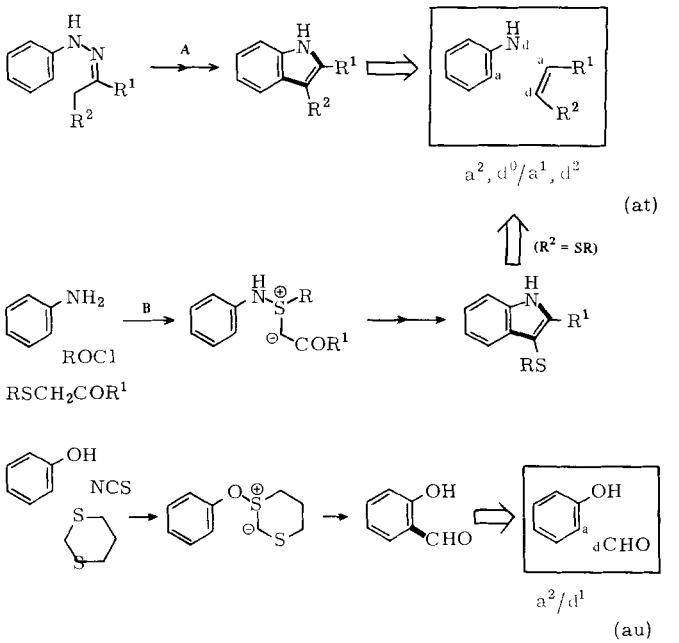


a [3,3]-shift which converts the product of a d^1-reaction into that of a d^5-reaction. On the other hand, in equation (ar) one starts with a 1,2-product (see Section 3, "black magic-box" and 1,2*n*-oxidations), a mandelic acid derivative, and furnishes a 1,6-bifunctionalized compound. This is also true of the oxide-Cope rearrangement[2,173] described in equation (as)[4f,142,144]; the reactivity umpolung proceeds *via* heteroatom exchange (Section 3.2).



(as)

If a molecule contains X—X'-hetero-hetero bonds [R—O—O—R, R—O—NR_2, R—N=O, R_2C=N(O)R, RO—N=CR_2, R_2N—NR_2, R_2C=N—NR_2, RN=NR, ... or heteroatom exchange analogues], it has a built-in 1,2-oxidation (see Section 3.1 and Table 3), and thus a reactivity umpolung. Therefore, we can consider *Fischer*'s indole synthesis[2] and *Gassman*'s recent modification[174] as a^2/d^2-combinations leading to a 1,4-disubstituted carbon framework [see eq. (at), routes A and B]. The Reimer-Tiemann-type[2] reaction in equation (au)[175] is obviously an a^2/d^1-combination; both components have reactivity *(10)*, and we must necessarily obtain a

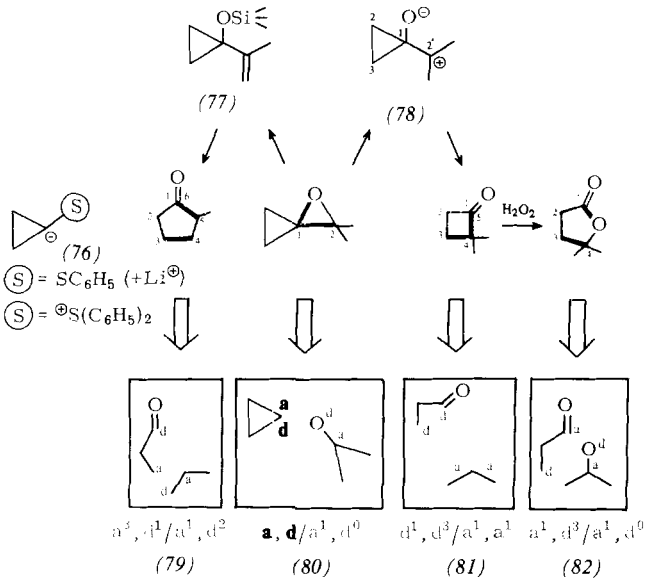


(at)

(au)

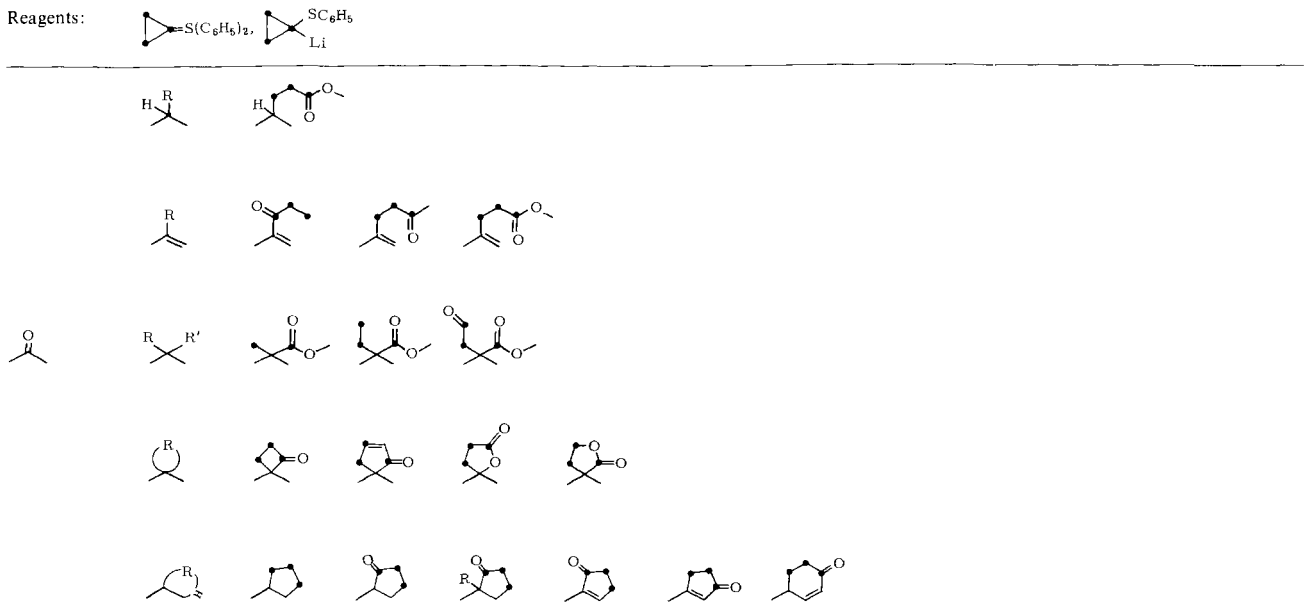
1,(2*n*+1)-bifunctional system—as in the reactivity pattern *(1)* (cf. postulate 1.4).

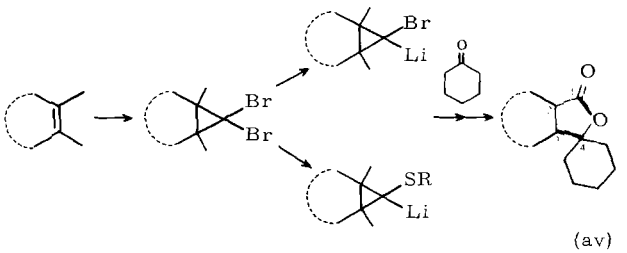
As is evident from Table 9, *Trost*'s cyclopropylidene sulfurane and phenylthiocyclopropyllithium *(76)*[176] are true synthetic chameleons; one can easily count ten different synthon combinations if one compares the products with the starting carbonyl compounds; all of them make at least one bond with reactivity umpolung [see *e.g. (79)—(82)*]. This plethora



of possibilities is obtained by a combination of: 1) heteroatom exchange [Section 3.2, see oxaspiropentane formation *(80)*], 2) the cyclopropane trick [Section 3.4, see *(77)* and *(78)* ($a^{2'}/d^3$)] and 3) the 1,2*n*-oxidation [Section 3.1, see *(82)*]. One limitation of the method, the general lack of availability of substituted reagents *(76)*, can be overcome[39b,177] by starting from dibromo cyclopropanes as outlined in equation (av); they are easily converted into Br/Li-carbenoids or RS-substi-

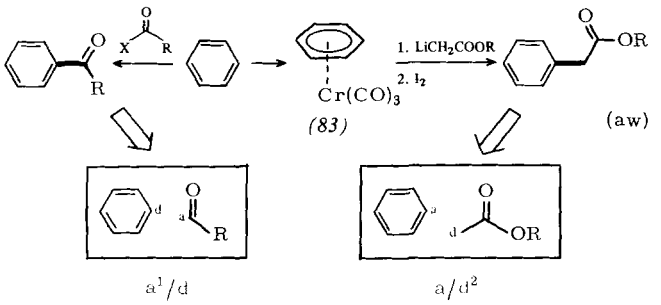
Table 9. Conversions of aldehydes and ketones with sulfur-substituted cyclopropyl nucleophiles of type *(76)*.





(av)

tuted·cyclopropyllithium derivatives, which may be up to tetrasubstituted, and which can be used just as the unsubstituted reagent *(76)*. In the overall reaction, the final product in *(46)* is made from cyclohexene, cyclohexanone, and bromoform, which illustrates that this approach constitutes a synthetic elaboration of the ketone *and* of the olefin [39b, 177]. The use of the Trost method for the preparation of 1,6- and 1,8-bifunctionalized carbon skeletons can only be alluded to here[178].



(aw)

As last example of a recent, useful development in the field of aromatic substitution with reactivity umpolung, *Semmelhack*'s method[179] is mentioned: formation of the benzene-(tricarbonyl)chromium complex *(83)* renders the benzene ring amenable to attack by nucleophiles; instead of the Friedel-Crafts products[2], aryl ketones, α-arylated carbonyl derivatives are formed [see eq. (aw), cf. eq. (am)]. The chromium metal atom decreases the electron density of the benzene ring (lowers the LUMO energy) sufficiently for nucleophilic attack to take place. At least formally, we may say that this is an umpolung by the redox method (Section 3.6).

6. Conclusion

The present article has tried to classify the methods by which reactivity umpolung can be achieved. Hopefully, it will help organic chemists to recognize the necessity of umpolung when planning a synthesis, to see new methods appearing in the literature in a systematic way, and to choose or even discover the best possible reagents for their synthetic problems. Reactivity umpolung is an essential part of synthetic strategy which is now also applied with the aid of computers[180]. It is still a controversial subject among synthetic chemists[181], but highly esteemed in many pharmaceutical and pesticidal industrial laboratories. A most important aspect of organic synthesis, stereochemistry, was naturally excluded from the present discussion, and it is appropriate to stress its importance by quoting: "Stereochemistry rears its ugly head" and "Multistage synthesis: logistics and stereochemistry combine to produce nightmares"[182].

I thank Miss R. Pfister, and Dipl.-Chem. E. Hungerbühler, M. Liesner, and Dr. N. Meyer for their most competent help in preparing the manuscript. Many valuable discussions with a number of colleagues, especially with Professor A. Eschenmoser are gratefully acknowledged. Our own work referred to in this article would not have been possible without the enthusiastic collaboration of my graduate students whose names are given in the list of references. We were generously supported financially by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the BASF AG (Ludwigshafen) and SANDOZ AG (Basel).

Received: November 2, 1978 [A 264 IE]
German version: Angew. Chem. *91*, 259 (1979)

[1] a) See textbooks of organic chemistry. b) Cf. *V. Gutmann*, The Donor-Acceptor Approach to Molecular Interactions, Plenum Press, New York 1978; c) For radical reactivity, the sign would be r [for the term radicophilic see *L. Stella, Z. Janousek, R. Merényi, H. G. Viehe*, Angew. Chem. *90*, 741 (1978); Angew. Chem. Int. Ed. Engl. *17*, 691 (1978)].

[2] *H. Krauch, W. Kunz:* Reaktionen der organischen Chemie. Hüthig, Heidelberg 1976; see also *J. E. Gowan, T. S. Wheeler*, Name Index of Organic Reactions, Longmans, London 1960.

[3] a) *E. J. Corey*, Pure Appl. Chem. *14*, 19 (1967); b) Previously, we have used the terms N^n- and E^n-synthon [4], indicating the affinity of the attacking moiety, and + and − signs denoting the electrophilicity and nucleophilicity, respectively, of the reagent related to a certain synthon. Although derived from a practical point of view, this terminology turned out to be subject to confusions; c) We do not use "synthetic equivalent" as a noun; "synthetic equivalents of acetaldehyde enolate" are simply acetaldehyde d^2-reagents.

[4] Reviews: a) *D. Seebach*, Angew. Chem. *81*, 690 (1969); Angew. Chem. Int. Ed. Engl. *8*, 639 (1969); b) *D. Seebach*, Synthesis *1*, 17 (1969); c) *D. Seebach, M. Kolb*, Chem. Ind. (London) *1974*, 687; d) *D. Seebach, D. Enders*, Angew. Chem. *87*, 1 (1975); Angew. Chem. Int. Ed. Engl. *14*, 15 (1975); e) Journal of Organometallic Chemistry Library. Elsevier, Amsterdam; f) *D. Seebach, K.-H. Geiss* in [4e], Vol. 1, 1976, p. 1; g) *D. Seebach, K.-H. Geiss, M. Kolb, A. K. Beck:* Modern Synthetic Methods 1976, Schweiz. Chemiker-Verband Zürich 1976, p. 173ff.; h) *B. Gröbel, D. Seebach*, Synthesis *1977*, 357; i) *D. Seebach, M. Kolb*, Justus Liebigs Ann. Chem. *1977*, 811; k) *D. Seebach, R. Bürstinghaus, B. T. Gröbel, M. Kolb, ibid.* *1977*, 830; l) *D. Seebach, E. W. Colvin, F. Lehr, Th. Weller*, Chimia, *33*, 1 (1979).

[5] We don't use the terms "latent" [*D. Lednicer*, Adv. Org. Chem. *8*, 179 (1972); *O. W. Lever, jr.*, Tetrahedron *32*, 1943 (1976); *L. Call*, Chem. Unserer Zeit *12*, 123 (1978)], "symmetrization of reactivity" [3a], "charge affinity inversion operation, consonant and dissonant relationships" [*D. A. Evans, G. C. Andrews*, Acc. Chem. Res. *7*, 147 (1974) and private communication], "control elements" [*St. Turner:* The Design of Organic Syntheses. Elsevier, Amsterdam 1976] and "illogical disconnections" [*St. Warren:* Designing Organic Syntheses, Wiley, Chichester 1978].

[6] Reviews: a) *T. Mukaiyama*, Angew. Chem. *89*, 858 (1977); Angew. Chem. Int. Ed. Engl. *16*, 817 (1977); b) *J. K. Rasmussen*, Synthesis *1977*, 91; c) *E. W. Colvin*, Chem. Soc. Rev. *7*, 15 (1978).

[7] *G. Büchi, H. Wüest*, J. Org. Chem. *34*, 1122 (1969); *H. J. J. Loozen, E. F. Godefroi, J. S. M. M. Besters, ibid.* *40*, 892 (1975); *A. A. Ponaras*, Tetrahedron Lett. *1976*, 3105.

[8] a) *Houben-Weyl-Müller:* Methoden der organischen Chemie. 4th Edit. Thieme, Stuttgart; b) *K. Nützel* in [8a], Vol. XIII/2a, 1973, p. 264.

[9] *I. Degani, R. Fochi*, J. Chem. Soc. Perkin Trans. *1* 1886 (1976).

[10] *J. Mathieu, J. Weill-Raynal:* Formation of C—C Bonds. Vol. I. Thieme, Stuttgart 1973, a) p. 168, b) p. 303.

[11] *R. H. Wollenberg, K. F. Albizati, R. Peries*, J. Am. Chem. Soc. *99*, 7365 (1977); *A. Alexakis, G. Cahiez, J. F. Normant, J. Villieras*, Bull. Soc. Chim. Fr. *1977*, 693; *K. S. Y. Lau, M. Schlosser*, J. Org. Chem. *43*, 1595 (1978); for the vinologous case (d^4) see: *R. H. Wollenberg*, Tetrahedron Lett. *1978*, 717.

[12] a) *A. I. Meyers:* Heterocycles in Organic Synthesis, Wiley-Interscience, New York 1974; b) Review: *K. Hirai, Y. Kishida*, Heterocycles 2, 185 (1974); c) Review: *J. ApSimon, A. Holmes, ibid.* 6, 731 (1977).

[13] *K.-H. Geiss, D. Seebach, B. Seuring*, Chem. Ber. *110*, 1833 (1977).

[14] *D. Vorländer*, Ber. Dtsch. Chem. Ges. *52*, 263 (1919); *A. Lapworth*, J. Chem. Soc. *121*, 416 (1922); *W. O. Kermack, R. Robinson, ibid.* *121*, 427 (1922); cf. the calculations by *J. A. Pople, M. Gordon*, J. Am. Chem. Soc. *89*, 4253 (1967); cf. also *S. W. Benson*, Angew. Chem. *90*, 868 (1978); Angew. Chem. Int. Ed. Engl. *17*, 812 (1978), and references cited therein.

[15] *E. Hückel:* Theoretische Grundlagen der organischen Chemie. 8th Edit., Vol. 2. Geest und Portig, Leipzig 1957.

[16] *H. Staudinger*, Ber. Dtsch. Chem. Ges. *41*, 2217 (1908).

[17] *P. Chaquin, J. P. Morizur, J. Kossanyi*, J. Am. Chem. Soc. *99*, 903 (1977).

[18] *D. Seebach* in [8a], Vol. IV/4, 1971, p. 1ff.

[19] *L. J. Dolby, Sh. Esfandiari, C. A. Elliger, K. S. Marshall*, J. Org. Chem. *36*, 1277 (1971).

[20] *P. A. Bartlett, F. R. Green*, J. Am. Chem. Soc. *100*, 4858 (1978).

[21] *D. Seebach, H.-O. Kalinowski*, Nachr. Chem. Tech. *24*, 415 (1976).

[22] *D. Seebach, B. Seuring, H.-O. Kalinowski, W. Lubosch, B. Renger*, Angew. Chem. *89*, 270 (1977); Angew. Chem. Int. Ed. Engl. *16*, 264 (1977); *B. Seuring, D. Seebach*, Helv. Chim. Acta *60*, 1175 (1977); Justus Liebigs Ann. Chem. *1978*, 2044.

[23] This is by no means a complete list but a rather deliberate selection of examples.

[24] *S. Tanaka, H. Yamamoto, H. Nozaki, K. B. Sharpless, R. C. Michaelson, S. D. Cuttnig*, J. Am. Chem. Soc. *96*, 5254 (1974).

[25] *V. Van Rheenen, R. C. Kelly, D. Y. Cha*, Tetrahedron Lett. *1976*, 1973; *V. Van Rheenen, D. Y. Cha, W. M. Hartley*, Org. Synth. *58*, in press.

[26] *D. W. Patrick, L. K. Truesdale, S. A. Biller, K. B. Sharpless*, J. Org. Chem. *43*, 2628 (1978).

[27] Review: *W. Adam*, Adv. Heterocycl. Chem. *21*, 438 (1977).

[28] *H. H. Wasserman, B. H. Lipshutz*, Tetrahedron Lett. *1975*, 1731.

[29] *E. Vedejs, D. A. Engler, J. E. Telschow*, J. Org. Chem. *43*, 188 (1978).

[30] *H. H. Wasserman, J. L. Ives*, J. Am. Chem. Soc. *98*, 7868 (1976).

[31] *R. Pütter* in [8a], Vol. X/3, 1965.

[32] *H. Metzger* in [8a], Vol. X/4, 1968.

[33] *G. Stork, E. W. Colvin*, J. Am. Chem. Soc. *93*, 2080 (1971); *G. M. Rubottom, J. M. Gruber*, J. Org. Chem. *43*, 1599 (1978).

[34] *E. Friedrich, W. Lutz*, Angew. Chem. *89*, 426 (1977); Angew. Chem. Int. Ed. Engl. *16*, 413 (1977).

[35] *J. Klein, R. Levene, E. Dunkelblum*, Tetrahedron Lett. *1972*, 2845; *G. L. Larson, D. Hernandez, A. Hernandez*, J. Organomet. Chem. *76*, 9 (1974); *G. L. Larson, E. Hernandez, C. Alonso, I. Nievers*, Tetrahedron Lett. *1975*, 4005.

[36] Cf. nitrene cyclization; reviews: *J. J. G. Cadogan, R. K. Mackie*, Chem. Soc. Rev. *3*, 87 (1974); *V. P. Semenov, A. N. Studenikov, A. A. Potekhin*, Khim. Geterotsikl. Soedin. *1978*, 291.

[37] See also: *J. Kaldova, J. Grob*, Helv. Chim. Acta *61*, 1996 (1978); cf. the electrochemical introduction of an amino group in the 4-position of a ketone: Review: *L. L. Miller, E. Kariv, J. R. Behling*, Annu. Rep. Med. Chem. *12*, 309 (1977).

[38] *D. S. Watt*, J. Am. Chem. Soc. *98*, 271 (1976).

[39] a) *B. M. Trost, M. J. Bogdanowicz*, J. Am. Chem. Soc. *93*, 3773 (1971); *B. M. Trost, D. E. Keely, H. C. Arndt, M. J. Bogdanowicz, ibid. 99*, 3088 (1977); b) *D. Seebach, M. Braun*, Angew. Chem. *86*, 279 (1974); Angew. Chem. Int. Ed. Engl. *13*, 277 (1974); *M. Braun, R. Dammann, D. Seebach*, Chem. Ber. *108*, 2368 (1975); *R. Dammann, M. Braun, D. Seebach*, Helv. Chim. Acta *59*, 2821 (1976).

[40] *S. Terahima*, J. Synth. Org. Chem. Jpn. *35*, 1045 (1977).

[41] *R. Criegee*, Ber. Dtsch. Chem. Ges. *77*, 722 (1944).

[42] *D. Hoppe, I. Hoppe, U. Schöllkopf*, Tetrahedron Lett. *1976*, 609; *J. F. Fitt, H. W. Gschwend*, J. Org. Chem. *42*, 2639 (1977); *P. Bey, J. P. Kevert*, Tetrahedron Lett. *1977*, 1455.

[43] *A. J. Birch*, J. Chem. Soc. *1944*, 314; *A. Dornow, H. D. Jordan*, Chem. Ber. *94*, 76 (1961); *E. J. Corey, L. S. Melvin, M. F. Haslanger*, Tetrahedron Lett. *1975*, 3117; Review: *W. Pritzkow et al.*, Wiss. Z. Hochschule Leuna-Merseburg *8*, 187 (1966); Chem. Abstr. *69*, 18337z (1968).

[44] *C. E. Sacks, P. L. Fuchs*, J. Am. Chem. Soc. *97*, 7372 (1975); *P. L. Fuchs*, J. Org. Chem. *41*, 2935 (1976); *G. Stork, A. A. Ponaras, ibid. 41*, 2937 (1976).

[45] Review: *D. L. J. Clive*, Tetrahedron *34*, 1049 (1978).

[46] Reviews: *E. Schacht*, Merck-Kontakte *1974* (3), 9; *1975* (2), 3; *R. Appel*, Angew. Chem. *87*, 863 (1975); Angew. Chem. Int. Ed. Engl. *14*, 801 (1975); *T. Mukaiyama, ibid. 88*, 111 (1976) and *15*, 94 (1976); *H. Loibner, L. Zbiral*, Helv. Chim. Acta *59*, 2100 (1976); *60*, 417 (1977); *Y. Tanigawa, H. Kanamaru, A. Sonoda, S.-I. Murahashi*, J. Am. Chem. Soc. *99*, 2361 (1977).

[47] *J. B. Hendrickson, R. Bergeron, A. Giga, D. Sternbach*, J. Am. Chem. Soc. *95*, 3412 (1973); *V. A. Curtis, H. S. Schwartz, A. F. Hartmann, R. M. Pick, L. W. Kolar, R. J. Baumgarten*, Tetrahedron Lett. *1977*, 1969.

[48] *R. Schlecker, D. Seebach, W. Lubosch*, Helv. Chim. Acta *61*, 512 (1978).

[49] *P. Beak, B. G. McKinnie*, J. Am. Chem. Soc. *99*, 5213 (1977); *P. Beak, M. Baillargeon, L. G. Carter*, J. Org. Chem. *43*, 4255 (1978).

[50] *P. Beak*, Chem. Rev. *78*, 275 (1978); cf. also *G. Büchi, M. Cushman, H. Wüest*, J. Am. Chem. Soc. *96*, 5563 (1974).

[51] *W. P. Jencks:* Catalysis in Chemistry and Enzymology, McGraw Hill, New York 1969.

[52] *H. Böhme, H. G. Viehe* in *E. C. Taylor:* Advances in Organic Chemistry. Vol. 9. Wiley, New York 1976.

[53] *P. Hullot, Th. Cuvigny*, Bull. Soc. Chim. Fr. *1973*, 2989; *Th. Kauffmann, H. Berg, E. Köppelmann, D. Kuhlmann*, Chem. Ber. *110*, 2659 (1977).

[54] *U. Schöllkopf*, Angew. Chem. *89*, 351 (1977); Angew. Chem. Int. Ed. Engl. *16*, 339 (1977); *D. Hoppe, ibid. 86*, 878 (1974), and *13*, 789 (1974).

[55] *U. Schöllkopf, H. Beckhaus*, Angew. Chem. *88*, 296 (1976); Angew. Chem. Int. Ed. Engl. *15*, 293 (1976).

[56] *D. Seebach, D. Enders*, Chem. Ber. *108*, 1293 (1975); *D. Enders, T. Hassel, R. Pieter, B. Renger, D. Seebach*, Synthesis *1976*, 548; *D. Seebach, D. Enders, B. Renger*, Chem. Ber. *110*, 1852 (1977); *B. Renger, H. O. Kalinowski, D. Seebach, ibid. 110*, 1866 (1977); *D. Seebach, D. Enders, R. Dach, R. Pieter, ibid. 110*, 1879 (1977); *B. Renger, D. Seebach*, Chem. Ber. *110*, 2334 (1977); *D. Seebach, R. Dach, D. Enders, B. Renger, M. Jansen, G. Brachtel*, Helv. Chim. Acta *61*, 1622 (1978); *B. Renger, H. Hügel, W. Wykypiel, D. Seebach*, Chem. Ber. *111*, 2630 (1978).

[57] *R. Schlecker, D. Seebach*, Helv. Chim. Acta *60*, 1459 (1977); *D. Seebach, T. Hassel*, Angew. Chem. *90*, 296 (1978); Angew. Chem. Int. Ed. Engl. *17*, 274 (1978); *T. Hassel, D. Seebach*, Helv. Chim. Acta *61*, 2237 (1978).

[58] *R. R. Schmidt, G. Berger*, Chem. Ber. *109*, 2936 (1976); *R. Schmidt, J. Talbiersky*, Angew. Chem. *88*, 193 (1976); Angew. Chem. Int. Ed. Engl. *15*, 171 (1976); Synthesis *1977*, 869, Angew. Chem. *90*, 220 (1978); Angew. Chem. Int. Ed. Engl. *17*, 204 (1978).

[59] *T. Saegusa, Y. Ito*, Synthesis *1975*, 291; *A. M. van Leusen, J. Wildeman, O. H. Oldenziel*, J. Org. Chem. *42*, 1153 (1977).

[60] *D. Seebach, D. Enders*, Angew. Chem. *85*, 1104 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1014 (1973); *D. Seebach, W. Lubosch, D. Enders*, Chem. Ber. *109*, 1309 (1976).

[61] *P. R. Ortiz de Montellano, Ch. K. Hsu*, Tetrahedron Lett. *1976*, 4215; *B. M. Trost, J. A. Rigby*, J. Org. Chem. *43*, 2938 (1978); for the thiolation of carbonyl compounds, see also *H. Horstmann* in [8a], Vol. VII, 2c, 1977, p. 2317; *D. Seebach, M. Teschner*, Tetrahedron Lett. *1973*, 5113; Chem. Ber. *109*, 1601 (1976); *B. M. Trost et al.*, J. Am. Chem. Soc. *98*, 4887 (1976); *99*, 4405 (1977); Chem. Rev. *78*, 363 (1978); Connective preparation of α-thiolated ketones: *M. Braun*, Tetrahedron Lett. *1978*, 3695.

[62] *A. Eschenmoser et al.*, Helv. Chim. Acta *56*, 2950, 2961, 2975 (1973) and references cited therein; *S. Levinger, Sh. Shatzmiller*, Tetrahedron *34*, 563 (1978).

[63] Reviews: *G. H. Posner*, Org. React. *22*, 253 (1975); *M. Schlosser*, Angew. Chem. *86*, 751 (1974); Angew. Chem. Int. Ed. Engl. *13*, 701 (1974); *J. F. Normant* in [4e], Vol. 1, 1976, p. 219; review on Barbier reaction: *C. Blamberg, F. A. Hartog*, Synthesis *1977*, 18; *N. Cohen, W. F. Eichel, L. J. Lopresti, Ch. Neukom, G. Sauncy*, J. Org. Chem. *41*, 3505 (1976).

[64] *D. J. Peterson*, Organomet. Chem. Rev. *A 7*, 295 (1972).

[65] *D. Seebach, N. Meyer*, Angew. Chem. *88*, 484 (1976); Angew. Chem. Int. Ed. Engl. *15*, 438 (1976) and unpublished results.

[66] *W. C. Still*, J. Am. Chem. Soc. *100*, 1481 (1978).

[67] Reviews: *J. P. Collman*, Acc. Chem. Res. *8*, 342 (1975); *A. P. Kozikowski, H. F. Wetter*, Synthesis *1976*, 561; *H. Alper* in *I. Wender, P. Pino:* Organic Synthesis *via* Metal carbonyls, Vol. 2, Wiley-Interscience, New York 1977, p. 545; *H.-A. Kurmeier*, Merck-Kontakte *1978* (1), 3; (2), 3; *P. Collman, R. G. Finke, J. N. Cawse, J. I. Braumann*, J. Am. Chem. Soc. *100*, 4766 (1978).

[68] Review: *J. Schwartz, J. A. Labinger*, Angew. Chem. *88*, 402 (1976); Angew. Chem. Int. Ed. Engl. *15*, 333 (1976); *J. Schwartz et al.*, J. Am. Chem. Soc. *99*, 638, 8045 (1977).

[69] *D. G. Smith, D. J. H. Smith*, J. Chem. Soc. Chem. Commun. *1975*, 459; *C. A. Scott, D. G. Smith, D. J. H. Smith*, Synth. Commun. *6*, 135 (1976).

[70] *D. A. Evans, G. C. Andrews*, Acc. Chem. Res. *7*, 147 (1974); *B. M. Trost, J. L. Stanton*, J. Am. Chem. Soc. *97*, 4018 (1975).

[71] Reviews: *P. D. Magnus*, Tetrahedron *33*, 2019 (1977); [4f]; *K. Kondo, D. Tunemoto et al.*, Tetrahedron Lett. *1975*, 1007, 1397, 2275; *L. J. Dolby et al., ibid. 1976*, 4675; J. Org. Chem. *42*, 1349 (1977); *G. A. Kraus, K. Frazier*, Synth. Commun. *8*, 483 (1978).

[72] *D. Seebach, N. Peleties*, Angew. Chem. *81*, 465 (1969); Angew. Chem. Int. Ed. Engl. *8*, 450 (1969); *D. Seebach, N. Peleties*, Chem. Ber. *105*, 511 (1972); *D. Seebach, A. K. Beck*, Angew. Chem. *86*, 859 (1974); Angew. Chem. Int. Ed. Engl. *13*, 806 (1974); *D. Seebach, N. Meyer, A. K. Beck*, Justus Liebigs Ann. Chem. *1977*, 846.

[73] *D. A. Evans, G. L. Carroll, L. K. Truesdale*, J. Org. Chem. *39*, 914 (1974); *I. Ojima, S. Inaba, K. Nakatsugawa*, Chem. Lett. *1975*, 331; *I. Ryu, S. Murai, T. Horiike, A. Shinonaga, N. Sonoda*, Synthesis *1978*, 154; *B. Uznanski, W. J. Stec, ibid. 1978*, 154; *P. G. Gassman, J. J. Talley*, Tetrahedron Lett. *1978*, 3773.

[74] *E. J. Corey, D. N. Crouse, J. E. Anderson*, J. Org. Chem. *40*, 2142 (1975).

[75] *M. Schlosser, Z. Brich*, Helv. Chim. Acta *61*, 1903 (1978).

[76] *M. Samson, M. Vandewalle*, Synth. Commun. *8*, 231 (1978).

[77] *W. Steglich et al.*, Angew. Chem. *83*, 725, 727 (1971); *89*, 408 (1977); Angew. Chem. Int. Ed. Engl. *10*, 653, 655 (1971); *16*, 394 (1977).

[78] *F. M. Schell, J. P. Carter, Ch. Wiaux-Zamar*, J. Am. Chem. Soc. *100*, 2894 (1978).

[79] *D. Seebach, W. Lubosch*, Angew. Chem. *88*, 339 (1976); Angew. Chem. Int. Ed. Engl. *15*, 313 (1976); *W. Lubosch*, Dissertation, University of Giessen 1979.

[80] *G. Stork et al.*, J. Am. Chem. Soc. *93*, 5286 (1971); *96*, 5272 (1974); Tetrahedron Lett. *1975*, 389.

[81] *G. Stork, T. Takahashi*, J. Am. Chem. Soc. *99*, 1275 (1977) and unpublished results.

[82] *R. Breslow et al.*, J. Am. Chem. Soc. *79*, 1762 (1957); *81*, 3080 (1959); Chem. Ind. (London) *1957*, 893; *J. P. Kuebrich, R. L. Schowen, M. Wang, M. E. Lupes*, J. Am. Chem. Soc. *93*, 1214 (1971); cf. also *K. H. Bräutigam, Th. Severin*, Chem. Ber. *108*, 379 (1975).

[83] Review: *H. Stetter*, Angew. Chem. *88*, 695 (1976); Angew. Chem. Int. Ed. Engl. *15*, 639 (1976). *H. Stetter, J. Nienhans*, Chem. Ber. *111*, 2825 (1978); *T. Chancellor, M. Quill, D. E. Bergbreiter, M. Newcomb*, J. Org. Chem. *43*, 1245 (1978) and references cited therein.

[84] *R. Lohmar, W. Steglich*, Angew. Chem. *90*, 493 (1978); Angew. Chem. Int. Ed. Engl. *17*, 450 (1978).

[85] *G. H. Posner*, Org. React. *19*, 1 (1972).

[86] *A. Debal, Th. Cuvigny, M. Larchevêque*, Tetrahedron Lett. *1977*, 3187; cf. *M. Larchevêque, Th. Cuvigny, ibid. 1975*, 3851; *A. Debal, Th. Cuvigny, M. Larchevêque*, Synthesis *1976*, 391 and references cited therein.

[87] *J. Ficini et al.*, Bull. Soc. Chim. Fr. *1964*, 871 and references cited therein; Tetrahedron Lett. *1971*, 1565, 1569.

[88] *D. Felix, R. K. Müller, U. Horn, R. Joos, J. Schreiber, A. Eschenmoser*, Helv. Chim. Acta *55*, 1276 (1972).

[89] *A. Kalir, D. Balderman*, Synthesis *1973*, 358.

[90] *S. Hünig et al.*, Synthesis *1976*, 416; *1975*, 180, 391; *1973*, 777.

[91] *J. P. Kuebrich, R. L. Schowen*, J. Am. Chem. Soc. *93*, 1220 (1971); *M. Hamana, T. Endo, S. Saeki*, Tetrahedron Lett. *1975*, 903.

[92] *B. C. Uff, A. Al-Kolla, K. E. Adamali, V. Harutunian*, Synth. Commun. *8*, 163 (1978).

[93] *Y. Masuyama, Y. Ueno, M. Okawara*, Tetrahedron Lett. *1976*, 2967 and references cited therein.

[94] *F. D. Popp*, Adv. Heterocycl. Chem. *9*, 1 (1968); *M. D. Rozawadowska, D. Brozda*, Bull. Acad. Pol. Sci., Sér. Sci. Chim. *26*, 33 (1978).

[95] *E. Leete, S. A. S. Leete*, J. Org. Chem. *43*, 2122 (1978); see also *S. F. Dyke et al.*, Tetrahedron *31*, 561, 1219 (1975); *G. Büchi, P. H. Liang, H. Wüest*, Tetrahedron Lett. *1978*, 2763.

[96] For the conversion of nitriles to ketones see [38]; *S. J. Selikson, D. S. Watt*, J. Org. Chem. *40*, 268 (1975); *E. Vedejs, J. E. Telschow, ibid. 41*, 740 (1976).

[97] *D. S. Watt et al.*, J. Org. Chem. *41*, 2846, 2939 (1976); J. Am. Chem. Soc. *99*, 182 (1977).

[98] *P. A. Grieco, C. L. J. Wang*, J. Chem. Soc. Chem. Commun. *1975*, 714; *B. M. Trost, Y. Tamaru*, J. Am. Chem. Soc. *99*, 3101 (1977).

[99] *G. Stork, A. Y. W. Leong, A. M. Tauzin*, J. Org. Chem. *41*, 3491 (1976).

[100] *H. H. Wasserman, B. H. Lipshutz*, Tetrahedron Lett. *1975*, 4611; *W. Adam, O. Cueto, V. Ehrig*, J. Org. Chem. *41*, 370 (1976).

[101] *R. A. Sheldon, J. K. Kochi*, Org. React. *19*, 279 (1972).

[102] *T. Wakamatsu, K. Akasaka, Y. Ban*, Tetrahedron Lett. *1974*, 3879; *1977*, 2751, 2755; *Y. Ueno, M. Okawara*, Synthesis *1975*, 268; *E. Nakamura, I. Kuwajima*, J. Am. Chem. Soc. *99*, 962 (1977).

[103] *A. Wissner*, Tetrahedron Lett. *1978*, 2749.

[104] *D. Wendisch* in [8a], Vol. IV/3, 1971.

[105] a) *P. Lipp et al.*, Ber. Dtsch. Chem. Ges. *54*, 1316 (1921); Justus Liebigs Ann. Chem. *499*, 1 (1932); *H. H. Wasserman, D. C. Clagett*, Tetrahedron Lett. *1964*, 341; Reviews: *J. Haywood-Farmer*, Chem. Rev. *74*, 315 (1974); *D. H. Gibson, C. H. De Puy, ibid. 74*, 605 (1974); *H. H. Wasserman, G. M. Clark, P. C. Turley*, Top. Curr. Chem. *47*, 73 (1974); *J. M. Conia, M. J. Robson*, Angew. Chem. *87*, 505 (1975); Angew. Chem. Int. Ed. Engl. *14*, 473 (1975); b) *W. A. Bone, W. H. Perkin*, J. Chem. Soc. *67*, 108 (1895); c) *R. W. Kierstead, R. P. Linstead, B. C. L. Weedon, ibid. 1952*, 3610, 3616; *J. M. Stewart, D. R. Olsen*, J. Org. Chem. *33*, 4534 (1968).

[106] *J. Buddrus*, Angew. Chem. *84*, 1173 (1972); Angew. Chem. Int. Ed. Engl. *11*, 1041 (1972); *J. Dockx*, Synthesis *1973*, 441; *H. E. Simmons, T. L. Cairns, S. A. Vladuchick*, Org. React. *20*, 1 (1973); *A. P. Marchand, N. M. Brockway*, Chem. Rev. *74*, 431 (1974); *E. V. Dehmlow*, Angew. Chem. *86*, 187 (1974); *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974); *16*, 493 (1977); *M. Makosza* in: Modern Synthetic Methods 1976. Schweizer Chemiker Verband, Zürich 1976, p. 7ff.; *W. P. Weber, G. W. Gokel*, Phase Transfer Catalysis in Organic Synthesis. Springer, Berlin 1977.

[107] A separate review on this subject by *D. Seebach et al.* is in preparation. Some aspects are covered in a Japanese review: *D. Tunemoto, K. Kondo*, J. Synth. Org. Chem. Jpn. *35*, 1070 (1977).

[108] *S. Danishefsky et al.*, J. Chem. Soc. Chem. Commun. *1972*, 821; *1975*, 7; J. Am. Chem. Soc. *96*, 1256 (1974); *97*, 3239 (1975); J. Org. Chem. *39*, 2658, 2924 (1974); *40*, 114, 2969 (1975); *41*, 1668 (1976); Tetrahedron Lett. *1975*, 79; review: Acc. Chem. Res. *12*, 66 (1979).

[109] *R. V. Stevens* in *J. W. ApSimon*: The Total Synthesis of Natural Products. Vol. 3, Wiley-Interscience, New York 1977, p. 439; *R. V. Stevens*, Acc. Chem. Res. *10*, 193 (1977).

[110] *E. Wenkert et al.*, J. Org. Chem. *42*, 2137 (1977); J. Am. Chem. Soc. *100*, 1267, 4893 (1978); cf. *S. Bernasconi, C. Capellini, M. Sisti*, Synth. Commun. *8*, 71 (1978).

[111] *S. Danishefsky et al.*, J. Org. Chem. *39*, 1979 (1974); Tetrahedron Lett. *1977*, 3029, 3031.

[112] *R. V. Stevens, J. M. Fitzpatrick, M. Kaplan, R. L. Zimmerman*, Chem. Commun. *1971*, 857.

[113] See also the use of this principle in prostaglandin synthesis: *A. Mitra*: The Synthesis of Prostaglandins: Wiley, New York 1977; *J. S. Bindra*: Prostaglandin Synthesis, Academic Press, New York 1977; Brefeldin A-Synthesis: *T. Livinghouse, R. V. Stevens*, J. Chem. Soc. Chem. Commun. *1978*, 754.

[114] *E. Nakamura, I. Kuwajima*, J. Am. Chem. Soc. *99*, 7360 (1977).

[115] *A. Suzuki et al.*, Synthesis *1975*, 317; Tetrahedron Lett. *1976*, 255.

[116] *E. J. Corey, P. Ulrich*, Tetrahedron Lett. *1975*, 3685.

[117] *P. L. Fuchs*, J. Am. Chem. Soc. *96*, 1607 (1974); *W. G. Dauben, D. J. Hart, ibid. 97*, 1622 (1975).

[118] *J. P. Marino, R. C. Landick*, Tetrahedron Lett. *1975*, 4531.

[119] *V. Jäger, H. G. Viehe*: in [8a], Vol. V/2a, 1977; *R. A. Raphael*: Acetylenic Compounds in Organic Synthesis. Butterworths, London 1955.

[120] Alkylations of ω-hydroxy-1-alkynes: *J. Flahaut, P. Miginiac*, Helv. Chim. Acta *61*, 2275 (1978); Acetylide of a propiolate: *R. M. Carlson, A. R. Oyler*, Tetrahedron Lett. *1974*, 2615; *L. J. Chinn, B. N. Desai, J. F. Zawadzki*, J. Org. Chem. *40*, 1328 (1975); *K. Mori, M. Oda, M. Matsui*, Tetrahedron Lett. *1976*, 3173; *K. Heyns, K.-M. Grühn, ibid. 1978*, 2861; 1-Amino-3-lithio-1-propyne: *E. J. Corey, D. E. Cane, J. Org. Chem. 35*, 3405 (1970); Metalated propargylamine derivatives: *B. W. Metcalf, P. Casara*, Tetrahedron Lett. *1975*, 3337; *R. Epsztein, F. Mercier*, Synthesis *1977*, 183; *D. Taub, A. A. Patchett*, Tetrahedron Lett. *1977*, 2745; Propargylphenyl selenide dianion: *H. J. Reich, Sh. K. Shah*, J. Am. Chem. Soc. *99*, 263 (1977).

[121] *H. Gerlach, P. Künzler, K. Oertle*, Helv. Chim. Acta *61*, 1226 (1978).

[122] *M. Baumann, W. Hoffmann, N. Müller*, Tetrahedron Lett. *1976*, 3585; cf. *M. Karpf, D. Walton, A. S. Dreiding*, Helv. Chim. Acta *61*, 527 (1978).

[123] *J. J. Bloomfield, D. C. Owsley, J. M. Nelke*, Org. React. *23*, 259 (1976).

[124] *F. Beck*: Elektroorganische Chemie, Verlag Chemie, Weinheim 1974; *A. J. Fry*: Synthetic Organic Electrochemistry. Harper & Row, New York 1972.

[125] *A. Schönberg*, Preparative Organic Photochemistry, Springer, Berlin 1968; *O. L. Chapman*: Organic Photochemistry, Edw. Arnold, London 1967.

[126] Review: *V. Kalyanaraman, M. V. George*, J. Organomet. Chem. *47*, 225 (1973) and ref. [1] therein; see also: *Ch. Grugel, W. P. Neumann, J. Sauer, P. Seifert*, Tetrahedron Lett. *1978*, 2847; *V. Rautenstrauch*, Synthesis *1975*, 787.

[127] *J. E. McMurry*, Acc. Chem. Res. *7*, 281 (1974).

[128] *J. E. McMurry, M. P. Fleming*, J. Org. Chem. *41*, 896 (1976), cf. *G. A. Olah et al.*, Synthesis *1976*, 318, 607.

[129] *T. Mukaiyama, T. Sato, J. Hanna*, Chem. Lett. *1973*, 1041; *S. Nishida, F. Kataoka*, J. Org. Chem. *43*, 1612 (1978).

[130] *E. J. Corey, R. L. Danheiser, S. Chandrasekaran*, J. Org. Chem. *41*, 260 (1976).

[131] *K. B. Sharpless, M. A. Umbreit, M. T. Nieh, Th. C. Flood*, J. Am. Chem. Soc. *94*, 6538 (1972); *Y. Fujiwara, R. Ishikawa, F. Akiyama, Sh. Teranishi*, J. Org. Chem. *43*, 2477 (1978); with $NaPO(OEt)_2$: *T. Minami, M. Matsumoto, T. Agawa*, J. Chem. Soc. Chem. Commun. *1976*, 1053.

[132] *H. Schäfer et al.*, Chem. Ber. *105*, 2398 (1972); *107*, 3640 (1974); cf. Angew. Chem. *90*, 483 (1978); Angew. Chem. Int. Ed. Engl. *17*, 460 (1978).

[133] *M. W. Rathke, A. Lindert*, J. Am. Chem. Soc. *93*, 4605 (1971); *T. J. Brocksom, N. Petragnani, R. Rodrigues, H. La Scala Teixeira*, Synthesis *1975*, 396; *Y. Kobayashi, T. Taguchi, E. Tokuno*, Tetrahedron Lett. *1977*, 3741; cf. also *H. O. Huisman*, Pure Appl. Chem. *49*, 1307 (1977); *C. Chassin, E. A. Schmidt, H. M. R. Hoffmann*, J. Am. Chem. Soc. *96*, 606 (1974); Reductive coupling of enones to 1,6-dicarbonyl derivatives: *J. Grimshaw, R. J. Haslett*, J. Chem. Soc. Chem. Commun. *1974*, 174; *R. Calas, J. Dunogues* in [4e], Vol. 2, 1976, p. 277; Intramolecular coupling: *Y. Kobayski, T. Taguchi, T. Morikawa*, Tetrahedron Lett. *1978*, 3555.

[134] *T. Saegusa et al.*, J. Am. Chem. Soc. *97*, 2912 (1975); *99*, 1487 (1977); *S. Torii, H. Tanaka, Y. Tomotaki*, Bull. Chem. Soc. Jpn. *50*, 537 (1977).

[135] Coupling of silyl enol ethers with $TiCl_4$: *S. Inaba, I. Ojima*, Tetrahedron Lett. *1977*, 2009; with Ag_2O: *Y. Ito, T. Konoike, T. Saegusa*, J. Am. Chem. Soc. *97*, 649 (1975); Dimerization of enol acetates with Mn^{III}: *R. M. Dessau, E. I. Heiba*, J. Org. Chem. *39*, 3457 (1974).

[136] *H. Schäfer:* Festschrift, 25 Jahre Fonds der Chemischen Industrie, Frankfurt 1975, p. 73; Abstract of IUPAC-Meeting on Natural Products, Bulgaria, Sept. 20–27, 1978; *H. Schäfer*, private communication.
[137] *E. J. Corey, R. L. Carney*, J. Am. Chem. Soc. *93*, 7318 (1971); *J. E. McMurry et al.*, J. Org. Chem. *42*, 2655 (1977); *43*, 3255 (1978); cf. also *M. F. Semmelhack, A. Yamashita, J. C. Tomesch, K. Hirotsu*, J. Am. Chem. Soc. *100*, 5565 (1978).
[138] *J. E. McMurry, L. R. Krepski*, J. Org. Chem. *41*, 3929 (1976).
[139] Review on insect pheromones: *R. Rossi*, Synthesis *1977*, 817; *1978*, 413.
[140] *J. Knolle, H. J. Schäfer*, Angew. Chem. *87*, 777 (1975); Angew. Chem. Int. Ed. Engl. *14*, 758 (1975).
[141] *N. L. Askerov, S. T. Meklitiev, V. M. Mamedova, A. P. Tomilov*, Zh. Obshch. Khim. *48*, 863 (1978).
[142] *K.-H. Geiss, B. Seuring, R. Pieter, D. Seebach*, Angew. Chem. *86*, 484 (1974); Angew. Chem. Int. Ed. Engl. *13*, 479 (1974).
[143] *D. Seebach, K.-H. Geiss*, Angew. Chem. *86*, 202 (1974); Angew. Chem. Int. Ed. Engl. *13*, 202 (1974).
[144] a) *M. Pohmakotr, K.-H. Geiss, D. Seebach*, Chem. Ber., in press; b) *M. Pohmakotr*, Dissertation, University of Giessen, 1978.
[145] *D. Seebach, R. Henning, F. Lehr*, Angew. Chem. *90*, 479 (1978); Angew. Chem. Int. Ed. Engl. *17*, 458 (1978).
[146] *D. Seebach, R. Henning, F. Lehr, J. Gonnermann*, Tetrahedron Lett. *1977*, 1161; Chem. Ber. *112*, 234 (1979).
[147] *R. Henning, F. Lehr, D. Seebach*, Helv. Chim. Acta *59*, 2213 (1976).
[148] *M. Pohmakotr, D. Seebach*, Angew. Chem. *89*, 333 (1977); Angew. Chem. Int. Ed. Engl. *16*, 320 (1977).
[149] *J. G. Smith, G. E. F. Simpson*, J. Org. Chem. *41*, 2878 (1976); *H. Hoberg, U. Griebsch*, Synthesis *1976*, 830; *A. N. Tischler, M. H. Tischler*, Tetrahedron Lett. *1978*, 3, 3407; *C. Degrand, C. Grosdemouge, P. L. Compagnon, ibid. 1978*, 3023; *D. A. Evans, P. J. Sidebottom*, J. Chem. Soc. Chem. Commun. *1978*, 753.
[150] *Y. Yamamoto, K. Kondo, I. Moritani*, J. Org. Chem. *40*, 3644 (1975); *H. N. Khatri, H. M. Walborsky, ibid. 43*, 734 (1978).
[151] *A. Butlerow*, Ann. Chem. Pharm. *120*, 295 *(1861)*; *E. Fischer*, Ber. Dtsch. Chem. Ges. *23*, 2114 (1890).
[152] *A. Eschenmoser*, Naturwissenschaften *61*, 513 (1974); *A. Eschenmoser, C. E. Wintner*, Science *196*, 1410 (1977); *A. Eschenmoser* in Jahrbuch der Akademie der Wissenschaften. Vandenhoeck & Ruprecht, Göttingen 1977, p. 29.
[153] *D. J. Peterson*, J. Org. Chem. *9*, 373 (1967).
[154] Review: *U. Schöllkopf*, Angew. Chem. *82*, 795 (1970); Angew. Chem. Int. Ed. Engl. *9*, 763 (1970).
[155] A complete coverage of this field up to 1976 is found in the review: *O. W. Lever, jr.*, Tetrahedron *32*, 1943 (1976); *R. K. Boeckman, K. J. Bruza, J. E. Baldwin, O. W. Lever, jr.*, J. Chem. Soc. Chem. Commun. *1975*, 519; *J. E. Baldwin, O. W. Lever, jr., N. R. Tzodikov*, J. Org. Chem. *41*, 2312 (1976); *C. N. Skold*, Synth. Commun. *6*, 119 (1976); *P. H. M. Schreurs, J. Meijer, P. Vermeer, L. Brandsma*, Tetrahedron Lett. *1976*, 2387; *A. B. Levy, St. J. Schwartz, ibid. 1976*, 2201; *D. A. Evans, P. J. Sidebottom*, J. Chem. Soc. Chem. Commun. *1978*, 753.
[156] *J. C. Clinet, G. Linstrumelle*, Tetrahedron Lett. *1978*, 1137.
[157] Review: *H. Ahlbrecht*, Chimia *31*, 391 (1977).
[158] *N. Meyer, D. Seebach*, Angew. Chem. *90*, 553 (1978); Angew. Chem. Int. Ed. Engl. *17*, 521 (1978) and unpublished results; cf. *W. E. Parham et al.*, J. Org. Chem. *37*, 1545 (1972); *39*, 2048 (1974); Synthesis *1976*, 116.
[159] *R. E. Ludt, J. S. Griffiths, K. N. McGrath, C. R. Hauser*, J. Org. Chem. *38*, 1668 (1973); *P. Beak, R. A. Brown, ibid. 42*, 1823 (1977) and references cited therein; *Ch. F. Beam*, Chem. Ind. (London) *1977*, 231.
[160] Review up to early 1976: *H. P. Abicht, K. Issleib*, Z. Chem. *17*, 1 (1977).
[161] *J. K. Crandall, A. C. Clark*, J. Org. Chem. *37*, 4236 (1977); *D. R. Dimmel et al., ibid. 38*, 2756 (1973); *40*, 132 (1975).
[162] Reviews: *R. A. Ellison*, Synthesis *1973*, 397; *T. Nakai*, J. Synth. Org. Chem. Jpn. *36*, 49 (1978); *Tse-Lok Ho*, Synth. Commun. *4*, 265 (1974); *G. Rio A. Lecas-Nawrocka*, Bull. Soc. Chim. Fr. *1976*, 317.
[163] For a recent application see: *E. J. Corey, K. C. Nicolaou, T. Toru*, J. Am. Chem. Soc. *97*, 2287 (1975).
[164] *E. J. Corey, R. H. Wollenberg*, J. Org. Chem. *40*, 2265 (1975); *G. Cahiez, A. Alexakis, J. F. Normant*, Tetrahedron Lett. *1978*, 3013; *G. Schill, Ch. Merkel*, Chem. Ber. *111*, 1446 (1978).
[165] *B. M. Trost, K. Hiroi, S. Kurozumi*, J. Am. Chem. Soc. *97*, 438 (1975); *W. Oppolzer, T. Sarkar, K. K. Mahalanabis*, Helv. Chim. Acta *59*, 2012 (1976); *W. E. Fristad, Th.-R. Bailey, L. A. Paquette*, J. Org. Chem. *43*, 1620 (1978); cf. *K. Hermann*, Nachr. Chem. Techn. Lab. *26*, 520 (1978); *S. Kano, T. Yokomatsu, T. Ono, S. Hibino, S. Shibuya*, J. Chem. Soc. Chem. Commun. *1978*, 414; Review: *T. Nakai, T. Mimura*, J. Synth. Org. Chem. Jpn. *35*, 964 (1977).
[166] *A. A. Ponaras*, Tetrahedron Lett. *1976*, 3105.
[167] a) *B. M. Trost, J. L. Stanton*, J. Am. Chem. Soc. *97*, 4018 (1975); *T. Nakai, T. Mimura, A. Ari-Izumi*, Tetrahedron Lett. *1977*, 2425; b) see also: *D. Seebach, H. Neumann*, Chem. Ber. *107*, 847 (1974); *H. Neumann, D. Seebach*, Tetrahedron Lett. *1976*, 4839; Chem. Ber. *111*, 2785 (1978).
[168] Reviews: *R. E. Gawley*, Synthesis *1976*, 777; *M. E. Jung*, Tetrahedron *32*, 3 (1976).
[169] Reviews: *A. T. Nielsen, W. J. Houlihan*, Org. React. *16*, 1 (1968); *G. Wittig, H. Reiff*, Angew. Chem. *80*, 8 (1968); Angew. Chem. Int. Ed. Engl. *7*, 7 (1968); *S. Swaminathan, K. V. Narayanan*, Chem. Rev. *71*, 429 (1971); *K. Hermann*, Nachr. Chem. Tech. Lab. *26*, 290 (1978); *I. Kuwajima, T. Sato, M. Arai, N. Minami*, Tetrahedron Lett. *1976*, 1817; *G. Schulz, W. Steglich*, Angew. Chem. *89*, 255 *(1977)*; Angew. Chem. Int. Ed. Engl. *16*, 251 (1977); *C. H. Heathcock et al.*, J. Am. Chem. Soc. *99*, 247, 8109 (1977); Tetrahedron Lett. *1978*, 1685.
[170] Review: *S. J. Rhoads, N. R. Raulins*, Org. React. *22*, 1 (1975); *F. E. Ziegler*, Acc. Chem. Res. *10*, 227 (1977); *G. B. Bennett*, Synthesis *1977*, 589; *N. Cohen et al.*, J. Org. Chem. *41*, 3497, 3505, 3512 (1976).
[171] See the discussion in ref. [4f] and [4g].
[172] *St. Raucher, A. S.-T. Lui*, J. Am. Chem. Soc. *100*, 4902 (1978).
[173] *D. A. Evans, A. M. Golob*, J. Am. Chem. Soc. *97*, 4765 (1975).
[174] *P. G. Gassman et al.*, J. Am. Chem. Soc. *96*, 5487, 5495, 5508, 5512 (1976); Tetrahedron Lett. *1977*, 2055.
[175] *P. G. Gassman, D. R. Amick*, Tetrahedron Lett. *1974*, 3463.
[176] *B. M. Trost et al.*, Acc. Chem. Res. *7*, 85 (1974); J. Am. Chem. Soc. *97*, 2224 (1975); *99*, 3080, 3088 (1977).
[177] *R. Dammann*, Dissertation, ETH Zürich 1978; *R. Dammann, D. Seebach*, Helv. Chim. Acta and Chem. Ber., in press.
[178] *B. M. Trost et al.*, J. Am. Chem. Soc. *99*, 6124 (1977); *100*, 5512 (1978).
[179] *M. F. Semmelhack* in [4e], Vol. 1, 1976, p. 361.
[180] *E. J. Corey et al.*, Science *166*, 178 (1969); Q. Rev. Chem. Soc. *25*, 455 (1971); J. Org. Chem. *43*, 2208 (1978); *M. Bersohn, A. Esack*, Chem. Rev. *76*, 269 (1976).
[181] *F. Näf, G. Ohloff*, Helv. Chim. Acta *57*, 1868 (1974).
[182] *R. E. Ireland*, Organic Synthesis. Prentice Hall, Englewood Cliffs 1969, Chap. 5, 6.

Alkenediazonium Salts: A New Chapter of Classical Organic Chemistry

By Kaspar Bott[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Whereas the protonation of α-diazo-β-diketones and α-diazo-β-oxo esters with hydrogen chloride and antimony pentachloride yields the corresponding hydroxyalkenediazonium hexachloroantimonates, the "acid-sensitive" α-diazomonocarbonyl compounds can be transformed into resonance-stabilized alkenediazonium salts by an analogous *O*-alkylation with triethyloxonium hexachloroantimonate. A general route for synthesizing these compounds consists in the transformation of the *p*-toluenesulfonylhydrazones of α-halogenated aldehydes and ketones with Lewis acids. Alkenediazonium ions which are not resonance stabilized can be isolated at room temperature only if their decomposition at higher temperatures leads, *via* evolution of nitrogen, to vinyl cations in particularly high energy levels. Facile substitution reactions at the CC double bond with anisole and methanol demonstrate the strongly electrophilic nature of alkenediazonium salts. When electron-donating substituents are attached to C2 of an ethylenediazonium ion, the bond order of the NN triple bond can be reduced to a level comparable with that in diazoacetic ester.

1. Introduction

Since their discovery by *Griess* in 1858, aromatic diazonium compounds have acquired considerable industrial and scientific importance[1, 2]. In contrast, their aliphatic analogues, the alkenediazonium salts, were known for a long time only as short-lived intermediates[3–6] which, up to a few years ago, could not be utilized in syntheses. The main reasons for this are the remarkably strong structure-dependence of the thermal stability of the alkenediazonium ions and their high reactivity toward nucleophilic agents. This account intends to describe methods which have been developed for the synthesis of stable alkenediazonium salts. The differences in behavior of alkenediazonium salts and aromatic diazonium compounds will be demonstrated by various substitution reactions. The IR spectra of substituted ethylenediazonium ions provide a good insight into the bond character of the diazonium group.

2. Synthesis of Alkenediazonium Salts

2.1. Diazonium Salts from α-Diazocarbonyl Compounds

Since their discovery, α-diazo-β-dicarbonyl compounds have been known to survive dissolution in cold, concentrated mineral acids[7, 8]. However, subsequent attempts[9] to isolate the protonation products assumed to be present in such solutions were unsuccessful.

A kinetic study of the decomposition of diazomalonic ester with chlorosulfonic acid and methylsulfuric acid in 1,2-dichloroethane led to the assumption of a proton-adduct corresponding to the diazonium salt *(1)*, which decomposes according to a first-order rate law with the elimination of nitrogen. As shown by Figure 1, the rate of the volumetrically determined nitrogen evolution is largely independent of the concentration

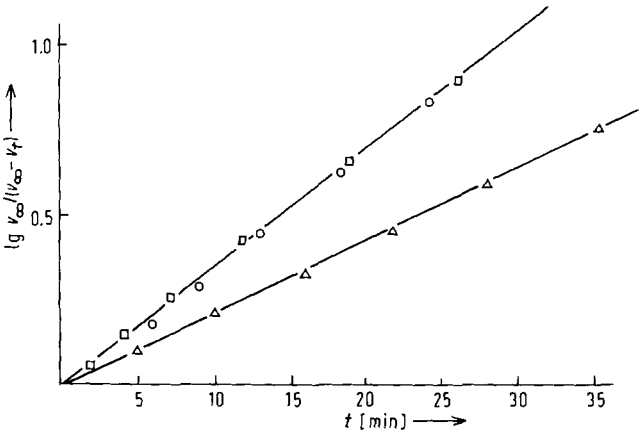
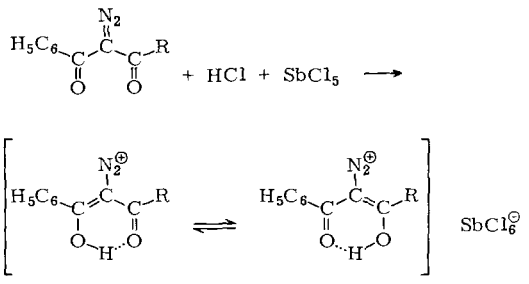


Fig. 1. Decomposition of diazomalonic ester at 16 °C in 1,2-dichloroethane (0.020 mol/l) with chlorosulfonic acid (△, 0.242 mol/l) or methylsulfuric acid (○, 0.238 mol/l; □, 0.443 mol/l).

and the strength of acid used in excess. Analogous measurements with α-diazo-β-disulfones have shown that, at the same temperatures and concentrations, chlorosulfonic acid reacts about 3000 times more rapidly than methylsulfuric acid[10].



(1)

R	Yield [%]	Decomposition at [°C]
OCH_3	81	114
CH_3	92	97
C_6H_5	96	116

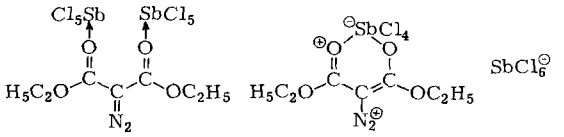
[*] Dr. K. Bott
Hauptlaboratorium der BASF Aktiengesellschaft
D-6700 Ludwigshafen (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0259 $ 02.50/0

Dissolution of hydrogen chloride, antimony pentachloride, and methyl benzoyldiazoacetate, or benzoyldiazoacetone, or benzoyldiazoacetophenone in dichloromethane affords crystalline salts *(1)* of hexachloroantimonic acid with the diazo compound[11].

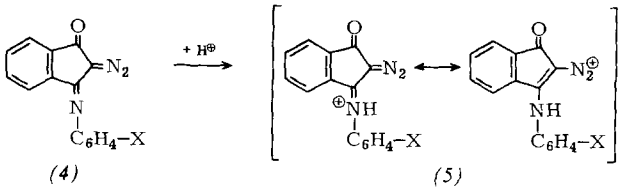
The colorless salts *(1)* contain diazonium ions derived from the enolic form of a β-oxo ester or a β-diketone. Because of the low vapor pressure of HCl (<1 torr at 25°C), it can be assumed that these hydroxyalkenediazonium ions have the *cis* configuration, with a strong intramolecular hydrogen bond[12]. The thermal stability of the salts *(1)* is remarkable; their chemical behavior is determined largely by their acidic character. Thus, the action of triethylamine leads to complete deprotonation and regenerates the α-diazo-β-dicarbonyl compounds.

In the presence of hydrogen chloride and antimony pentachloride, diazomalonic ester does not add a proton, but reacts with two molecules of the Lewis acid[11]. Regarding the two structural possibilities, namely an addition complex *(2)* or a diazonium chelate *(3)* with salt character, measurement of the electrical conductivity in liquid sulfur dioxide provides evidence in favor of *(3)*.



(2) *(3)*

Boron trichloride and boron trifluoride also combine with dicarbonyl diazo compounds, to form 2:1 addition products, for which *Fahr* and *Hörmann*[9] suggest structures analogous to the complex *(2)*. The more strongly basic imines *(4)* are already protonated in ethanol/water by mineral acids yielding salts of type *(5)*, whose properties are in agreement with the two resonance structures, *viz.* diazoimonium ion and aminoalkenediazonium ion[13].

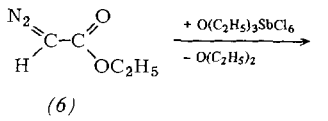


(4) *(5)*

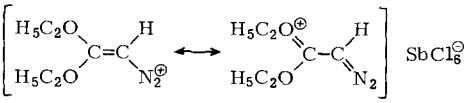
X = H, *p*-Cl, $-NO_2$, $-CH_3$, -I, $-OCH_3$

Although the acid-sensitivity of α-diazomonocarbonyl compounds such as diazoacetic ester *(6)* or *p*-nitrophenyldiazoacetic acid piperidide *(7)* excludes salt formation with strong protonic acids, the alkylation of the carbonyl oxygen with triethyloxonium hexachloroantimonate affords the substituted ethylenediazonium salts *(8)* and *(9)*[11], which can also be regarded as oxonium or as imonium compounds. *(8)* decomposes at 115°C and *(9)* at 127°C.

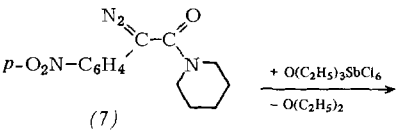
When *(6)* and *(7)* are transformed into the ions *(8)* and *(9)*, the frequencies of the respective NN stretching vibrations are shifted by 80 and 30 cm^{-1}. The magnitude of this frequency shift ($\Delta\tilde{\nu}$NN) and the position of the diazo absorption band



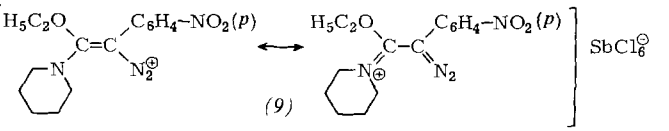
(6)



(8)



(7)

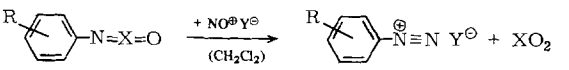


(9)

provide a simple means of estimating the approach to a real nitrogen-nitrogen triple bond (see Section 4).

2.2. Diazonium Salts from Isocyanates and Sulfinylamines

The observation crucial to the development of syntheses of ethylenediazonium salts without substituents at C2 capable of displaying resonance was that the salt *(8)* is resistant to acetic acid at room temperature but loses nitrogen spontaneously with methanol. This shows that methanol adds to the activated carbon-carbon double bond of *(8)*, to give a very short-lived alkanediazonium ion. The transformations selected as model reactions, namely those of nitrosyl salts with aryl isocyanates *(10a)* or arylsulfinylamines *(10b)* should permit preparation of arenediazonium ions in the absence of alcohols and water. Whereas the sulfinylamines *(10b)* are transformed almost quantitatively into aryldiazonium salts *(11)*[14], the desired reaction does not occur with phenyl isocyanate *(10a)*, R = H.



(10) *(11)*

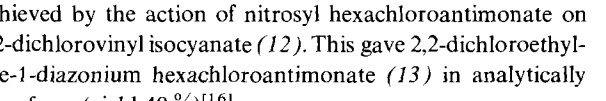
(10a), X = C, R = H

(10b), X = S, R = *p*-Cl, *p*-O_2N, *m*-O_2N

Y = $SbCl_6$, ClO_4

Our assumption that the nitrosyl cation preferentially attacks the benzene ring in the case of phenyl isocyanate was later confirmed by *Olah*[15]: alkyl isocyanates react with nitrosyl salts to give alkanediazonium salts, identified by their secondary products.

The analogous synthesis of an alkenediazonium salt was achieved by the action of nitrosyl hexachloroantimonate on 2,2-dichlorovinyl isocyanate *(12)*. This gave 2,2-dichloroethylene-1-diazonium hexachloroantimonate *(13)* in analytically pure form (yield 40%)[16].

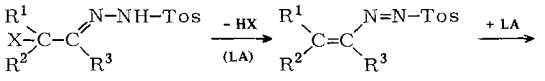


(12) *(13)*

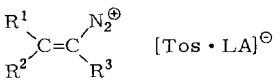
It still remains to be established whether other vinyl isocyanates are also suitable for these reactions. Vinylsulfinylamines, which could also be considered as potential starting materials, are still unknown.

2.3. Alkenediazonium Salts from Sulfonylhydrazones

The action of Lewis acids on the *p*-toluenesulfonylhydrazones *(14)* of α-halo aldehydes or ketones constitutes a simple and efficient synthesis of alkenediazonium salts of the type *(16)*[17–19]. Suitable Lewis acids are antimony pentachloride, stannic chloride, and aluminum trichloride, and in this reaction sequence they fulfil several functions. They catalyze the elimination of hydrogen halide from the sulfonylhydrazones *(14)*, and they remove the *p*-toluenesulfinate anion from the azosulfone intermediate *(15)* in the subsequent step. Finally, they are necessary for the formation of the complex anion in the final product *(16)*. The hydrazones *(14)* can also contain an alkoxy or acyloxy group instead of the halogen, provided that their elimination is favored by geminal substituents R^1 and R^2.



(14) *(15)*

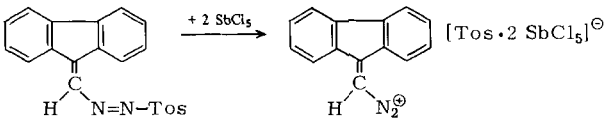


(16)

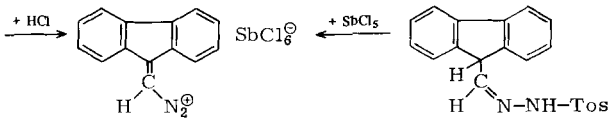
LA = Lewis acid
X = F, Cl, Br
Tos = *p*-CH_3–C_6H_4–SO_2

The rates of the formation of *(16)* parallel the well known sequence of strengths of the Lewis acids in Friedel-Crafts reactions[20], *i.e.* $AlCl_3 > SbCl_5 > SnCl_4$. As the first step of this sequence, hydrogen halide elimination can sometimes become rate-determining for the overall reaction, when relatively weak Lewis acids such as $SnCl_4$ are used. In such cases it is advantageous to produce the sulfonylazoalkene *(15)* separately, using a suitable base[21] (see Section 2.3.1).

Antimony pentachloride is preferred as the Lewis acid, since the diazonium hexachloroantimonates were found to be well-crystalline compounds. The salt *(18)*, which results from the azofulvene *(17)* and two molecules of $SbCl_5$, is transformed almost quantitatively into crystalline hexachloroantimonate *(19)* by the action of hydrogen chloride.



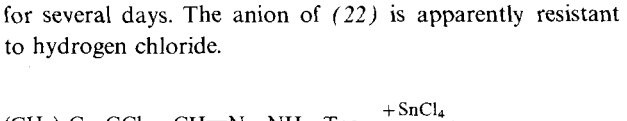
(17) [≡*(15a)*] *(18)*



(19) *(20)*

Furthermore, *(19)* arises directly from 9-fluorenecarbaldehyde *p*-toluenesulfonylhydrazone *(20)* and antimony pentachloride, the latter also acting as an oxidizing agent in this case.

2-Chloro-3,3-dimethyl-1-butene-1-diazonium tetrachloro(toluenesulfinato)stannate *(22)* crystallizes from a solution of 2,2-dichloro-3,3-dimethylbutyraldehyde tosylhydrazone *(21)* and stannic chloride in dichloromethane on standing for several days. The anion of *(22)* is apparently resistant to hydrogen chloride.



(21) *(22)*

2.3.1. Preparation of the Toluenesulfonylazoalkene Intermediate

The production of the azo compounds *(15)* which appear as short-lived intermediates in the synthesis of alkenediazonium salts can be considered as a variant of the Chattaway reaction[22]. The chemical behavior of *p*-toluenesulfonylazoalkenes *(15)* in the absence of strong acids has been investigated by several authors and was utilized for the synthesis of alkynes[23–25] or alkylidenecyclopropanes[26].

Table 1 shows a selection of azoalkenes *(15a–g)* accessible in pure form[19,21]. The reactions of *p*-toluenesulfonyl hydra-

Table 1. Synthesis of *p*-toluenesulfonylazoalkenes *(15a–g)* $R^1R^2C{=}CR^3{-}N{=}N{-}SO_2{-}C_6H_4{-}CH_3(p)$.

Starting materials	Products *(15)*	R^1	R^2	R^3	Yield [%]	Dec. pt. [°C]
9-Bromo-9-fluorenecarbaldehyde + tosyl hydrazide	*(15a)*	2,2'-Biphenylylene		H	84	125–126
(20) + Br_2/pyridine [27]	≡ *(17)*				87	
9-Acetyl-9-bromofluorene + tosyl hydrazide	*(15b)*	2,2'-Biphenylylene		CH_3	77	140–141
(20a) [a] + I_2/pyridine [27]					89	
Tetrachloro-3-butenal + tosyl hydrazide	*(15c)*	$Cl_2C{=}CCl$	Cl	H	—	88
(14), X = Br + NaOH	*(15d)*	Br	Br	H	83	90–91
(14), X = Cl + $N(C_2H_5)_3$	*(15e)*	Cl	Cl	CH_3	69	108–109
(14), X = Cl + $N(C_2H_5)_3$	*(15f)*	$(CH_3)_3C$	Cl	H	69	70
(14), X = Br + $N(C_2H_5)_3$	*(15g)*	$(CH_3)_3C$	Br	H	67	72–74

[a] *(20a)* = 9-Acetylfluorene-*p*-toluenesulfonylhydrazone.

zide with α-halogenated aldehydes and ketones that also contain a C_α-aryl or -vinyl groups lead directly to the sulfonylazoalkenes [for example *(15a—c)*]. Apparently, aryl and vinyl groups strongly accelerate the subsequent reaction of the sulfonylhydrazones *(14)* to *(15)*, since this reaction occurs with a gain in resonance energy. The azoalkenes *(15a)* [≡ *(17)*] and *(15b)* can also be prepared by oxidation of the halogen-free sulfonylhydrazones according to a method described by *Schantl*[27].

Toluenesulfonylhydrazones of aldehydes and ketones bearing only halogen atoms or a halogen and *tert*-alkyl groups attached to C-2 require a base for elimination of hydrogen halide (*e.g.* triethylamine or aqueous sodium hydroxide). Among the azoalkenes *(15d—g)* synthesized by this route, *(15f)* and *(15g)* are stable at room temperature for only a few hours.

2.3.2. Diazonium Salts from Aldehyde Sulfonylhydrazones[19]

Table 2 lists the β-substituted ethylenediazonium compounds that have been prepared by the toluenesulfonylhydrazone method, in the order of decreasing decomposition temperatures. The stabilizing effect of chlorine is clearly evident. If one chlorine atom of *(13)* is replaced by hydrogen or

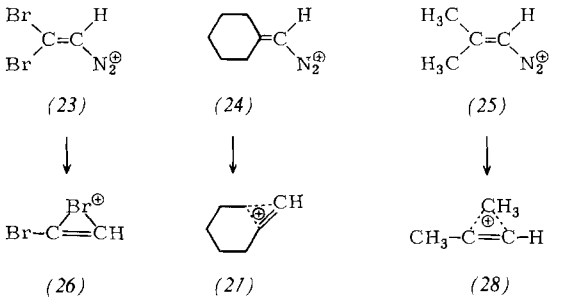
Table 2. β-Substituted ethylenediazonium hexachloroantimonates and tetrachloro(toluenesulfinato)stannates $R^1R^2C{=}CH{-}N_2^{\oplus}Y^{\ominus}$.

	R^1	R^2	Y	Decomposition at [°C]	Color
(13)	Cl	Cl	$SbCl_6$	131—132	colorless
(49)	$Cl_2C{=}CCl$	Cl	[Tos·$SnCl_4$]	112 [a]	yellow
(48)	Cl	H	$SbCl_6$	97—98	colorless
(19)	2,2′-Biphenylylene		$SbCl_6$	95	green-brown
(46)	$(CH_3)_3C$	Cl	$SbCl_6$	86—87	colorless
(22)	$(CH_3)_3C$	Cl	[Tos·$SnCl_4$]	78—80	colorless
	Br	Br	$SbCl_6$	58 [b]	pale yellow
	$(CH_3)_3C$	Br	[Tos·$SnCl_4$]	58	colorless
	1-Adamantyl	Br	$SbCl_6$	50—52	pale yellow
	H_5C_2	Cl	$SbCl_6$	[c]	—

[a] $CCl_2{=}CCl{-}CCl{=}CH{-}N_2^{\oplus}$ [$2SbCl_5$·Tos]$^{\ominus}$ decomposes at 90°C. [b] Compare *(23)*. [c] The compound can only be obtained as a solution (CH_2Cl_2) stable at room temperature.

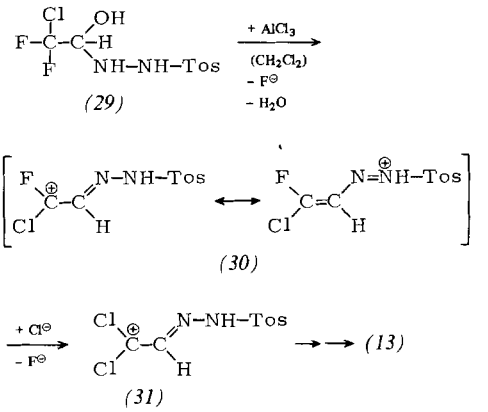
by a *tert*-butyl group, or if both chlorine atoms are replaced by a *tert*-butyl group and bromine, or by the 1-adamantyl substituent and bromine, the thermal stability of the resulting diazonium salt is decreased. A similar introduction of a trichlorovinyl or 2,2′-biphenylyl group decreases the stability to a smaller extent.

A plausible explanation for the different thermal stabilities of the β-substituted ethylenediazonium salts is that, in general, the elimination of nitrogen does not yield the particularly unstable primary vinyl cations [*e.g.* as in the case of *(13)*], but rather bridged cations such as *(26)*—*(28)*, which can already profit from the lower energy level of a completely rearranged intermediate[28–31]. Thus, it is not surprising that the alkenediazonium ions *(24)* and *(25)*, derived from 1-chlorocyclohexanecarbaldehyde- and α-chloroisobutyraldehyde toluenesulfonylhydrazone respectively, spontaneously eliminate nitrogen at temperatures as low as 5 to 10°C. The pronounced tendency of the cyclohexylidenemethanediazonium ion *(24)* to undergo decomposition corresponds to

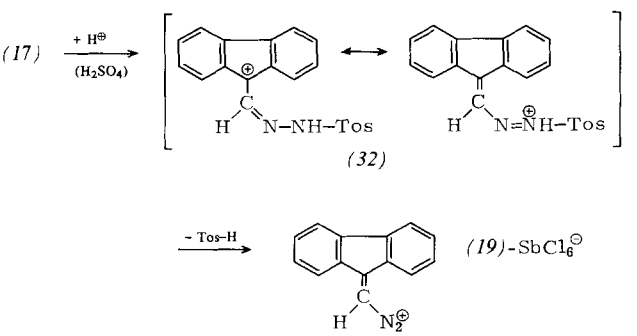


the accelerated solvolysis of cyclohexylidenemethyl trifluoromethanesulfonate, which undergoes ring expansion to give cycloheptanone, probably *via (27)*[32].

The influence of fluorine in the β-position upon the strength of the bonding of the diazonium group is of interest in this connection. While antimony pentachloride, antimony pentafluoride, or aluminum trichloride does not react with trifluoroacetaldehyde tosylhydrazone (as hydrate), reaction of the corresponding chlorodifluoro derivative *(29)* and aluminum trichloride in dichloromethane gives a solution of the 2,2-dichloroethylenediazonium ion. This ion is precipitated by the readily soluble isopentadecylammonium hexachloroantimonate as the salt *(13)*[33]. The replacement of fluorine by chlorine, necessary for the formation of *(13)*, probably takes place in the resonance-stabilized cationic intermediate *(30)*.



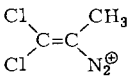
The protonation product *(32)* of the azo compound *(17)* [≡ *(15a)*], which corresponds to the short-lived intermediates *(30)* and *(31)*, can be observed directly in sulfuric acid, since transformation of the dark red *(32)* into the olive-green cation of *(19)* goes to completion only after one or two minutes even at room temperature.



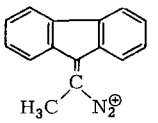
2.3.3. Diazonium Salts from Ketone Sulfonylhydrazones[19]

The diazonium group plays an outstanding role[34] in the generation of carbenium ions by heterolytic bond fission because of the great ease with which a nitrogen molecule can be eliminated. This is why alkenediazonium ions with an alkyl or aryl substituent on the diazo carbon can exist under normal conditions only if the energy level of the resultant vinyl cations is raised by an opposing effect.

For example, in compounds *(13)* and *(19)*, replacement of the α-hydrogen by a methyl group leads to the ions *(33)* and *(34)*. The salts of the 1,1-dichloropropene-2-diazonium ion *(33)* can only be isolated and characterized at temperatures below −20 °C, since they decompose with evolution of



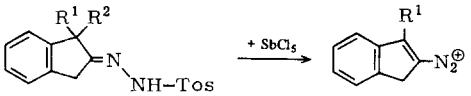
(33)



(34)

nitrogen even at −10 to 0 °C both as solids and in solution. Even at −20 °C, the reaction of the azo compound *(15b)* with antimony pentachloride gives no indication that *(34)* can exist for only a few minutes under these conditions.

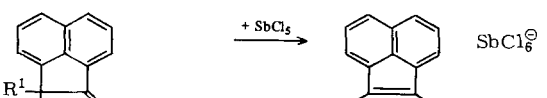
As shown by solvolyses of cyclic vinyl trifluoromethanesulfonates[35], vinyl cations with nonlinear σ-bonds are less stable than those with linear bonds. According to our investigations[36], however, the higher energy level of the 1-cyclopentenyl and 1-cyclohexenyl cations still does not permit the isolation of cyclopentene- or cyclohexenediazonium salts at 0 °C. Only in the indene-2-diazonium ion *(36a)*, and in its 3-phenyl derivative *(36b)*, does the five-membered ring become so rigid by the incorporation of four sp^2-centers that *(36a)* and *(36b)* fail to eliminate nitrogen at room temperature.



(35a, b) *(36a, b)*

(a), R^1 = H, R^2 = AcO
(b), R^1 = C_6H_5, R^2 = H

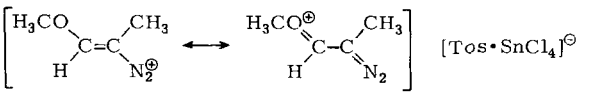
Reaction of the hydrazones *(37a)* and *(37b)* with antimony pentachloride yields the even more strained acenaphthylene-1-diazonium hexachloroantimonates *(38a)*, or *(38b)* with an aryl substituent at the diazonium carbon atom. The remarkable stability of *(38a)*, which is even greater in its derivative *(38b)*, due to fluorine substitution, arises for geometric reasons: in the diazonium ion *(38a)* the aryl substituent can only stabilize the vinyl cation resulting from loss of nitrogen when it is oriented perpendicularly to the σ-bond skeleton of the olefinic carbons. Such an orientation is completely ruled out because of the "fusion" of the five-membered ring with the naphthalene system. Likewise, the 3-phenyl-2-indenyl cation which corresponds to the indenediazonium ion *(36b)* is unable to lower its energy level by migration of the phenyl group to C-2.—"Aromatic" diazonium ions of acenaphthylene are still unknown.



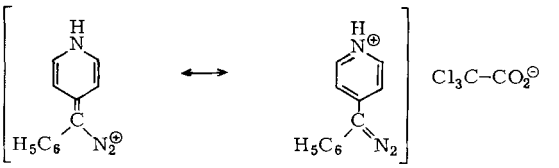
(37a, b) *(38a, b)*

	R^1	R^2	Decomposition of *(38)* at [°C]
(a)	H	OCH_3	140—141
(b)	F	F	187—188

In addition, the stability of α-alkyl- or α-aryl-ethylenediazonium compounds can be increased by substituents capable of resonance with the diazonium group. Thus, the 1-methoxypropene-2-diazonium salt *(39)* obtained from 1,1-dimethoxyacetone tosylhydrazone and stannic chloride does not decompose below 95 °C.



(39)



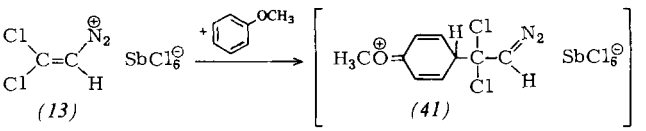
(40)

Both in the α-(*p*-nitrophenyl)ethylenediazonium salt *(9)* and in the salt *(40)*[37] (decomposition at 97 °C), promotion of nitrogen elimination by the phenyl substituent is completely suppressed by the resonance stabilization.

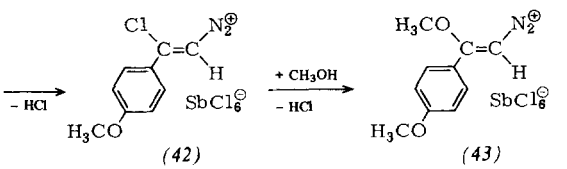
3. Reactions of Alkenediazonium Salts[19]

In contrast to the arenediazonium ions, the alkenediazonium ions can only exist with the anions of very strong acids, and they react spontaneously, even below room temperature, with water, alcohols, carboxylic acids, and other carbonyl compounds.

As shown by the substitution reactions of *(13)* and *(42)*, nucleophiles expectedly attack the β-carbon of the ethylenediazonium group. The particularly electrophilic salt *(13)* can enter the *p*-position in anisole at 0 to 20 °C. Subsequent elimination of hydrogen chloride forms the 2-chloro-2-(*p*-methoxyphenyl)-ethylene-1-diazonium salt *(42)*. While an excess of



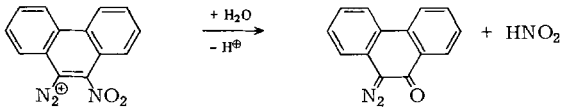
(13) *(41)*



(42) *(43)*

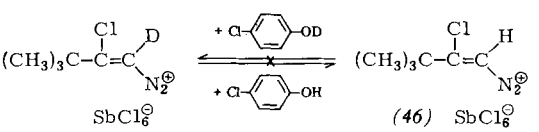
anisole does not react with *(42)*, the more strongly basic methanol can also substitute the second chlorine atom. The yields of the hexachloroantimonates *(42)* and *(43)*, isolated in an analytically pure state and free from isomers, are 61 and 56 %, respectively. The postulated intermediate *(41)* comprises a strong protonic acid and an acid-sensitive diazoalkane group united in a single molecule, but the usual displacement of nitrogen does not occur. The reaction *(42)*→*(43)* is expected to proceed *via* an analogous compound. This reaction requires two or three moles of methanol per mole of *(42)*, presumably because some of the alcohol is "bound" by the hydrogen chloride which is produced. Compound *(43)* ultimately decomposes on addition of yet more methanol.

The NO_2 group of the 10-nitrophenanthrene-9-diazonium ion *(44)*, whose C^9—C^{10} bond partly has an alkene-like character, is also displaced by water in dilute mineral acids, forming diazophenanthrone *(45)*[38].

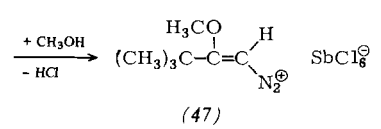


(44) *(45)*

In the 2-chloro-3,3-dimethyl-1-butene-1-diazonium salt *(46)*, the addition of a nucleophilic agent at C-2 is strongly hindered by the bulky *tert*-butyl group. Thus, under the conditions mentioned earlier, neither anisole nor phenol can effect halogen exchange. However, the rapid transformation of *(46)* into 2-methoxy-3,3-dimethyl-1-butene-1-diazonium hexachloroantimonate *(47)* by methanol can be confirmed spectroscopically, since this reaction is accompanied by a characteristic shift of the diazo stretching band toward longer wavelengths (Section 4).



(46)



(47)

The strong deshielding effect of the *tert*-butyl group on the β-carbon in *(46)* provides a method of checking whether the acidity of the α-hydrogen atom is sufficient to establish an acid-base equilibrium in the presence of *p*-chlorophenol. In 1:3 mixtures of *(46)* with *O*-deuterated *p*-chlorophenol in 1,2-dichloroethane, the spectroscopically observed ratio of the two species of protons $[(CH_3)_3C—/{=}CH—N_2^{\oplus}]$ is still 9:1, even after three hours at room temperature.

In the light of the foregoing investigations, it is worth noting the observations by *Newman et al.*[5] and by *Kirmse et al.*[39] that the β,β-dialkylethylenediazonium ions *(24)* and *(25)*, obtained from *N*-nitrosooxazolidones, can be deprotonated to α-diazoolefins by sodium methoxide, and transformed into vinyl azides by alkali azides, in spite of their short lifetimes.

4. Diazo Stretching Vibrational Spectra

Taking the salts *(8)* and *(9)* as examples, it has already been mentioned that electron-donating substituents on C-2 of an ethylenediazonium ion are able to accept a positive charge and can thus reduce the bond order of the NN triple bond. Therefore, with increasing proportion of this resonance structure the frequency of the relevant diazo stretching vibration should decrease. Examples of this are shown in Table 3. 2-Chloroethylenediazonium hexachloroantimonate *(48)* and the next five compounds with halogens and *tert*-alkyl groups on C-2 exhibit diazo absorption bands with the shortest wavelengths. In the two subsequent compounds *(49)* and *(19)* a trichlorovinyl or biphenylylene group is involved in the resonance with the diazonium nitrogen. In the diazonium compounds *(47)*, *(39)*, *(42)*, *(43)*, and *(8)* the presence of *p*-methoxyphenyl and alkoxy groups leads to an even more marked shift of the NN vibrational frequencies. Owing to its long wave absorption maximum, the salt *(9)* can already be compared with diazoacetic ester ($\tilde{\nu}_{NN} = 2105\,cm^{-1}$), while Reimlinger salt *(40)* must be regarded as *N*-protonated phenyl-4-pyridyldiazomethane according to its IR spectrum.

Table 3. NN stretching frequencies of alkenediazonium salts $R^1R^2C{=}CR^3—N_2^{\oplus}Y^{\ominus}$.

	R^1	R^2	R^3	Y	$\tilde{\nu}$ [cm^{-1}]
(48)	Cl	H	H	$SbCl_6$	2260 [a]
(13)	Cl	Cl	H	$SbCl_6$	[b]
(46)	$(CH_3)_3C$	Cl	H	$SbCl_6$	[a]
	Br	Br	H	$SbCl_6$	2240 [b]
	1-Adamantyl	Br	H	$SbCl_6$	[a]
	$(CH_3)_3C$	Br	H	[Tos·$SnCl_4$]	[a]
(49)	$Cl_2C{=}CCl$	Cl	H	[Tos·$SnCl_4$]	2220 [a]
(19)	2,2'-Biphenylylene		H	$SbCl_6$	2210 [c]
(47)	$(CH_3)_3C$	H_3CO	H	$SbCl_6$	2205 [a]
(39)	H_3CO	H	CH_3	[Tos·$SnCl_4$]	2200 [a]
(42)	*p*-$H_3COC_6H_4$	Cl	H	$SbCl_6$	2200 [c]
(43)	*p*-$H_3COC_6H_4$	H_3CO	H	$SbCl_6$	2190 [c]
(8)	H_5C_2O	H_5C_2O	H	$SbCl_6$	2180 [d]
(9)	Piperidino	H_5C_2O	*p*-$O_2NC_6H_4$	$SbCl_6$	2110 [d]
(40)	—CH=CH—NH—CH=CH—		C_6H_5	$Cl_3C—CO_2$	2062 [d]

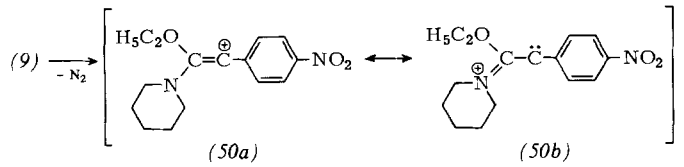
[a] Solid in Nujol. [b] In 1,2-dichloroethane. [c] In nitrobenzene. [d] KBr disk.

The influence of nuclear substituents in aromatic diazonium salts upon the position of the NN absorption bands has already been investigated[40]. The parent compound of the arenediazonium salts, benzenediazonium tetrafluoroborate, whose vibrational band is at 2280 cm^{-1}, should accordingly be placed at the head of Table 3.

5. Final Remarks and Outlook

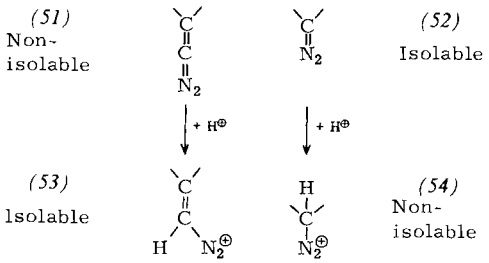
From the various syntheses of alkenediazonium salts considered, we can conclude that those alkenediazonium ions are generally stable enough to be isolated which form high-energy vinyl cations on elimination of nitrogen. The only exceptions to this rule are the resonance-stabilized β-alkoxy- and β-dialkylaminoethylenediazonium salts. These compounds, products of the *O*-alkylation of α-diazocarboxylic acid amides, α-diazocarboxylic acid esters, α-diazoketones, and α-diazoaldehydes, are the links between real alkenediazonium ions and the uncharged aliphatic diazo compounds.

The vinyl cation *(50a)*, obtained in the decomposition of the resonance-stabilized alkenediazonium compound *(9)*,



assumes a similar transition state since, in another resonance form *(50b)*, it can also be regarded as an imonium ion with a β-alkoxycarbene partial structure. The gain in energy due to the resonance between *(50a)* and *(50b)* must however be considerably smaller than the loss in resonance energy that the alkenediazonium salt *(9)* must accept as a consequence of the elimination of the diazonium nitrogen. This was derived from the fact that in *(9)* the nitrogen is no longer the good leaving group that it normally is.

When alkenediazonium ions have an H-atom on the α-carbon, they can be regarded as protonated α-diazoalkenes. A comparison of the α-diazoalkenes *(51)* with the diazoalkanes *(52)* shows that in the first case only the protonated species *(53)* can be isolated, whereas the alkyldiazonium ions *(54)* derived from the isolable diazoalkanes *(52)* occur only as short-lived intermediates.



The introduction of the diazonium group into alkenes produces species surpassing even tetracyanoethylene in their electrophilic properties. For this reason the reactions of ethylenediazonium salts with other alkenes and "1,3-dipoles" most likely possess considerable synthetic potential. An indication of cycloadditions of alkenediazonium ions to the nitro group is provided by the observation that the particularly reactive compounds *(13)* and *(38a)* eliminate nitrogen in nitrobenzene solution even at room temperature.

Furthermore, alkenediazonium ions provide a means of investigating the stability of vinyl cations in a range that is inaccessible by the heterolysis of vinyl perfluoroalkanesulfonates. In this field, interest is centered mainly on the generation of primary vinyl cations which have so far only been unequivocally detected on the addition of 1-adamantyl cations to acetylene[41] or on the photolysis of iodoolefins[42].

Received: December 1, 1978 [A 265 IE]
German version: Angew. Chem. *91*, 279 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] *K. H. Saunders:* The Aromatic Diazo-Compounds and their Technical Application. Edward Arnold, London 1949.
[2] *H. Zollinger:* Diazo and Azo Chemistry. Wiley-Interscience, New York 1961.
[3] *D. Y. Curtin, J. A. Kampmeier, B. R. O'Connor*, J. Am. Chem. Soc. *87*, 863 (1965); *D. Y. Curtin, J. A. Kampmeier, M. L. Farmer, ibid. 87*, 874 (1965).
[4] *W. M. Jones, F. W. Miller*, J. Am. Chem. Soc. *89*, 1960 (1967).
[5] *M. S. Newman, A. O. M. Okorodudu*, J. Org. Chem. *34*, 1220 (1969).
[6] *M. S. Newman, C. D. Beard*, J. Am. Chem. Soc. *92*, 7564 (1970).
[7] *L. Wolff, P. Bock, G. Lorentz, P. Trappe*, Justus Liebigs Ann. Chem. *325*, 129 (1902).
[8] *H. Staudinger, J. Becker, H. Hirzel*, Ber. Dtsch. Chem. Ges. *49*, 1978 (1916).
[9] *E. Fahr, W. D. Hörmann*, Justus Liebigs Ann. Chem. *682*, 48 (1965).
[10] *F. Klages, H. A. Jung, P. Hegenberg*, Chem. Ber. *99*, 1704 (1966).
[11] *K. Bott*, Angew. Chem. *76*, 992 (1964); Angew. Chem. Int. Ed. Engl. *3*, 804 (1964); Tetrahedron *22*, 1251 (1966).
[12] *F. Klages, E. Zange*, Chem. Ber. *92*, 1828 (1959).
[13] *M. Regitz, H. Schwall*, Justus Liebigs Ann. Chem. *728*, 99 (1969).
[14] *K. Bott*, Angew. Chem. *77*, 132 (1965); Angew. Chem. Int. Ed. Engl. *4*, 148 (1965).
[15] *G. A. Olah, N. Friedman, J. M. Bollinger, J. Lukas*, J. Am. Chem. Soc. *88*, 5328 (1966).
[16] *K. Bott*, Tetrahedron Lett. *1971*, 2227.
[17] *K. Bott*, DOS 2042986 (1970), Chemische Werke Hüls; Chem. Abstr. *76*, 126374n (1972).
[18] *K. Bott*, Angew. Chem. *82*, 953 (1970); Angew. Chem. Int. Ed. Engl. *9*, 954 (1970).
[19] *K. Bott*, Chem. Ber. *108*, 402 (1975).
[20] *K. Bodendorf, H. Böhme*, Justus Liebigs Ann. Chem. *516*, 1 (1935).
[21] *K. Bott*, Synthesis *1973*, 161.
[22] *F. D. Chattaway, R. Bennett*, J. Chem. Soc. *1927*, 2850.
[23] *A. Eschenmoser, D. Felix, G. Ohloff*, Helv. Chim. Acta *50*, 708 (1967).
[24] *P. Wieland*, Helv. Chim. Acta *53*, 171 (1970).
[25] *G. Rosini, S. Cacchi*, J. Org. Chem. *37*, 1856 (1972).
[26] *P. J. Stang, D. P. Fox*, J. Org. Chem. *42*, 1667 (1977).
[27] *J. Schantl*, Monatsh. Chem. *103*, 1705 (1972).
[28] *G. Modena, U. Tonellato*, Adv. Phys. Org. Chem. *9*, 185 (1971).
[29] *M. Hanack*, Acc. Chem. Res. *9*, 364 (1976).
[30] *M. Hanack*, Angew. Chem. *90*, 346 (1978); Angew. Chem. Int. Ed. Engl. *17*, 333 (1978).
[31] *P. J. Stang*, Acc. Chem. Res. *11*, 107 (1978).
[32] *P. J. Stang, T. E. Dueber*, Tetrahedron Lett. *1977*, 563.
[33] *K. Bott*, Fette, Seifen, Anstrichm. *76*, 443 (1974).
[34] *W. Kirmse*, Angew. Chem. *88*, 273 (1976); Angew. Chem. Int. Ed. Engl. *15*, 251 (1976).
[35] *W. D. Pfeifer, C. A. Bahn, P. v. R. Schleyer, S. Bocher, C. E. Harding, K. Hummel, M. Hanack, P. J. Stang*, J. Am. Chem. Soc. *93*, 1513 (1971).
[36] *H. Klingelhöfer*, Ingenieurarbeit, Fachhochschule Münster 1972.
[37] *H. Reimlinger*, Angew. Chem. *75*, 788 (1963); Angew. Chem. Int. Ed. Engl. *2*, 482 (1963).
[38] *J. W. Barton, A. R. Grinham, E. K. Whitaker*, J. Chem. Soc. *C 1971*, 1384.
[39] *W. Kirmse, O. Schnurr*, J. Am. Chem. Soc. *99*, 3539 (1977).
[40] *K. B. Whetsel, G. F. Hawkins, F. E. Johnson*, J. Am. Chem. Soc. *78*, 3360 (1956).
[41] *K. Bott*, Justus Liebigs Ann. Chem. *766*, 51 (1972).
[42] *S. A. McNeely, P. J. Kropp*, J. Am. Chem. Soc. *98*, 4319 (1976).

Kinetics of Sorption, Desorption, and Diffusion in Zeolites

By Hans-Joachim Doelle and Lothar Riekert[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Sorption and desorption in zeolites (molecular sieves) have to be considered as complex processes, involving simultaneous diffusion in zeolite crystals, mass transfer in the intercrystalline voids of a pellet, and heat transfer between the zeolitic sorbent and its surroundings. The kinetics of sorption and desorption, respectively, of n-C_4H_{10} in zeolite X and of CO_2 in zeolite A have been investigated: only the initial rates of uptake or release of the sorbate are controlled by mass transfer alone whereas ultimately they also depend on the rate of heat transfer from the sorbent to its surroundings or *vice versa*. Diffusivities of the sorbate in the zeolite crystals can be obtained from the kinetics of mass transfer, provided the resistance due to viscous or Knudsen flow between the crystals of the zeolitic sorbent can be eliminated. A sample consisting of a monolayer of single crystals had to be used for this purpose in the n-butane/zeolite X system; the intracrystalline diffusivity obtained in this way is not in conflict with data obtained by NMR spectroscopy. The intracrystalline diffusivities obtained in this way—taking into account the coupling of several processes during sorption—are higher than values reported in the literature.

1. Introduction: Sorption, Diffusion, and Self-Diffusion in Zeolites

Zeolites (natural or synthetic crystalline aluminosilicates) have found important applications as sorbents and catalysts in commercial processes[1]. On conventional sorbents or catalysts adsorption takes place in a two-dimensional phase boundary whereas in zeolites guest molecules can penetrate into the relatively open crystal structures. These guest molecules can be considered as dissolved in a solid rather than being adsorbed at a surface, since the size of the "cavities" in the crystal structures (0.5—2 nm) is of the same order of magnitude as are the collision cross-sections of small molecules. At equilibrium, the sorbate will be distributed randomly in the crystal. The kinetics of sorption and desorption in zeolites as well as the activity and selectivity of zeolite catalysts may be strongly dependent on the rate of migration of the sorbate in the solid.

It therefore appears expedient to have some knowledge about the diffusivities of sorbed molecules in zeolite crystals when considering various applications. Zeolites can be synthesized as crystals with diameters of about 1 μm; crystal diameters up to 100 μm can be prepared by special methods. It is therefore not possible to measure diffusivities in zeolites *via* steady state rates of permeation—as for example in a foil of plastic material. Diffusivities can be deduced from material fluxes in zeolites only by observing rates of sorption or desorption, *i.e.* by studying non-steady-state kinetics. Information about the mobility of sorbed molecules in zeolites can also be obtained independently by NMR spectroscopy. Unfortunately, the results of several investigations along these lines appear inconsistent. For example, different values of the diffusivity of C_2H_6 in Na-mordenite have been found for sorption and desorption; the coefficient of diffusion thus depends on the direction of the net flux[2]. A diffusivity that is different by a factor of roughly 10^2 was found for the same system by a chromatographic pulse method[3]. The discrepancies between diffusion coefficients which have been found from observed rates of sorption on the one hand and coefficients of self-diffusion as obtained by the NMR spin-echo method on the other hand are even more striking.

The mean square displacement $\langle \Delta X^2 \rangle$ of a molecular species in sorption equilibrium during a given time interval Δt is observed by spin-echo experiments. $\langle \Delta X^2 \rangle$ will depend only on the random movement of the sorbate in the zeolite crystals if the amount of this substance in the gas phase is negligible compared to the amount which is sorbed in the solid, which will be the case at low temperatures. For sufficiently small time intervals Δt, the root mean square displacement $\langle \Delta X^2 \rangle^{1/2}$ will furthermore be small compared to the linear dimensions of the crystallites. Under these conditions the coefficient D^* of self-diffusion of the sorbate follows from $\langle \Delta X^2 \rangle$ and Δt as[4]:

$$D^* = \frac{\langle \Delta X^2 \rangle}{6 \Delta t}$$

This coefficient D^* characterizes the mobility of sorbed particles in a system where sorption equilibrium is established, the density of sorbed particles being constant in space and time. The diffusivity D as obtained from the kinetics of sorption or desorption on the other hand is defined by the diffusion equation

$$\frac{\partial c}{\partial t} = \operatorname{div}(D \operatorname{grad} c) \qquad (1)$$

(c = concentration of sorbate in a zeolite crystal) which is used in its integrated form to describe the net flux of material with respect to the coordinates of the solid. As long as the sorbed particles do not interact—their random movements thus being independent (at low degrees of saturation θ)—the

[*] Prof. Dr. L. Riekert, Dr. H.-J. Doelle
Lehrstuhl für Chemische Verfahrenstechnik der Universität
Postfach 6380, D-7500 Karlsruhe (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0266 $ 02.50/0

coefficients D^* and D should be equal, whereas at higher degrees of saturation a simple theory of random movement of sorbed particles requires that D^* be smaller than D[5]. The same condition should be expected from a widely assumed relation (2) between the ratio D^*/D and the slope of the equilibrium isotherm

$$\frac{D^*}{D} = \frac{d\ln c}{d\ln p} = \frac{d\ln \theta}{d\ln p} \qquad (2)$$

which is (incorrectly) known as *Darken*'s equation. Within the linear range of the isotherm, equation (2) requires $D^* = D$, whereas at higher degrees of saturation (θ) its validity appears to be dubious[6]. Theory thus requires that D^* and D be of the same order of magnitude at least within a wide range of θ and also, that D^* should *not* be greater than D at a given temperature. Values of D^* obtained from NMR spectroscopy, however, are greater by factors between 10^3 and 10^5 than values of D found from sorption kinetics for the same sorbate-zeolite systems[7]. In view of these rather striking contradictions it was suspected that the kinetics of sorption in zeolites is not controlled exclusively by diffusion in the solid, and it has been proposed that coefficients of diffusion D in zeolites obtained from sorption kinetics be considered as compound quantities, which may also be influenced by processes other than the migration of the sorbate in the solid[7, 8].

In order to obtain "true" diffusivities of the sorbate in the zeolite crystals from sorption kinetics we have attempted to determine experimentally the relative influence of the following processes on the rate of uptake or desorption:

- mass transfer of sorbate in the gas phase and in the intercrystalline voids of the zeolite sample,
- transfer through the gas/solid phase boundary,
- diffusion in the volume of the crystals,
- heat transfer between solid and surroundings.

It was also a goal of this investigation[9] to gain some insight into the kinetics of sorption in commercial applications of zeolites, information which might perhaps be useful with respect to the optimal size, structure, *etc.* of zeolitic sorbents.

2. Experimental Investigation of Sorption Kinetics

The kinetics of sorption or desorption was observed in a system consisting of a gas phase and the solid, initially at equilibrium, the amount of sorbate in the solid being recorded following an increase or decrease of pressure in the gas at time zero. The gas phase consisted of only one component; any external resistance to mass transfer can thus arise only from the flux of the gas in the voids (macroscopic pores) between the crystals of the zeolite sample. The change of pressure at time zero should ideally be instantaneous, a condition which can only be approximated. The change of the gas pressure with time must be symmetrical in sorption and in desorption; otherwise different initial conditions could be responsible for an apparent discrepancy between the rate of sorption as compared to desorption. The finite rates of response of sensors and recording equipment has to be considered in evaluating the observations.

The apparatus shown schematically in Figure 1 has been used to determine sorption isotherms as well as the kinetics

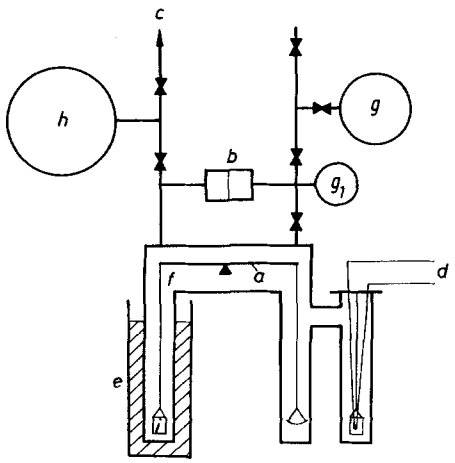


Fig. 1. Apparatus (schematic): a, balance (Cahn R 100); b, differential pressure transducer (MKS baratron 77); c, turbomolecular pump; d, thermocouple (Pt/PtRh, 0.1 mm diam.); e, constant temperature water bath; f, volume with sample and balance (3.075 l); g, storage vessel; g_1, storage vessel (0.285 l); h, evacuated buffer volume (50 l); i, sample pan.

of sorption and desorption. The zeolite sample in the form of either a bed of small crystals or a monolayer of larger single crystals was placed in the sample pan of an electric microbalance (sensitivity 0.5 μg); the pressure in the system was observed through a membrane-capacitance manometer. The overall time constants for the recording of changes of sample mass or pressure were found to be 0.15 s. The system was evacuated by a turbomolecular pump; the temperature of the glass leg containing the sample was kept constant within ±0.1 K during sorption experiments; an electric furnace was used for outgassing. The volume f containing the sample was connected at time zero for 0.2 s to the storage volume g_1 in order to obtain an increase in pressure; a decrease in pressure was obtained by connecting for 0.2 s to the evacuated vessel h. The change of the amount of sorbate in the solid was then recorded *via* the balance, the control volume of the closed system being always the same. The pressure p in the system changes linearly with the amount n of sorbate in the solid, because the total amount of substance either in the gas or in the solid is constant during each run. This condition had to be taken into account when diffusion coefficients were evaluated; solutions of the diffusion equation for this particular condition have been given by *Barrer*[10] and by *Crank*[11]. The variation of the temperature of the zeolite due to sorption or desorption was monitored in separate experiments but under identical conditions by a miniature thermoelement (0.1 mm diameter) embedded in the sample. The zeolite samples were degassed for 3 h at 573 K and $p < 10^{-2}$ Pa before starting the first sorption experiment.

Zeolites NaX and NaA were synthesized as relatively large crystallites (diameters ranging from 5 to 100 μm) by the method described by *Charnell*[12]. Crystal structures were verified by X-ray diffraction; the composition of the dry materials was analyzed as

zeolite NaX: $Na_2O \cdot Al_2O_3 \cdot (SiO_2)_{2.26}$
zeolite NaA: $Na_2O \cdot Al_2O_3 \cdot (SiO_2)_{2.0}$

Samples with a fairly narrow size distribution of the crystals (80±10 μm for NaX; 30±5 μm for NaA) were obtained by wet sieving. The gases used were *n*-butane (purity better than

99.8 mol %) and carbon dioxide (purity better than 99.995 mol %).

3. The *n*-Butane/Zeolite NaX System

Equilibrium isotherms of *n*-butane sorbed in NaX are shown in Figure 2 for temperatures between 25 and 40 °C. A constant isosteric heat of sorption $\Delta H_s = -39\,\mathrm{kJ\,mol^{-1}}$ follows from these data with the equation

$$\Delta H_s = RT^2 \left(\frac{\partial \ln p}{\partial T}\right)_{n/m}$$

for sorbate concentrations up to 6 wt %.

All kinetic observations were conducted in this range of saturation, where the isotherm at 25 °C can be represented with an accuracy of ±5 % by the linear relation

$$\frac{n}{m} = K \cdot p \text{ with } K = 3 \times 10^{-5}\ \mathrm{mol\ g^{-1}\ Pa^{-1}} \qquad (3)$$

(n = amount of sorbed butane, m = mass of sorbate-free, dry zeolite).

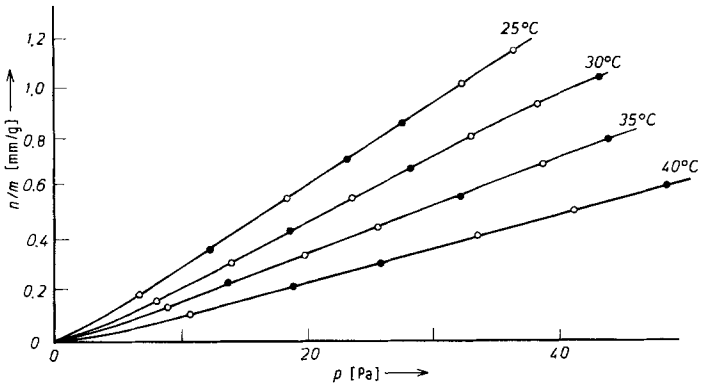


Fig. 2. Isotherms of *n*-butane in zeolite NaX; equilibrium reached in sorption (○) and in desorption (●).

The kinetics of sorption and desorption was studied with samples consisting of loose piles (beds) of the same crystals but of different heights, in order to find out whether mass transfer in the void fraction along the height of the bed has any influence on the observed rates. The observed kinetics are represented by plotting the dimensionless quantity $\Delta n/(\Delta n)_f$ as a function of time t or $\sqrt{t}$. $\Delta n/(\Delta n)_f$ gives the (positive or negative) change Δn of the amount n of sorbate in the solid as a fraction of the final change $(\Delta n)_f$

$$\frac{\Delta n}{(\Delta n)_f} \equiv \frac{(n)_t - (n)_{t=0}}{(n)_{t\to\infty} - (n)_{t=0}}$$

It will run from 0 to 1 in any sorption or desorption experiment. A plot of this quantity as a function of time must be independent of the height of the sample bed if mass-transfer resistance in the voids of the bed has no effect on the kinetics. In this case the composition (or pressure) of the gas will only change with time but must be independent of the location in the bed, being the same for each crystal. The reverse must be true if mass transfer through the bed causes appreciable gradients of concentration along its height.

Kinetic experiments have been conducted with three zeolite samples, all containing crystals of the same size:

(a) $m = 92$ mg, bed height 3 mm
(b) $m = 39.5$ mg, bed height 1.3 mm
(c) $m = 18$ mg, monolayer of crystals (≤80 μm)

Sample (c) was spread evenly in a special sample pan of large diameter and thus consisted of less than one monolayer of crystals; any mass-transfer resistance in the gas surrounding the crystals was excluded with this configuration.

The kinetics of sorption in samples (a)—(c) at 25 °C and at approximately the same final degree of saturation are shown in Figure 3; in Figure 4 the kinetics of sorption is compared with that of desorption. Experimental conditions are listed in Table 1.

Table 1. Conditions of kinetic experiments for the NaX/*n*-C_4H_{10} system.

Run no.	Sample weight m [mg] (bed height)	Initial/final loading [mmol/g]	Initial/final pressure [Pa]
1	92 (3 mm)	0/0.43	46.6/14.9
1′	92 (3 mm)	0.43/0.89	62.9/28.9
2	39.5 (1.3 mm)	0/0.41	27.3/14.4
3	18 (≤80 μm)	0/0.37	21.9/12.9
4	18 (≤80 μm)	0.49/0.82	34.0/26.3
5	18 (≤80 μm)	0.82/0.50	10.0/16.9
6	91 (2.9 mm)	0.74/0.90	43.5/37.0
7	91 (2.9 mm)	0.90/0.74	24.7/31.1

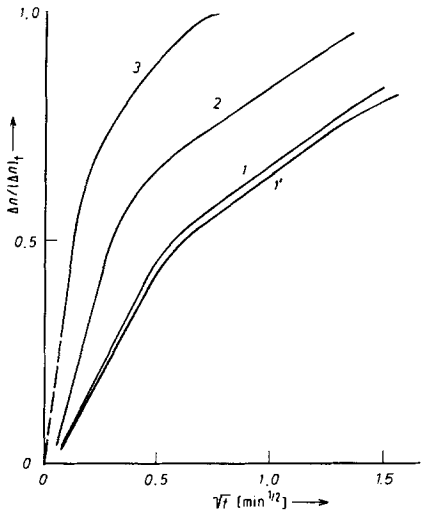


Fig. 3. Kinetics of sorption of *n*-butane in zeolite NaX at 298 K for three different samples of mass 92 mg (1 and 1′), 39.5 mg (2), and 18 mg (3).

The change Δn of the amount of sorbate is linear in $\sqrt{t}$ up to $\Delta n/(\Delta n)_f \approx 0.5$ within the accuracy of experimental observation[*]; its rate is independent of the direction of the flux, $\Delta n/(\Delta n)_f$ being the same function of t in sorption and desorption for a given sample configuration. This pattern—in particular

[*] The initiation of the change of pressure in the system was taken as the origin of the time axis ($t = 0$). Extrapolated curves of $\Delta n/(\Delta n)_f$ vs. $\sqrt{t}$ intersect with the line $\Delta n = 0$ at $\sqrt{t} \approx 3 \times 10^{-2}$ min$^{1/2}$, corresponding to a delay of 0.05 s due to the finite rate of response of balance and recorder.

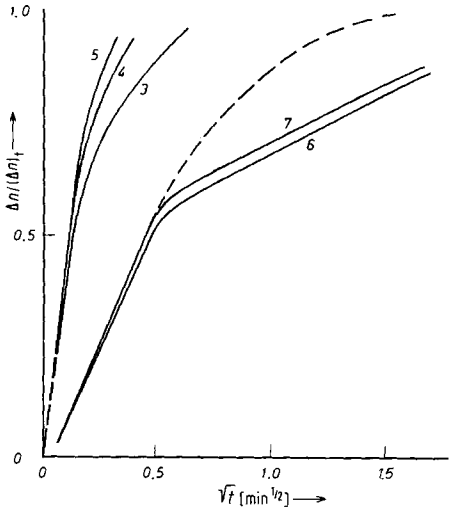


Fig. 4. Kinetics of sorption (3, 4, 6) and of desorption (5, 7) of *n*-butane in zeolite NaX at 298 K for two samples with mass 91 mg (6, 7) and 18 mg (3, 4, 5); broken line: advancement of $\Delta n/(\Delta n)_f$ as expected from the initial slope for run no. 7 on the basis of the diffusion equation with constant *D*.

the initially linear relation between Δn and $\sqrt{t}$—is generally to be expected if the rate-controlling flux of the sorbate in the sample is proportional to a gradient of concentration, no matter whether (laminar or Knudsen) flow in the voids of the sample-bed or diffusion in the crystals is rate controlling[13,14]. However, the initial slope of $\Delta n/(\Delta n)_f$ *vs.* $\sqrt{t}$ was found to be nearly proportional to the inverse of the height of the bed (or sample mass) in runs no. 1, 2, 6, and 7—and thus depends on the geometric configuration of the bed.

This observation indicates that at least initially [for $\Delta n/(\Delta n)_f < 0.5$] mass transfer through the bed is rate controlling, whereas diffusion in the crystals was of only minor influence on the rates of sorption or desorption in these experiments. If mass transfer through the bed is rate controlling then in the limit every crystal in the bed would always be in equilibrium with the gas phase contingent to it and we would have to expect the same rate law as for diffusion and localized adsorption in a porous material[13,14], the individual crystals in the bed being analogous to sorption sites on the pore walls. This type of rate behavior was also observed for the sorption of *n*-butane in commercial pellets of zeolite X, the kinetics depending essentially on the macroscopic dimensions and on the macropore structure of the pellets[9].

Any external mass transfer resistance is excluded if the zeolite sample consists of a single crystal or a monolayer of crystals (runs no. 3, 4, and 5). In this case the observed rates can be controlled by diffusion of the sorbate in the zeolite crystals only if transfer through the solid/gas phase boundary causes no appreciable resistance to the flux. The diffusivity *D* of the sorbate in the zeolite can then be obtained from the observed initial slope of $\Delta n/(\Delta n)_f$ *vs.* $\sqrt{t}$. This evaluation was based on the solution of the diffusion-equation for short times ($\Delta n/(\Delta n)_f < 0.3$), spherical geometry, and the appropriate initial and boundary conditions, *e.g.* sorption in a closed system and linear isotherm[10,11]:

$$\frac{\Delta n}{(\Delta n)_f} = \frac{12}{d}\left(\frac{1+E}{E}\right)\left(\frac{Dt}{\pi}\right)^{1/2} \tag{4}$$

with

$$E = \left(\frac{n_{gas}}{n}\right)_{equil.} = 2.4$$

d = crystal diameter = 8×10^{-5} m.

In runs no. 3, 4, and 5 the initial slope

$$\lim_{\Delta n \to 0}\left(\frac{1}{(\Delta n)_f}\frac{dn}{d\sqrt{t}}\right) \geq 0.59\,s^{-1/2} \tag{5}$$

was observed and from eq. (4) we have

$$D > 2 \times 10^{-7}\ cm^2\ s^{-1}$$

for *n*-butane in zeolite X at 298 K.

This value of *D* has to be regarded as a lower limit considering the finite rate of response of balance and recorder and a possible phase transfer resistance, sorption (or desorption) being 50 % complete after only 0.7 s.

The group D/d^2—which can be obtained from the initial slope of $\Delta n/(\Delta n)_f$ *vs.* $\sqrt{t}$—should also determine the further progress of Δn with t according to the diffusion equation. However, all observed curves of Δn *vs.* $\sqrt{t}$ deviate considerably

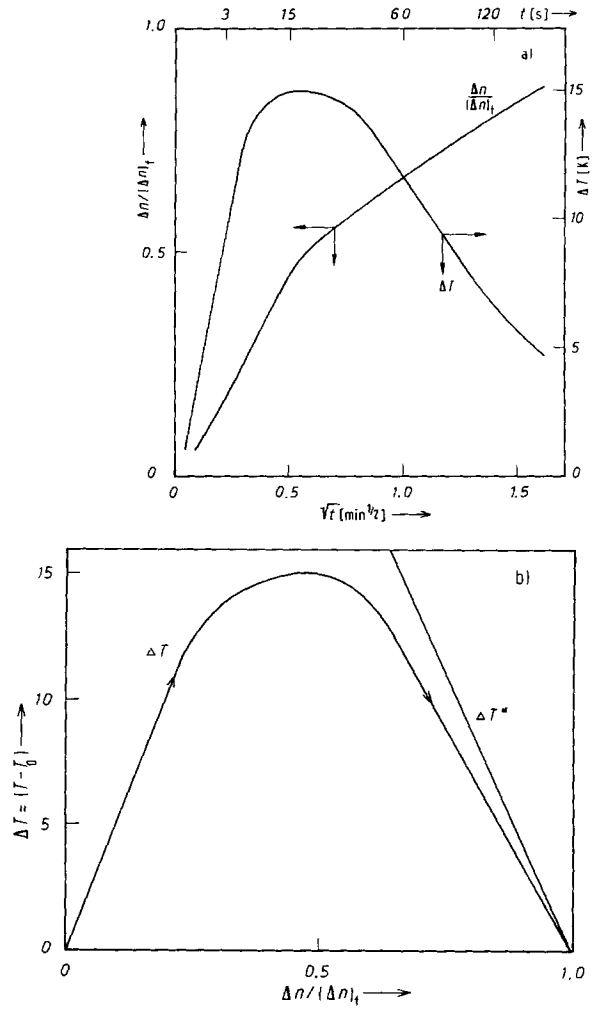


Fig. 5. Relative exchange $\Delta n/(\Delta n)_f$ of sorbate and temperature excursion ΔT in the n-C_4H_{10}/NaX system, conditions as in run no. 1 (see Table 1): a) as a function of $\sqrt{t}$; b) ΔT and equilibrium excess temperature ΔT^* as function of $\Delta n/(\Delta n)_f$.

from what should be expected (*e.g.* dotted curve for run no. 7 in Fig. 4) on this basis: a "bend" towards the $\sqrt{t}$-axis around $\Delta n/(\Delta n)_f \approx 0.5$ was found throughout, this bend being less pronounced for the monolayer configuration than for samples in form of a bed. This observation can *not* be explained as due to a concentration dependence of the diffusivity since the curves of $\Delta n/(\Delta n)_f$ *vs.* $\sqrt{t}$ for a given sample are identical in sorption and desorption as well as for different ranges of sorbate concentration. The deviation of Δn from expectation—based on the laws of isothermal diffusion—appears to be due to temperature changes in the sample, sorption being an exothermic process whereas desorption is endothermic. The temperature in the sample during sorption has been monitored by a miniature thermocouple and is shown together with $\Delta n/(\Delta n)_f$ as function of $\sqrt{t}$ in Figure 5a for the conditions of run no. 1. In Figure 5b the temperature increase $\Delta T = T - T_0$ is plotted as a function of $\Delta n/(\Delta n)_f$, together with the temperature increase ΔT^* of the sample which would be necessary to establish sorption equilibrium in the closed system for any value of the independent variable $\Delta n/(\Delta n)_f$. In order to compute ΔT^* the constant K in Figure 3 was approximated as a linear function of T within the temperature interval under consideration. The temperature increase ΔT as a function of Δn approaches the equilibrium line ΔT^* (Δn) for $\Delta n/(\Delta n)_f > 0.7$. The observed kinetics is controlled by mass transfer in the range $\Delta n/(\Delta n)_f < 0.5$, whereas the kinetics of the final approach to equilibrium depends mainly on the heat transfer between the sample and its surroundings. Sorption equilibrium is nearly established in the range $\Delta n/(\Delta n)_f > 0.7$ ($\Delta T \approx \Delta T^*$), while the temperature of the sample is not in equilibrium with its surroundings until the closed nonadiabatic system has reached equilibrium at $T = T_0$ and $\Delta n = \Delta n_f$. The change of sample temperature with time will thus control the rate of sorption in this second stage of the experiment. Both the deviation of the amount of sorbate from its final value and the excess temperature ΔT of the sample decrease exponentially with time at this stage, the same time constant (1.8 min) being found independently from observations of either quantity. The bend in the plot of $\Delta n/(\Delta n)_f$ *vs.* $\sqrt{t}$ was less pronounced with a sample consisting of a monolayer of crystals, the maximal temperature excursion being limited to $|\Delta T| < 6$ K due to the relatively important contribution of the sample pan to the combined heat capacity of the sample and its container.

It is possible to obtain diffusivities from the initial kinetics, in spite of the nearly adiabatic behavior of the system at small times ($\Delta n/(\Delta n) < 0.5$), since the kinetics of sorption or desorption is controlled by mass transfer in this range. The temperature diffusivity a of a zeolite crystal will be approximately

$$a = \frac{\lambda}{\rho c_p} \approx 5 \times 10^{-3} \text{ cm}^2 \text{ s}^{-1}$$

(with thermal conductivity $\lambda \approx 0.8$ W m^{-1} K^{-1}, density $\rho \approx 2$ g cm^{-3}, and specific heat $c_p \approx 0.75$ J g^{-1} K^{-1}); the Lewis number in the solid must thus be $Le = a/D \gg 1$ and temperature gradients in the crystals will be negligible. The crystal is therefore a heat sink (or source) of temperature T_0 at $t = 0$; the initial slope of Δn *vs.* $\sqrt{t}$ must be the same as in an isothermal system at T_0.

Comparing the thermal diffusivity in a bed of crystals with the apparent diffusivity of the sorbate in the bed leads to the conclusion that temperature differences within the bed will generally be less important than temperature differences between the bed and its surroundings. The rate of the final approach to equilibrium—which is controlled by heat transfer—will therefore depend on the thermal contact between the sample and the thermostat at T_0.

4. The Carbon Dioxide/Zeolite NaA System

Equilibrium isotherms for the CO_2/zeolite NaA system are shown in Figure 6; from these isotherms a constant heat of sorption of -44.7 kJ mol^{-1} is obtained for loadings up to 5 wt % CO_2, in good agreement with the value reported by *Barrer* and *Coughlan*[15].

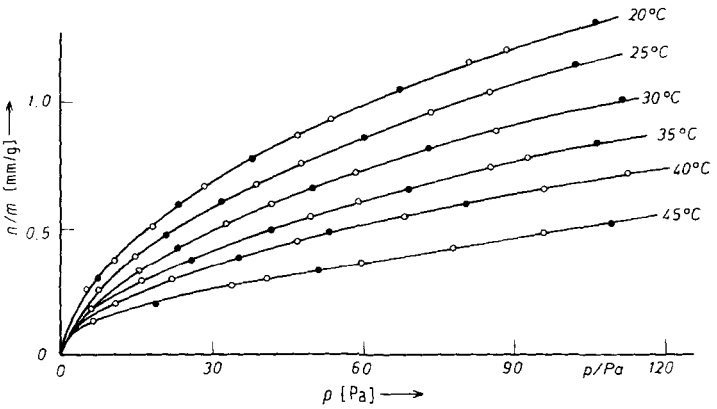


Fig. 6. Isotherms of CO_2 in zeolite NaA; equilibrium reached in sorption (○) and in desorption (●).

The kinetics of sorption and desorption was investigated at $T_0 = 293$ K using two samples of different weight (48.3 and 23.5 mg), the height of the beds being different by a factor of 15 since sample pans of different diameters were used.

Table 2. Conditions of kinetic experiments for the NaA/CO_2 system.

Run no.	Sample weight [mg] (bed height)	Initial/final loading [mmol/g]	Initial/final pressure [Pa]
1	48.3 (2.1 mm)	0/0.71	70.5/43.2
2	48.3 (2.1 mm)	0/1.01	118.4/89.8
3	23.5 (0.13 mm)	0/0.42	23.9/16.6
4	48.3 (2.1 mm)	0.82/0.61	23.9/33.3
5	48.3 (2.1 mm)	0.61/0.82	63.8/55.9

Experimental conditions are listed in Table 2; results are shown in Figures 7 and 8. The initial change of $\Delta n/(\Delta n)_f$ is always proportional to $\sqrt{t}$; it is independent of the direction of the flux, being the same for sorption or desorption over a given range of saturation of the sorbent. The initial slope of $\Delta n/(\Delta n)_f$ *vs.* $\sqrt{t}$ does not depend on the height of the bed; therefore the observed rate of mass transfer in the range $\Delta n/(\Delta n)_f < 0.4$ must be controlled by the uptake into or the release from the individual crystals, any influence of mass transfer in the voids of the bed being negligible in this case. The diffusivity D of CO_2 in zeolite A can hence be evaluated from eq. (4), on the basis of observations on a bed of crystals. Within the saturation range investigated we have $E = 2.1$ and

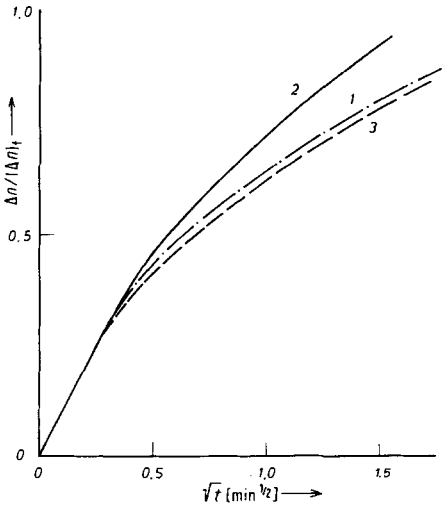


Fig. 7. Kinetics of sorption of CO_2 in zeolite NaA at 293 K for two samples with mass 43.3 mg (1, 2) and mass 23.5 mg (3).

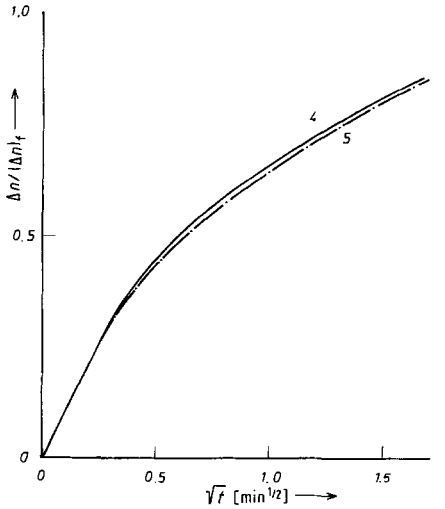


Fig. 8. Kinetics of sorption (5) and of desorption (4) of CO_2 in zeolite NaA at 293 K.

no. 1; the influence of an increase in thermal conductivity of the gas phase (due to increased pressure) on the kinetics is evident from Figure 7.

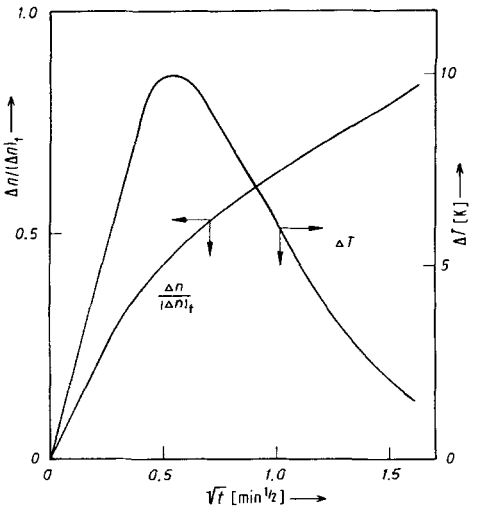


Fig. 9. Relative exchange $\Delta n/(\Delta n)_f$ and temperature excursion ΔT in the sample for sorption of CO_2 in NaA, conditions as in run no. 1 (see Table 2).

5. Discussion and Comments

Diffusivities D in the volume of zeolite crystals as obtained here from the kinetics of sorption and desorption are compared with values from the literature for the same or for similar systems in Table 3.

Diffusivities reported in the literature are considerably smaller than the values found here, with the exception of the coefficient of self-diffusion of *n*-butane in zeolite NaX as obtained from NMR experiments with the pulsed field gradient technique[4, 17]. Some of the values in Table 3 have been observed with the respective zeolites after partial or complete ion exchange of Na^+ against Ca^{2+}; however, this fact can hardly explain the appreciable discrepancies. Rather,

Table 3. Values of D, present results as compared to previous data.

Sorbate	Zeolite	T[K]	Method	Result [cm^2 s^{-1}]	Ref.
n-C_4H_{10}	$Ca_{0.42}Na_{0.16}X$	308	sorption	$D = 1.9\times10^{-14}$	[16]
n-C_4H_{10}	NaX	273	NMR spin-echo	$D^* = 10^{-5}$	[4, 17]
n-C_4H_{10}	NaX	298	sorption	$D > 2\times10^{-7}$	[a]
CO_2	CaA	298	exchange $^{12}CO_2/^{14}CO_2$	$D^* = 1.4\times10^{-11}$	[18]
CO_2	NaA	293	sorption	$D = 1.1\times10^{-9}$	[b]

[a] See Section 3; [b] see Section 4.

with $d = 3\times10^{-5}$ m a diffusity of $D = 1.1\times10^{-9}$ cm^2 s^{-1} follows for CO_2 in zeolite NaA at 293 K.

Excursion of the sample temperature and its re-equilibration is again of considerable influence on the kinetics of sorption or desorption when $\Delta n/(\Delta n)_f$ exceeds a value of 0.6. However, in the present system the final equilibration is not entirely controlled by heat transfer as was the case in the system *n*-C_4H_{10}/NaX. The excess temperature ΔT in the bed is shown in Figure 9 as a function of $\sqrt{t}$ under the conditions of run

it appears likely that the influence of external mass transfer and of mass transfer in the intercrystalline voids of pelleted sorbents on the kinetics has been underestimated in the work of *Ma* and *Lee*[16] and of *Sargent* and *Whitford*[18]. In both cases the gas phase consisted of a mixture of two components, pellets made from relatively small crystals (about 1 μm diameter) having been used as sorbents; the influence of external and intercrystalline mass transfer on the kinetics was evaluated from the shape of the curves of uptake or exchange *vs.* time

and not by experimentation with samples of different macroscopic sizes. The uptake as a function of time must follow the diffusion equation exactly if either intracrystalline or intercrystalline diffusion alone controls the rate of sorption or exchange; its shape will be identical in both limiting cases. Only in the intermediate case will isothermal uptake or exchange *not* follow the straightforward solution of the diffusion equation. However, the deviation should be most pronounced at the very beginning of an experiment, where it is difficult to measure the respective rate exactly.

A resistance due to the transfer through the phase boundary (crystal surface) will appear in the shape of the uptake *vs.* $\sqrt{t}$ curves also only as a "foot" near the origin, unless it controls the rate predominantly[19]. Such a resistance can be excluded on the basis of our experiments in the CO_2/NaA system; in the n-C_4H_{10}/NaX system it was not possible to obtain the exact shape of Δn *vs.* $\sqrt{t}$ near the origin. This is one reason for quoting only a lower limit for the diffusivity of n-butane in NaX, which as such is not in conflict with the coefficient of self-diffusion as reported by *Kärger* and *Pfeifer*[4] for the same system. It appears difficult, if not impossible, to measure diffusivities in zeolites greater than 10^{-7} $cm^2 s^{-1}$ by means of sorption kinetics, in view of the limitations of experimental equipment and of the size of synthetic zeolite crystals. Measurement of self-diffusion in zeolite crystals by means of NMR spectroscopy is limited to values of D^* above 10^{-7} $cm^2 s^{-1}$[20]; both methods thus complement each other.

Diffusivities can be obtained within this limit from the kinetics of sorption or desorption, no matter whether the system is adiabatic, nearly adiabatic, or isothermal, provided intracrystalline diffusion is rate controlling and the evaluation is based on proper boundary conditions. By observing certain precautions this condition can be fulfilled, at least for a limited range of the relative exchange $\Delta n/(\Delta n)_f$. In any case mass transfer into or out of a zeolite will necessarily cause an excursion of the temperature of the sample[21]. In the limit the kinetics of sorption can be entirely controlled by heat transfer; then it is of course not possible to obtain diffusivities from the respective rate data, as has been shown by *Wicke*[22]. The unsteady sorption or desorption in zeolites can never proceed strictly isothermally, a fact which seems important with respect to the interpretation of kinetic data as well as with respect to commercial applications.

Rather elaborate precautions were necessary in order to observe intracrystalline diffusion through sorption kinetics in the system n-C_4H_{10}/NaX. Intracrystalline diffusion may consequently not necessarily be relevant for the kinetics in this system under different conditions, *e.g.* in commercial operation. It appears that intracrystalline diffusion has frequently been assumed *a priori* to be rate determining in sorption or desorption in zeolites. This assumption seemed dubious after coefficients of self-diffusion have been found by NMR spectroscopy, which are orders of magnitude greater than those obtained from sorption kinetics. It is now evident that processes other than diffusion in the crystals but necessarily coupled with sorption or desorption—namely the flow in the intercrystalline voids and heat transfer—can be of considerable influence on the rate of mass transfer between a gas and a zeolitic sorbent. From this observation it follows that not only crystal structure and chemical composition but also crystallite size as well as dimensions and macropore structure of pellets can possibly be important for the properties of commercial sorbents and catalysts containing zeolites.

Dr. H.-J. Pätow's help in synthesizing large crystals of zeolites X and A as well as financial support from the Fonds der Chemischen Industrie are gratefully acknowledged.

Received: November 16, 1978 [A 267 IE]
German version: Angew. Chem. *91*, 309 (1979)

[1] *D. W. Breck:* Zeolite Molecular Sieves. Wiley, New York 1974; see also: *K. Unger*, Angew. Chem. *84*, 331 (1972); Angew. Chem. Int. Ed. Engl. *11*, 267 (1972); *F. Schwochow, L. Puppe, ibid. 87*, 659 (1975) and *14*, 620 (1975).
[2] *C. N. Satterfield, A. S. Frabetti*, AIChE J. *13*, 731 (1967).
[3] *Y. H. Ma, C. Mancel*, Adv. Chem. Ser. *121*, 392 (1973).
[4] *J. Kärger, H. Pfeifer*, Z. Chem. *16*, 85 (1976).
[5] *L. Riekert*, AIChE J. *17*, 446 (1971).
[6] *J. Kärger*, Surf. Sci. *59*, 749 (1976).
[7] *J. Kärger, J. Caro*, J. Chem. Soc. Faraday Trans. I *73*, 1363 (1977).
[8] *L. Riekert*, Adv. Catal. *21*, 281 (1970).
[9] *H.-J. Doelle:* Das Zusammenwirken von Stoff- und Wärmetransport bei der Sorption und Desorption in Zeolithen. Dissertation, Karlsruhe 1978.
[10] *R. M. Barrer*, Trans. Faraday Soc. *45*, 358 (1949).
[11] *J. Crank:* The Mathematics of Diffusion. Oxford University Press, London 1970, pp. 53f., 88f.
[12] *J. F. Charnell*, J. Cryst. Growth *8*, 291 (1971).
[13] Ref. [11], pp. 121f.
[14] *P. B. Weisz*, Trans. Faraday Soc. *63*, 1801 (1967).
[15] *R. M. Barrer, B. Coughlan* in Molecular Sieves, Soc. Chem. Industry, London 1968, pp. 241f.
[16] *Y. H. Ma, T. Y. Lee*, AIChE J. *22*, 147 (1976).
[17] *J. Kärger, H. Pfeifer, M. Rauscher, A. Walter*, Z. Phys. Chem. (Leipzig) *259*, 784 (1978).
[18] *R. W. H. Sargent, C. J. Whitford*, Adv. Chem. Ser. *102*, 155 (1971).
[19] Ref. [11], pp. 91f.
[20] *H. Pfeifer, W. Schirmer, H. Winkler*, Adv. Chem. Ser. *121*, 430 (1973).
[21] *J. D. Eagan, B. Kindl, R. B. Anderson*, Adv. Chem. Ser. *102*, 164 (1971).
[22] *E. Wicke*, Kolloid Z. *86*, 167 (1939).

Polymer Alloys—Their Structure, Morphology, and Properties

By Burghard J. Schmitt[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Polymeric materials with novel properties for new technological applications are increasingly obtained by combining existing polymers, while the synthesis of new monomers has receded into the background. These polymer combinations or "alloys" (polyblends) are characterized by their chemical composition, the conformation of the chain molecules, and the morphology, *i.e.* the state of order at supramolecular level. Multiphase constitution is a typical characteristic of these substances, with a decisive influence on their macroscopic properties. The morphology of multiphase polymer alloys can be controlled to a limited extent *via* the chemical composition of their components when homopolymers are mixed in the melt or as dispersions. Graft copolymerization, on the other hand, makes it possible to achieve the desired morphology at a given chemical composition. Furthermore, transparent two-phase polymer alloys can be obtained under certain conditions. In multiphase polymers the reduction of stress without fracture, caused by mechanical loading will be treated using models. Certain combinations of properties such as hardness and toughness are connected with the coexistence of disperse and continuous phases. Equilibrium thermodynamical criteria for liquid mixtures will be used to explain demixing phenomena in polymers. In the last few years it has become possible to determine the chain conformation experimentally using neutron scattering.

1. Basic Phenomena

Macromolecular materials with new technical properties can be obtained by the synthesis of new monomers, by new methods of polymerization, and by the combination of existing polymers[**] having various properties. Preparative chemistry has produced about 1000 compounds that can be polymerized in chain or stepwise reactions[***], forming the basic repeating units of the resulting polymers. About 50 of these monomers are used on an industrial scale, and this number has not increased in the past few years. In applied polymer research the interest has instead been turned more and more toward methods of polymerization and the combination of existing polymers. The simple idea behind this second method is to build up required composite industrial materials by combining known polymers[2-4]. For example, it seemed obvious to combine the hard and stiff, but at the same time brittle homo- and copolymers of styrene (repeating unit $-[CH(C_6H_5)-CH_2]-$) with the soft and resilient butadiene polymers (repeating units $(-[CH_2-CH=CH-CH_2]-$ or $-[CH_2-CH(CH=CH_2)]-)$ by polymerizing the former in the presence of prepolymerized butadiene to produce a material exhibiting hardness and stiffness as well as impact resistance. According to their composition, composites are to be regarded as polymer mixtures. They can be described as polymer alloys, because they often have qualitatively new characteristics not possessed by their constituents.

Figure 1 shows schematically the constitution of chain molecules. A polymer mixture or polyblend is obtained when in an assembly of polymer molecules some are present, whose chemical composition of the repeating unit differs from that of the remaining polymer molecules. By this definition, random copolymers are not polyblends. Random copolymers should be considered as polymer mixtures when polymer molecules with large differences in chemical composition are present. In block copolymers with sufficiently long sequences of one and then of the other repeating unit, the blocks behave like independent polymer molecules, so that they may be considered as analogous to polyblends[5].

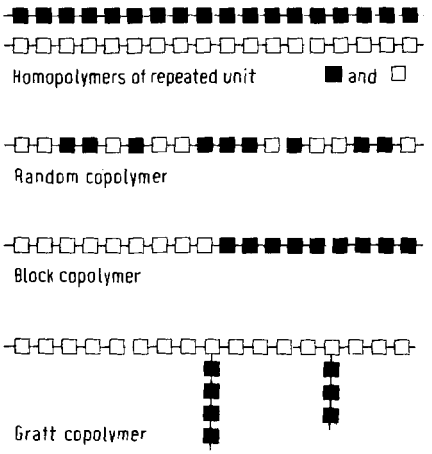


Fig. 1. Schematic representation of chain molecules.

The main characteristic of all polymer alloys is their multiphase constitution. A cross-section through such a material contains a number of regions that differ from one another in their characteristics such as chemical composition, density, refractive index, mechanical-dynamic properties, and softening temperature. These regions are separated from one another by phase boundaries. Generally there are two discrete phases: a continuous and a disperse phase. The dimensions of the disperse regions vary from 5 nm to a few thousand nm. It

[*] Dr. B. J. Schmitt
Kunststofflaboratorium der BASF-AG
D-6700 Ludwigshafen (Germany)

[**] The term 'polymer' denotes an assembly of macromolecules which are built up of a large number of interconnected repeating units; the mechanism of the linking process is not specified.

[***] For the definition of these reactions, also called chain-growth and step-growth polymerization reactions, see [1].

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0273 $ 02.50/0

is unimportant whether the two phases are chemically different from each other, for according to the phase rules it is enough to have an abrupt change, amounting to a discontinuity, in a characteristic along the space coordinate, including therefore a change from the crystalline to the amorphous state alone, and a chemically homogeneous chain molecule can have both amorphous and crystalline sections at the same time[6].

When characterizing multiphase macromolecular materials, a distinction is made between structural features or elements of molecular dimensions and those of supermolecular dimensions[7]. The former are of a chemical nature and they impress their character on all the chain molecules, irrespective of the state of aggregation. They include the composition, molecular-weight distribution, steric arrangement of the substituents (tacticity), branching of the chains, and—in copolymers—the succession and amount of the repeating units.

The spatial arrangement of these chemical or molecular structural features according to crystallographic, kinetic, thermodynamic, and statistical rules is called morphology. This describes the state of order at the supermolecular level and largely determines the macroscopic properties of multiphase materials. Deliberate modification of the morphology offers a new degree of freedom at a given chemical structure of an assembly of macromolecules. In the case of polyblends the morphology is largely determined by phase-separation or demixing phenomena, *i.e.* by the separation of a homogeneous phase into at least two discrete phases.

No less important than the chemical structure is the physical form of the macromolecules, for example the different conformations of the chains in the amorphous and the crystalline domain (made possible by rotation around C—C bonds) and the mobility of chains, chain segments, and side groups. These mobilities are temperature-dependent, and they can all be frozen in at a sufficiently low temperature, *e.g.* at −130 °C for siloxanes, with the repeating unit $-[Si(CH_3)_2—O]-$, and the polymer is then either glassy and amorphous with no long-range order of the molecular chains, or it is partially crystalline, if it contains regions with a periodic order. When subjected to mechanical loads, these materials are almost elastic up to the point of brittle fracture. The slopes of the stress-deformation curves (see Fig. 35) are defined as moduli and give a measure of the stiffness (these slopes vary with the stresses to different extents). Polymers with frozen-in segmental mobilities have moduli of 10^5—10^7 N/cm^2, the modulus for steel being 10^8 N/cm^2.

Figure 2 shows schematically the temperature-dependence of the moduli of amorphous and partially crystalline polymers. Heating first produces a temperature region with secondary dispersion, where the side groups become mobile. This is followed by a relatively narrow temperature region in which the chain segments become mobile, the viscosity of the system falls by several orders of magnitude, and changes in the conformation of the macromolecules become possible; at the same time, there is a marked change in the temperature coefficients of the specific volume and the refractive index. Instead of a temperature range, one generally specifies a characteristic temperature—the glass temperature—for a polymer or a homogeneous polyblend. The glass temperature *e.g.* for polystyrene is about 100 °C, and that for polybutadiene is −85 °C.

Above the glass temperature, the polymer is soft and—unlike low-molecular liquids—still quite elastic, with moduli

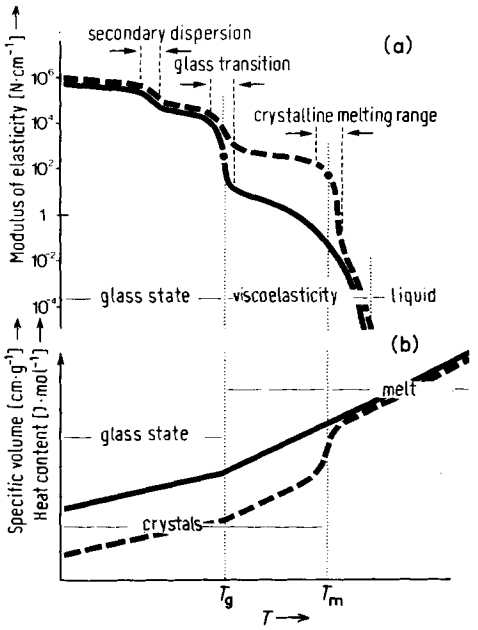


Fig. 2. a) Thermomechanical curves for amorphous (—) and partially crystalline (---) high molecular weight polymers (schematic), b) heat content and specific volume as a function of the temperature on melting and glassy solidification of high molecular weight polymers. T_g—glass temperature, T_m—crystalline melting point.

of 1—10 N/cm^2. This elasticity of softened polymers, called rubber-like or rubbery elasticity, stems from the network structure of the materials. Due to linkages between chain molecules either by chemical bonding, entanglement in amorphous domains or folds in crystalline domains, restoring forces come into operation on deformation. The coexistence of viscous and elastic properties is named viscoelasticity.

When the temperature is raised further, softened polymers become more and more like liquids, and the elasticity of the melt decreases. This is particularly noticeable in the melting region of crystallites. Figure 2 shows that the crystallites are formed from the melt. The state of glassy solidification below the glass temperature is not an equilibrium state with a minimum energy content, for the crystalline state has a lower energy than the glassy one. Yet the transition from the glassy state to crystallites occurs extremely slowly or not at all in practice, owing to the frozen-in segmental mobility. In polymers that do not crystallize because of insufficiently long sequences of the same tacticity one can observe only the transition from the glass amorphous state to the amorphous melt state. Polymers often fail, even at high temperatures, to reach the state of an ideal liquid without any elasticity, because they decompose before this would happen. A typical example of this is high-molecular poly(methyl methacrylate) with the repeating unit $-[CH_2—C(CH_3)\cdot(COOCH_3)]-$, which exhibits depolymerization and amorphous elastic behavior at about 200 °C.

The material properties of polymers show characteristic differences according to whether they exhibit a glassy state or rubber-like elasticity at a given temperature; crystallites can also be present in both cases. Multiphase polymeric materials can be arranged in a list according to their moduli[8, 9] (see Table 1). About 90 % of industrial polymers used today are multiphase materials; they include partially crystalline polymers and combinations with inert fillers such as glass fibers and air.

Table 1. Classification of multiphase polymeric materials.

Type of material	Disperse phase, with modulus G_D	Continuous phase, with modulus G_K	Relationship between moduli at room temperature
Reinforced rubber	inorganic filler	rubbery polymer	$G_D \gg G_K$
Thermoplastic elastomer	glassy amorphous or crystalline polymer	rubbery polymer	$G_D \gg G_K$
Reinforced thermoplastic	inorganic filler	glassy amorphous or partially crystalline polymer	$G_D > G_K$
Partially crystalline polymer	crystalline polymer	glassy amorphous polymer	$G_D \approx G_K$
Soft foam	gas	rubbery polymer	$G_D < G_K$
Impact-resistant stiff plastic	rubbery polymer	glassy amorphous or partially crystalline polymer	$G_D \ll G_K$
Rigid foam	gas	glassy amorphous polymer	$G_D \ll G_K$

The present review is restricted to polymer-polymer combinations. The designation "polymer alloys" used for these is not correct if it is intended to express an analogy with metal alloys, whose melts are homogeneous and whose products of solidification contain crystallites of the pure substances in a wide range of compositions. In polyblends, on the other hand, phase-separation phenomena must be borne in mind from the outset, the melts are often not homogeneous like a single phase, and the demixed phases are not pure substances but contain all the components in various concentrations. Pure substances occur as separate phases only in the case of partially crystalline polymers.

2. Preparation of Polyblends

The most direct way of preparing polyblends is to mix the preformed polymers in the molten state ("melt mixing"). The extent of mixing depends on the rate of diffusion of the chain molecules. *Bueche et al.* have measured the rate of diffusion of isotopically labeled polybutyl acrylate with the repeating unit $-[CH_2-CH(COOC_4H_9)]-$[10] and polystyrene[11] in a matrix composed of the same polymer in each case, as a function of the temperature and the molecular weight, while *Bresler et al.* have measured the rate of diffusion of labeled polyisoprene with the repeating unit $-[CH_2-C(CH_3)=CH-CH_2]$ in vulcanized rubber[12]. The diffusion coefficients lie in the range of 10^{-10}—10^{-13} cm^2/s, which means that the center of gravity of the chain molecules undergoes an average displacement of 10^{-5}—10^{-6} cm in the melt. This value is two orders of magnitude lower than that for the diffusion of low-molecular compounds in a polymeric matrix, and the thermodynamic equilibrium is established here considerably more slowly. Even so, the displacement is still about 10—100 times as great as the diameter of a polymer coil in the melt (cf. Section 4). The establishment of equilibrium is influenced by the time of mixing, the shear gradient, the temperature, and the rheological properties of the polymers[13–16]. A thorough mixing in molecular dimensions is possible only when the mobility of the chains is not frozen in, *i.e.* only above the glass temperature.

Strong shearing forces often decompose polymers, and the resulting radicals can then participate in cross-linking or in the formation of graft or block copolymers (cf. Fig. 1), leading to new chemical structures in the polyblend. For example, intensive kneading of polyisoprene with chloroprene rubber having the repeating units $-[CH_2-CH(CCl=CH_2)]-$ is enough to produce graft, block, and cross-linked copolymers even at low temperatures[17]. If the chemical structure is not to be changed, mixing in the melt must be restricted to thermally stable polymers and polymers that are not sensitive to shearing forces.

Polymer latexes are often combined by mixing. They consist of spherical or irregular polymer particles, emulsifiers, and dispersing agents such as water. The polyblend is obtained by coagulating the latex or evaporating the dispersing agent. When the mixture is dried, the components are present in the form of separate particles measuring 100—1000 nm. This method makes it possible to fix the particle size of the disperse phase without interfering with the properties of the components. The composition of the particles remains unchanged until the powder is melted, when again decomposition and grafting take place, with an increasing change in the particle composition. These changes, caused by the migration of one polymer component into the particles of the other, occur less often if cross-linking through chemical bonds has taken place in the latex particles. The electron micrographs in Figure 3 show increasingly sharper phase boundaries and phase contrast due to the reduced degree of mixing caused by increasing crosslinking, *e.g.* for a poly(butyl acrylate).

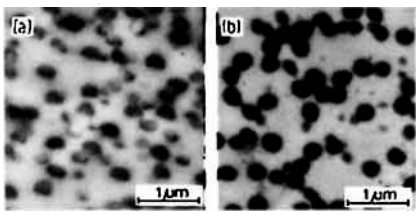


Fig. 3. Molten latex mixtures composed of poly(methyl methacrylate) and poly(butyl acrylate). a) Slightly cross-linked poly(butyl acrylate), b) strongly cross-linked poly(butyl acrylate). Contrast by electron etching, with the elastomeric phase as dark areas.

Another method is to mix the polymers in a mutual solvent, followed by precipitation and/or drying. The view that evaporation always leads to mixing at the molecular level, though occasionally encountered[18], is incorrect. Ternary systems consisting of two polymers and a solvent exhibit wide miscibility gaps[19–22]. Phase separation begins already at a polymer concentration of a few percent. As drying advances, a nonequilibrium state is frozen in. Coprecipitation also gives a heterogeneous material if the components have different solubilities.

Only through chemical bonds can polymer chains be fixed in a "forced" mixture. For this purpose the monomers are polymerized in the presence of a polymer prepared in advance. If the latter has functional groups such as hydroxyl or amino groups or halogen atoms at its ends, or if it comprises cations, anions, or free radicals, the monomer will add on there and block copolymers are formed. These can of course also be obtained by coupling reactions with preformed polymers. If the second polymer chain adds on not at the chain end but

at another site activated *e. g.* by double bonds, graft copolymers will be formed. This method is used to prepare a large part of rubber-reinforced thermoplastics. For example, polybutadiene is dissolved in the monomer which is to form the glassy component, and either bulk polymerization or solution polymerization in an inert solvent is then carried out. Alternatively, the reaction mixture is suspended in water after partial conversion, and the polymerization is completed with intense stirring[23, 24]. Pure glassy polymer and graft copolymer are formed side by side, *i. e.* a two-phase mixture is obtained directly. Many morphological variants can be prepared by an appropriate choice of the concentrations, the molecular weight of the polybutadiene, and the conditions of the preparation (cf. Section 5).

Graft copolymers are often prepared in emulsion. The monomers added to a chemically different polymer latex polymerize both on the surface and inside the latex particles. This method gives networks that penetrate into one another to various extents and are formed either by chemical bonds or by the looping-together of the chain molecules. Despite this fixation, the system exhibits demixing and a multiphase character with a domain structure within the dimensions determined by the latex particles (see Fig. 4).

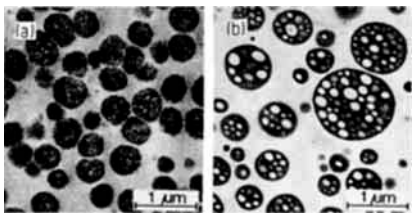


Fig. 4. Acrylonitrile-butadiene-styrene copolymers. a) Emulsion polymerization of styrene and acrylonitrile in the presence of a preformed polybutadiene latex, b) bulk polymerization of styrene and acrylonitrile in the presence of dissolved polybutadiene (for comparison). Dark areas: elastomeric phase.

3. Thermodynamics of Polyblends

Apart from mixing in the melt, all methods used for the preparation of polyblends are expected to lead initially to thermodynamically nonequilibrium systems, the attainment of equilibrium being inhibited by high viscosities and the network structure. In polymer melts, on the other hand, equilibrium states can be reached at sufficiently high temperatures. This is proved by a) the reversibility in the experimental determination of the turbidity limits, *e. g.* for mixtures of poly(methyl methacrylate) with styrene-acrylonitrile copolymers having the repeating units $-[CH(C_6H_5)-CH_2]-$ and $-[CH(CN)-CH_2]-$[25] (see also Fig. 9), and b) by reproducible adjustment of the molecular conformations according to the temperature in these mixtures and in mixtures of poly(methyl methacrylate) with poly(α-methylstyrene)[26]. Inspection under a light and an electron microscope shows directly that a multiphase system is formed in melts of poly(methyl methacrylate) and styrene-acrylonitrile copolymers in less than 1 minute if a sudden rise in the temperature transfers the system from the stable single-phase region to the multiphase region[27]. Annealing for 2 h simply makes the particles in the demixed regions twice as large. The finely dispersed state after phase separation favors the establishment of equilibrium concentrations in the demixed regions (for quantitative considerations see [28–30]).

The establishment of equilibrium is also inhibited in melts if the polymers are chemically cross-linked or the crystallites are not fully melted. In this second case, according to a widely confirmed model[31, 32], the number of possible chain segment conformations in the amorphous domains is reduced due to restrictions of the volume available for conformational changes because of crystallites of differing sizes (see Fig. 5).

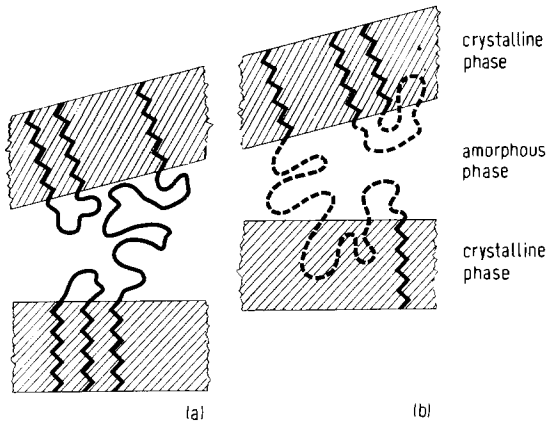


Fig. 5. Conformational restriction in the melting or crystallization of chain molecules (schematic). a) Possible conformations, b) conformations not possible, because of the excessively small volume of the amorphous phase.

Consequently the entropy contribution of a noncrystalline chain portion is smaller than that of a chain of the same length in an amorphous melt. During melting, the entropy changes not only for the repeating units changing phase but also for the entire noncrystalline chain sections. The entropy change per monomeric unit is therefore not constant, and partially crystalline polymers have a melting range rather than a fixed melting point:

$$T_S = \Delta H_S / \Delta S_S \qquad (1)$$

where ΔH_S is the enthalpy of melting and ΔS_S is the entropy of melting.

If the temperature of a melt mixture containing crystallizable polymers sinks below the melting range of one of the components, the latter will partially separate out as a solid crystalline phase and the composition of the remaining melt will be shifted. The free enthalpy of a polymer is lower in the crystalline state than in the melt, and the free enthalpy of the mixture is therefore reduced by partial crystallization. If the temperature is below the melting range of another crystallizable component, this component also crystallizes out in part. If two crystallizable polymers in the melt form a single-phase mixture, yet on crystallization form their own crystallites instead of mixed ones, plotting the melting temperature against the composition gives two curves that intersect at the eutectic point (see Fig. 6a)[33].

Figure 6b shows the phase diagram for a mixture of a crystallizable polymer and an amorphous polymer. Poly(vinylidene difluoride) with the repeating unit $-[CH_2-CF_2]-$ and poly(methyl methacrylate) form a homogeneous mixed melt[35], from which the former crystallizes out at any mixing ratio if the temperature is between the melting temperature of its crystallites and the glass temperature of the mixture.

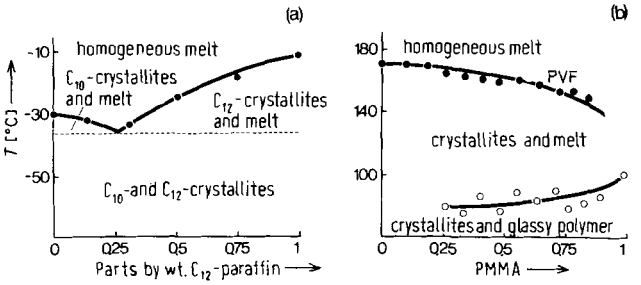


Fig. 6. Melting and glassy solidification of binary polymer mixtures. ●--Melting point; ○-- glass temperature. a) C_{10} and C_{12} paraffins as model polymers, both crystallizable (measurements by *Killian*) [33]; b) poly(vinylidene difluoride) (PVF) (crystallizable) and poly(methyl methacrylate) (PMMA) (amorphous) (measurements by *Nishi* and *Wang*) [35].

In the solid state we have the crystalline melting point and the glass temperature. Both depend on the ratio of the components in the mixture. As the amount of the poly(methyl methacrylate) is increased, the melting temperature of poly(vinylidene difluoride) decreases. The fact that the glass temperature of the mixture is lower than that of pure poly(methyl methacrylate) indicates that considerable amounts of uncrystallized poly(vinylidene difluoride) are still present[36]. It is now being investigated using neutron scattering whether this substance is mixed with poly(methyl methacrylate) in the form of a molecular dispersion[34]. When a homogeneous mixed melt is quenched below the freezing temperature, poly(vinylidene difluoride) remains in the amorphous state[36]. Since the condition for the homogeneous miscibility of chemically different polymers is rarely satisfied, this simple consideration can be used in few cases. Usually, crystallites are formed from which a non-crystallizable second component is omitted. However, the crystallites are in turn embedded in a multiphase amorphous matrix. Only a slow after-crystallization occurs near the glass temperature[37].

An equilibrium state reached in the melt at a high temperature can be frozen in by rapid cooling. There is then no equilibrium with respect to the lower temperature. The frozen-in systems are unstable and change with time even below the glass temperature[38]. For example, the moduli of elasticity increase during the storage of quenched melts of polycarbonates with the repeating unit $-[O-C_6H_4-O-CO]-$ and poly(methyl methacrylates)[39]. Since the changes with time are comparatively slow below the glass temperature and polyblends need to be melted in the case of thermoplastic processing, it has been recommended that the time-dependent effects should be ignored, and the criteria of the thermodynamics of mixtures should be used[20, 40-42]. If the parameters that determine the equilibrium state are known, it is possible to make predictions also for the nonequilibrium state as to the course of later changes. The magnitude, sign, and course of the free enthalpy of mixing[*], as a function of the composition, decide whether the polyblend gives a stable single-phase system or tends to separate into a number of phases under the given conditions. It is immaterial here in principle whether these states are actually established. However, conveniently, only the temperature range where the segmental mobility is not frozen in is observed since in practice an equilibrium state cannot be obtained at all below the glass temperature.

[*] This is defined as the difference between the free enthalpy of the mixture and the sum of the free enthalpies of the pure components.

The free enthalpy of mixing per mole is given by eq. (2) for two polymers 1 and 2 that are uniform with respect to the molecular weight:

$$\Delta G_m/(n_1+n_2)=RT[x_1\ln\Phi_1+x_2\ln\Phi_2+\chi_{12}\Phi_1\Phi_2(m_1x_1+m_2x_2)] \quad (2)$$

where x_1 and x_2 are the mole fractions and Φ_1 and Φ_2 the partial volumes of polymers 1 and 2, respectively, R and T have the usual meanings, n_1 and n_2 are the numbers of molecules, and m_1 and m_2 the numbers of segments per chain molecule (these numbers are relative to a reference volume that is the same for both polymers and approximately corresponds to the molar volume of the monomers). The correction term χ_{12} at first takes account only of the enthalpic interaction between a segment of polymer 1 and a segment of polymer 2. Equation (2) has been derived on the basis of a model in which the polyblend forms a three-dimensional lattice whose points are randomly occupied by the segments of the polymer chains (lattice theory)[43-45]. Figure 7 shows a two-dimensional model for mixtures of a polymer with a low-molecular compound and with another polymer. In the second case the number of possible arrangements in the given volume is considerably smaller, because of the linking of the polymer segments into chains. This is why the entropy of mixing (ΔS_m)

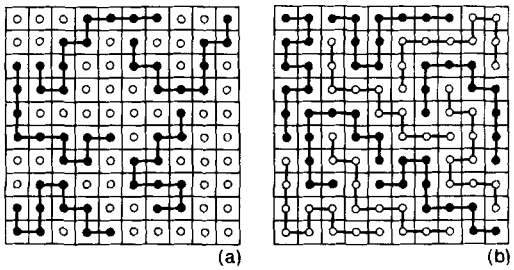


Fig. 7. Possible arrangements in binary mixtures of a polymer with a) a low-molecular weight compound, and b) another polymer (two-dimensional and schematic). Number of segments per chain molecule $m_1=m_2=10$.

reaches a lower value in the case of polyblends. A further reduction in the number of possible arrangements results from the stiffer chains[46, 47]. On the other hand, the number of contacts with neighboring segments is little affected, and the enthalpy of mixing (ΔH_m) is not so different for the two cases. The value of ΔH_m, which is positive for most polyblends[48, 49] is only partially compensated by ΔS_m[47] and ensures positive values for the free enthalpy of mixing ΔG_m on account of the relation:

$$\Delta G_m=\Delta H_m-T\Delta S_m \quad (3)$$

This gives a qualitative explanation for the increasing tendency toward demixing with increasing chain length of the components.

Figure 8 shows for a binary polyblend the variation in the free enthalpy of mixing with the composition (represented here by the mole fraction x_2 of polymer 2). If the curves have more than one minimum, there is a miscibility gap, despite the negative values of the free enthalpy of mixing over the whole range. The points of contact of the double tangents at the two minima of the individual curves lie on the binodal curve, which forms the boundaries of the area

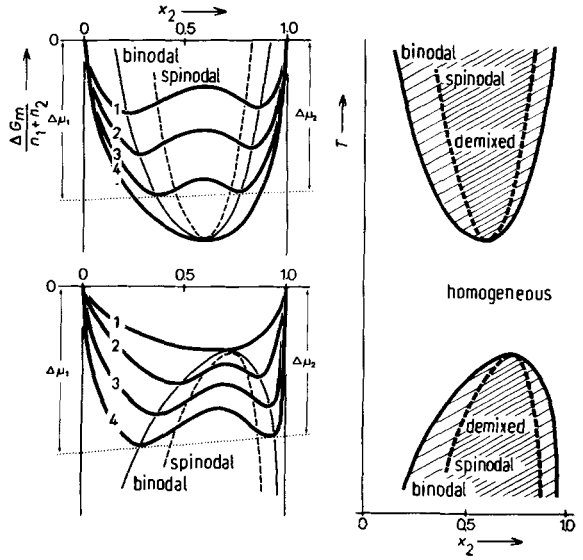


Fig. 8. Free mixing enthalpy ΔG_m, binodal and spinodal curves for binary polyblends with upper and lower miscibility gaps (schematic). T—temperature, n_1 and n_2—numbers of molecules, $\Delta\mu_1$ and $\Delta\mu_2$—chemical potentials, x_2 mole fraction of polymer 2. Curves 1—4 at T_1 to T_4; $T_1 > T_2 > T_3 > T_4$.

of stable homogeneous mixtures. This means that a homogeneous mixture is not stable within the enclosed area. Demixing shifts the free enthalpy of mixing toward the negative values. Connecting the points of inflection of the curves gives the spinodal curve, which acts as a boundary between the unstable and the metastable region. The main significance of the spinodal curve is that it can be calculated in the closed form from the expressions for the free enthalpy of mixing which cannot be done in the case of the binodal curve. The combination of eq. (2) with the condition for the point of inflection

$$\frac{\partial^2 \Delta G_m}{\partial x_1^2} = 0 \tag{4}$$

leads to

$$\chi_{12}^{Spin} = \frac{1}{2(m_1 \Phi_2 + m_2 \Phi_1)} \left[\frac{1}{\Phi_1 \Phi_2} + \frac{(m_2 - m_1)^2}{m_1 m_2} \right] \tag{5}$$

The spinodal curve shows the miscibility gap and its variation with the experimental conditions in qualitatively the same way as the binodal curve.

The components are miscible in any proportion if:

$$\left(\frac{\partial^2 \Delta G_m}{\partial x_1^2} \right)_{p,T=const.} > 0 \quad \text{for} \quad 0 < x_1 < 1 \tag{6}$$

If the value of this differential derivative is negative for a given interval of x_1, then there is a miscibility gap. This gives a thermodynamically exact definition of polymer compatibility and incompatibility, independently of the subjective assessment based on optical or mechanical properties of polyblends. The polymers of a mixture are said to be "compatible" if there is no miscibility gap anywhere in the composition domain at a given temperature and pressure; otherwise they are "incompatible". On the basis of equilibrium thermodynamics, there is no general incompatibility over the whole composition region in the case of amorphous polyblends: the miscibility gaps often extend to very small concentrations of one component, but they never encompass the pure substance. We therefore always have compatibility if one of the components is in a sufficiently large excess. A phase can form from just one of the components of the mixture only in the case of very extensively cross-linked or partially crystalline polymers[37].

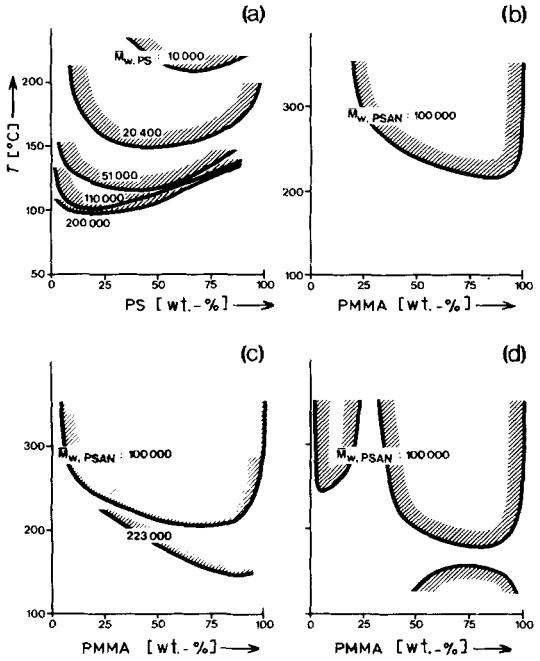


Fig. 9. Turbidity limits in quasibinary polyblends. a) Poly(methyl vinyl ether) ($\bar{M}_w = 51\,500$) and polystyrene (PS) (measurements by *Nishi* and *Kwei*) [50], b) poly(methyl methacrylate) (PMMA) ($\bar{M}_w = 100\,000$) and styrene-acrylonitrile copolymers (PSAN) with an acrylonitrile content of 26.8 wt.-%, c) 28 wt-%, and d) 28.7 wt-%. Curve for $\bar{M}_{w,PSAN} = 223\,000$, after [51]. $\bar{M}_w$ is the weight-average molecular weight; demixed regions are shaded.

Figure 9 shows the turbidity limits for mixtures of polystyrene and poly(methyl vinyl ether)[50] having the repeating unit $-[CH_2-CH(OCH_3)]-$ and for mixtures of poly(methyl methacrylate) and styrene-acrylonitrile copolymers[27,51]. There are certain differences here from mixtures of polymers and low-molecular compounds[52]: mixtures of high polymers always exhibit upper miscibility gaps, *i.e.* a diminished mutual solubility with increasing temperature. The position of the miscibility gaps in a temperature/composition diagram depends on the molecular weight to a great extent. In the case of copolymers there are drastic shifts in the turbidity limits even at small changes in the average composition. The upper and low miscibility gaps have also been found to merge. The lower miscibility gaps can be observed only if they lie above the glass temperature.

Mixtures of oligomers show strongly asymmetric and bimodal turbidity curves (see Fig. 10), as for example in the case of the oligomers of dimethylsiloxane and isobutylene with the repeating unit $-[CH_2-C(CH_3)_2]-$[53], or the oligomers of styrene and isoprene[20]. The mutual solubility increases with rising temperature as in the case of combinations with oligomeric glycols[54]. It is always lower miscibility gaps that are observed in oligomer mixtures.

Equation (2), derived from the lattice model, can be used for qualitative and quantitative description of the phase relationships in "liquid-liquid" systems of the type mentioned above. The first two terms account for the combinatorial

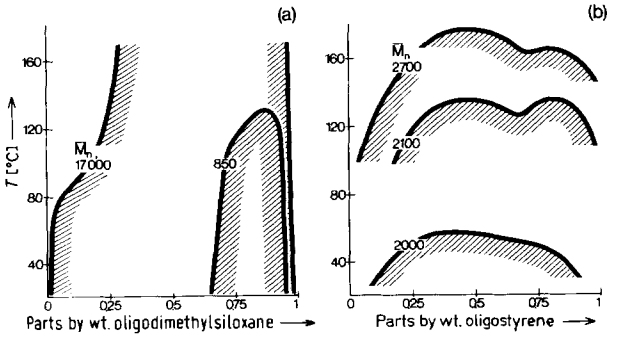


Fig. 10. Turbidity curves for binary oligomer mixtures. a) Oligoisobutylene ($\bar{M}_n \approx 250$) and oligodimethylsiloxanes ($\bar{M}_n = 17000$ and 850) (measurements by *Allen et al.*) [53]; b) oligoisoprene ($\bar{M}_n = 2700$) and oligostyrenes ($\bar{M}_n = 2700$, 2100, and 2000) (measurements by *Konigsveld et al.*) [20]. $\bar{M}_n$ is the number-average molecular weight; demixed regions are shaded.

entropy of mixing. As mentioned before, the correction term χ_{12} originally served only to describe the enthalpic interactions between a segment of polymer 1 and a segment of polymer 2. If this term is zero (when the interactions 1—2 are energetically equal to the sum of the interactions 1—1 and 2—2), the mixture is said to be athermal. The molecular nonuniformity, which is generally encountered with polymer components, is taken into account in the following multicomponent version of eq. (2)[55]:

$$\Delta G_m/(n_1+n_2) = RT\left[\sum_i x_{1i}\ln\Phi_{1i} + \sum_j x_{2j}\ln\Phi_{2j} + \chi_{12}\Phi_1\Phi_2\left(\sum_i x_{1i}m_i + \sum_j x_{2j}m_j\right)\right] \quad (7)$$

where $\Phi_1 = \sum_i \Phi_{1i}$ and $\Phi_2 = \sum_j \Phi_{2j}$

The subscripts i and j refer here to the chains with a number (m_i) of segments in polymer 1, and to the chains with a number (m_j) of segments in polymer 2, respectively. Since the full expression is unwieldy, the treatment is restricted to "quasi-binary" mixtures, and average values of the molecular-weight distributions of the two components are inserted for the relative chain lengths m_1 and m_2. This simplification at once means that a noncombinatorial entropy is assigned to the correction term χ_{12}. The lattice model can be used for the quantitative description of the phase relationships in amorphous polyblends as a function of the composition, temperature, pressure, molecular weight, and molecular-weight distribution only if suitable functional relationships for these factors are available for the correction term χ_{12}. The latter is then a largely empirical correction for the free enthalpy of the athermal mixture with an enthalpy component and a noncombinatorial entropy component. *Koningsveld et al.* have described bimodal turbidity curves for oligomer mixtures of isobutene and dimethylsiloxane with the aid of *e.g.* a quadratic concentration function of χ_{12}[20, 56, 57]. However, this method is merely descriptive and does not permit any predictions to be made about the mixing behavior of chemically different polymers.

On the other hand, *Hildebrand*'s solubility parameters δ permit such predictions to be made without the determination of χ_{12}, which is difficult with high-polymer mixtures[58]. These parameters are a measure of the internal heat of evaporation E needed for overcoming all the intermolecular forces in 1 mole of a liquid, the relevant relationship being:

$$\delta = (E/V_{mol})^{1/2} \quad (8)$$

where V_{mol} is the molar volume. For the change of enthalpy on mixing two liquids, we have that:

$$\Delta H_m = V_{tot}(\delta_1 - \delta_2)^2 \Phi_1 \Phi_2 \quad (9)$$

and using eq. (2), we obtain from this that:

$$\chi_{12} = \frac{V_{tot}}{RT(m_1 x_2 + m_2 x_2)}(\delta_1 - \delta_2)^2 \quad (10)$$

According to *Small*[59], the solubility parameter of a polymer i is obtained as:

$$\delta_i = \rho_i \sum \frac{F_i}{M_{0,i}} \quad (11)$$

where ρ_i is the density of the homopolymer, $M_{0,i}$ is the molecular weight of the repeating unit, and the F_i terms are the attraction constants of the chemical structural elements in the repeating unit (for numerical values, see [60]). The solubility parameters for copolymers are obtained by a linear combination of the partial volumes of the repeating units[61], while the change in the solubility parameter δ occurring when a reference temperature T_0 is replaced by a temperature T is taken into account with the aid of:

$$\ln(\delta_{T_0} - \delta_T) = -\alpha(T_0 - T) \quad (12)$$

where α is always the coefficient of thermal expansion that applies above the glass temperature. If δ is the same for two polymers, eqs. (10) and (2) show respectively that χ_{12} and ΔG_m are zero. A homogeneous single-phase mixture should then be stable. Although eq. (10) can be used only with positive enthalpies of mixing and fails both with partially crystalline polymers and with polymers containing hydrogen bonds, *Krause*[61] and *Casper*[62] have successfully used the concept of solubility parameters for an *a-priori* evaluation of the miscibility of polyblends of technical interest as a function of temperature, composition, and molecular weight. With mixtures of homopolymers and copolymers, the solubility parameter of the copolymer can be equalized with that of the homopolymer by choosing a suitable average composition for the copolymer. This was successful, for example with styrene-acrylonitrile copolymers and poly(methyl methacrylate) (see Fig. 11). The miscibility limits calculated *via* the solubility parameters[62] show at least a qualitative agreement with the experimental values. Although there are also numerous examples where this is not the case, the concept of solubility parameters is increasingly used with oligomer mixtures as well[54, 63].

Extended theories of polymer solutions include, *via* the degrees of freedom of the mobilities, non-combinatorial entropies of mixing as structural defects which for mixtures of liquids are due to differences in packing densities[64–69]. The free enthalpy of mixing is related to experimentally measurable quantities by relatively complicated expressions (thermal coefficients of expansion, compressibility, volume requirement of a chain segment). The property of the mixture can thus be found from the material characteristics of the pure components. In this way, *McMaster* has calculated the phase relationships in polyblends without any empirical correction

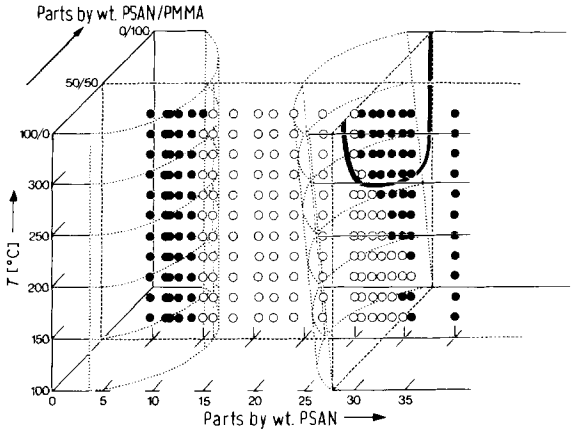


Fig. 11. Miscibility of poly(methyl methacrylate) (PMMA) with styrene-acrylonitrile copolymers (PSAN) as a function of temperature and composition. ○ = optically clear, ● = turbid. Unbroken curve: phase diagram for copolymer composition 72 wt-% styrene, 28 wt-% acrylonitrile (see Fig. 9). Concave surfaces: miscibility limits calculated according to [62] by means of solubility parameters.

terms[51, 70]. In agreement with experimental results, the calculation indicates both a close dependence of the turbidity limits on the molecular weight and the existence of upper miscibility gaps as the normal case for high-polymer mixtures. However, the thermodynamic material data needed for the calculation have been determined with sufficient accuracy only for a few substances. For this reason and because of the mathematics involved, these equations of state are not yet in frequent use.

Structural defects in a mixture, which are also regarded as changes in the free volume, can again be basically combined in the correction term χ_{12} featuring in Eq. (2)[70], in which case the first two terms in this equation remain unchanged[71, 72]. According to *Huggins*, however, we must consider the effect of the surroundings of the chain segments on the chain flexibility, in addition to the possibilities of arrangement, which—as mentioned before—are more limited here than in the case of low-molecular mixtures[73, 74]. The addition of stiff chains makes flexible chains less flexible, so that they will expand. According to *Silberberg*, it should be possible to formulate this effect in the form of a concentration-dependence of the radii of gyration in polyblends[75]. These corrections of *Huggins*' for the entropy of mixing can be combined with *Flory*'s equation of state[65] (changes in free volume on mixing), and they enable us to give a quantitative description of the thermodynamic properties of polyblends solely on the basis of molecular quantities that can be determined experimentally (for details, see [76, 77]).

Polyblends must tend toward a state of minimum free entropy if we are to apply equilibrium thermodynamic criteria to them. This is achieved in the case of demixing if the chemical potential of a component is the same in all the phases. The chemical potential is defined as the differential derivative of the free enthalpy of mixing ΔG_m with respect to the concentration of this component. We have from eq. (2) that:

$$\Delta\mu_1 = \frac{\partial(\Delta G_m/(n_1+n_2))}{\partial x_1} = RT[\ln\Phi_1 + (1-m_1/m_2)\Phi_2 + m_1\chi_{12}\Phi_2^2] \quad (13)$$

An identical chemical potential in demixed phases is indicated by a double tangent at the curve for the free enthalpy of mixing (cf. Fig. 8). This defines the compositions of the coexisting phases, which form the binodal curve at the temperature in question; this curve is identical with the turbidity limit in the case of strictly binary mixtures. It must therefore be ascertained whether the composition of the demixed phases in the miscibility gaps of "quasibinary" polyblends corresponds to the turbidity limit. This has been done successfully for the system composed of poly(methyl methacrylate) and styrene-acrylonitrile copolymer with the aid of broad-line nuclear magnetic resonance. The spectra were recorded for a pure polymer and for mixtures containing increasing amounts of the other polymer. In the miscibility region the spectra for the two pure polymer components are not additive. The homogeneous mixture with a specific composition must be regarded as an individual species with a characteristic spectrum. Just before the turbidity limit is exceeded, one obtains the spectrum of one of those polymer compositions the system is to give by decomposition in the nonmiscible region. Since in the case of immiscibility the nuclear resonance spectra are additive, we can accurately build up the spectra for the polymer compositions in the miscibility gap from the spectra for the polymer mixtures at the turbidity limits, provided that we know the proportions of the phases. The method and results for mixtures of styrene-acrylonitrile copolymers with poly(methyl methacrylate) are shown in Figure 12. The phases have been separated according to the rules of equilibrium thermodynamics for

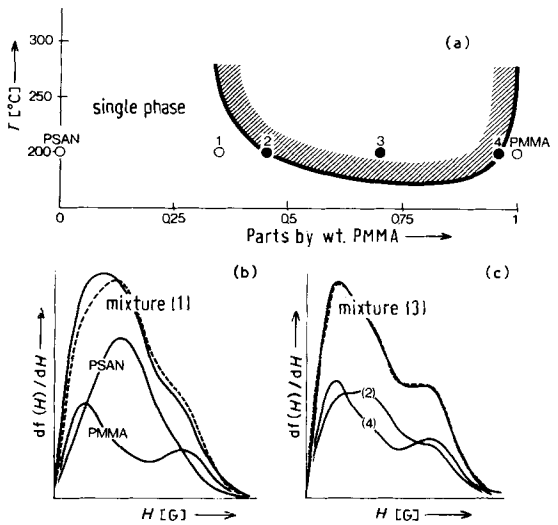


Fig. 12. Additivity and non-additivity of broadline NMR spectra of single- and multi-phase blends of poly(methyl methacrylate) (PMMA) and styrene-acrylonitrile copolymer (PSAN; 71.3 wt-% styrene, 28.7 wt.-% acrylonitrile). a) Turbidity curve, b) and c) resonance signals. Blend (1): PSAN/PMMA = 65/35, blend (3): PSAN/PMMA = 30/70 (phase ratio (2): 0.49, phase ratio (4): 0.51); — experimental curves, ---- curves calculated according to the composition (b), and using the stated phase ratios (c).

liquid mixtures. In quasibinary mixtures, however, the turbidity limit and the binodal curve do not coincide, on account of the inevitable molecular weight distributions[42], and the turbidity limit then by no means represents the composition of the coexisting phases (cf. [78, 79]).

The chemical potential $\Delta\mu_1$ of a component of a polyblend in the homogeneous single-phase region can be determined by small-angle neutron scattering. For this purpose all the hydrogen atoms in one part of the molecules of a component must be replaced by deuterium atoms. Since these isotopes differ in their scattering distances, a small-angle neutron scat-

tering, which—similarly to conventional light scattering—can be evaluated with the aid of eq. (14), is given by a dilute solution of the deuterated polymer in a nondeuterated matrix, or by the opposite system, which is simpler to use from the point of view of the scattering technique but is more difficult to prepare:

$$\frac{Kc_2}{R(\varkappa)} = \frac{1}{M_2 P(\varkappa)} + 2A_2 c_2 + \cdots \tag{14}$$

where $\varkappa$ [$=(4\pi/\lambda)\sin\theta$] is the scattering parameter, c_2, M_2, and A_2 are respectively the concentration, molecular weight, and the second virial coefficient of the polymer component present in the lower concentration, $R(\varkappa)$ is the ratio between the scattered and the incident intensities, $P(\varkappa)$ is *Debye*'s one-particle scatter function[80,81], λ is the neutron wavelength, and θ is the scattering half-angle. The constant K contains the scattering distances of hydrogen and deuterium as the most important quantities. The average scattering mass radius r of the polymer is calculated from $P(\varkappa)$ with the aid of:

$$P(\varkappa) = 1 - \langle r^2 \rangle_z \frac{\varkappa}{3} + \cdots \tag{15}$$

The conversion of $\langle r^2 \rangle_z$ into the weight-average scattering mass radius R_w is done in the usual way, on the assumption of a Schulz-Flory distribution. According to *Zimm*[82], we plot $Kc_2/R(\varkappa)$ against the sum of the concentration of polymer 2 and the square of the scatter parameter $\varkappa$. Extrapolation to $c_2 = 0$ and $\kappa = 0$ gives $P(\varkappa)$ and A_2, respectively. The intercept with the ordinate gives the reciprocal of M_2. Figure 13 shows such graphs for styrene-acrylonitrile copolymers in a matrix of perdeuterated poly(methyl methacrylate) at two temperatures[26]. The second osmotic virial coefficient of polymer 2 (here styrene-acrylonitrile copolymer) can therefore be obtained directly from experiment. It is connected by eq. (16) with the chemical potential $\Delta\mu_1$ of the polymer component 1 present in the higher concentration [here perdeuterated poly(methyl methacrylate)][52]:

$$\Delta\mu_1 = -RT\left[\frac{V_1}{M_2} c_2 + A_2 V_1 c_2^2\right] \tag{16}$$

where V_1 is the partial molar volume of polymer 1. If the chemical potential and the composition of the mixture are known, integration of eq. (13) gives also the value of the

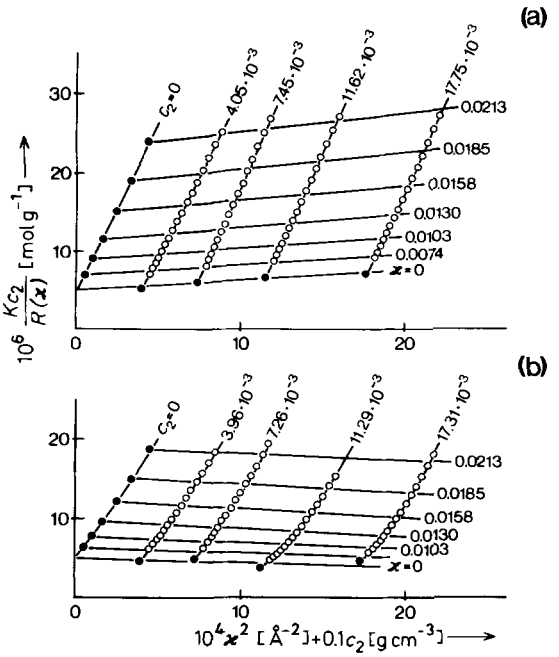


Fig. 13. Zimm diagram for styrene-acrylonitrile copolymer (71 wt-% of styrene, 29 wt-% of acrylonitrile) in perdeuterated poly(methyl methacrylate) at a) 110 °C and b) 130 °C. c_2 = Concentration of the styrene-acrylonitrile copolymer in g/cm^3. $\varkappa$ = scatter parameter, ○ = experimental points, ● = extrapolated values, K = scatter constant.

free enthalpy of mixing ΔG_m. The equation holds in this form only for dilute systems.

Neutron scattering experiments enable us to decide for the first time whether polyblends are molecular disperse in the optically clear domain. This cannot be done with certainty by means of the other methods used to determine whether the system is a multiphase one (dynamic and mechanical measurements, electron microscopy, and calorimetry). The state of the samples remains unchanged during scattering experiments; this method can be used at low concentrations and detects individual molecules. Molecular aggregates can be detected even at high dilutions. The molecular weights that the Zimm diagram (Fig. 13) gives for the styrene-acrylonitrile copolymer in a mixture with poly(methyl methacrylate) agree with the values obtained using conventional methods for the polymers employed. This indicates that in the range of compositions examined the mixtures are molecular disperse. Outside the miscibility gaps there is thorough mixing at the molecular level. Table 2 gives the numerical values for the molecular weights together with the other results obtained

Table 2. Neutron scattering by styrene-acrylonitrile copolymers in deuterated poly(methyl methacrylate). Composition in wt-%. R_w = scattering mass radius. A_2 = second virial coefficient. DMF = dimethylformamide. MEK = methyl ethyl ketone.

Styrene/acrylonitrile	$\bar{M}_w$ from light scattering in DMF	MEK	$\bar{M}_w$ from neutron scattering	T [°C]	R_w [Å]	$A_2 \cdot 10^4$ [mol cm^3 g^{-2}]	$A_{2,n} \cdot 10^4$ [mol cm^3 g^{-2}]	$A_{2,S} \cdot 10^4$ [mol cm^3 g^{-2}]
90/10	64000	60000	70000	110	74	−1.00	1.6	− 2.65
				130	70	−1.10		
81/19	134000	132000	180000	110	114	1.20	2.3	− 1.1
				130	111	1.13		
81/19	263000	255000	270000	110	152	1.15	5.3	− 4.2
				130	142	0.93		
81/19	444000	455000	440000	110	205	1.15	4.9	− 3.9
				130	192	0.89		
71/29	238000	204000	200000	110	134	0.52	16.0	−15.8
				130	120	−0.20		

by the neutron scattering method. As the temperature increases, the scattering mass radius R_w of the styrene-acrylonitrile copolymer decreases, as does the second osmotic virial coefficient A_2. This indicates a diminished dissolving power of poly(methyl methacrylate), in agreement with the existence of upper miscibility gaps. At the same time, when the miscibility limits are approached, the A_2 values decrease according to the acrylonitrile content of the copolymers, as an indication of the decreasing dissolving power of poly(methyl methacrylate) near these limits. The resolution of the A_2 values into an enthalpy term and an entropy term as in eqs. (17) and (18), which are valid for low concentrations[52]:

$$A_{2,H} = -T\left[\left(\frac{\partial A_2}{\partial T}\right)_p - \alpha_1 A_2\right] = -\frac{\Delta H_1}{RTc_2^2 V_1} \tag{17}$$

$$A_{2,S} = A_2 - A_{2,H} = \frac{\Delta S_1^E}{R c_2^2 V_1} \tag{18}$$

where α_1 is the coefficient of expansion, gives a negative sign for the heat of dilution ΔH_1 (indicating an exothermal interaction between the two polymers) and an excess entropy ΔS_1^E, which is surprisingly high for polyblends. The amorphous polyblend can therefore be treated as a liquid mixture.

In mixtures of styrene-acrylonitrile copolymers with a random constitution and various average compositions, the interaction between the two polymer components is endothermal. Despite the negative virial coefficients, the mixtures remain molecular dispersions until the variations in the acrylonitrile content of the component exceed about ±6 wt-%. As the deviation in the composition increases, the scattering mass radii decrease, and the second virial coefficient becomes more and more negative. Table 3 gives some relevant data obtained

Table 3. Neutron scattering by styrene-acrylonitrile copolymer mixtures with various average compositions of the components (monomer ratio in wt-%). $\bar{M}_w = 280000$. $T = 25\,^\circ C$. $\bar{R}_w$ = scattering mass radius. A_2 = second virial coefficient.

Styrene/acrylonitrile		R_w [Å]	$A_2 \cdot 10^4$
Component 1	Component 2	Component 2	[mol cm^3 g^{-2}]
84.5/15.5	81.0/19.0	128	−0.65
83.0/17.0	81.0/19.0	137	−0.08
81.0/19.0	81.0/19.0	138	0
79.5/20.5	81.0/19.0	137	−0.15
78.1/21.9	81.0/19.0	136	−0.2
75.0/25.0	81.0/19.0	134	−0.3

by the neutron scattering method[113]. Clusters are formed when the differences in the ratio of the repeating units of the components are large. The number of chain molecules per aggregate can be determined from the ratio between the molecular weight of the cluster and that of the initial copolymers.

4. Chain Conformation

The conformation of chain molecules in polyblends is basically the same as in homopolymers. Partially crystalline polymers are described by a two-phase model; crystalline regions are separated here by amorphous ones. Individual chain molecules belong partly to crystallites and partly to the amorphous phase. In the lamellar crystallites the chains are closely packed and have either a zigzag or a helical conformation. Owing to varying configuration of the main chains and because of branching, chain ends, and chemical heterogeneity, lattice defects occur in copolymers. As a result of these lattice defects and the amorphous regions, these systems give more or less diffuse X-ray diagrams, with broadened reflections, from which the unit cell for an ideal crystal without any lattice defects can be derived with the aid of stereochemical considerations. From this we can determine the equilibrium conformations of the chain molecules and derive the intramolecular and intermolecular interaction potentials. For example, *Natta et al.*[83] calculated in this way the potential surfaces for isotactic polypropylene with the repeating unit $-[CH_2-CH(CH_3)]-$ as a function of the angle of rotation between two successive monomer units.

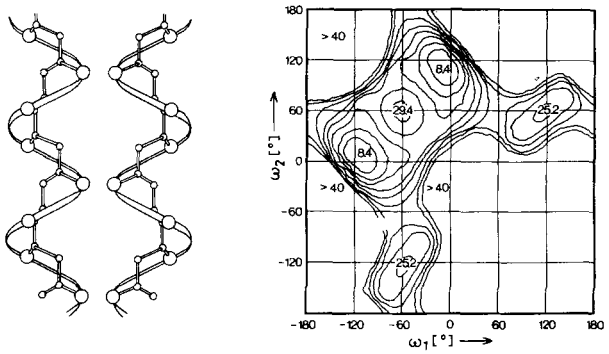


Fig. 14. Helical conformation and potential surfaces for isotactic polypropylene as a function of the angles of rotation ω_1 and ω_2 of two successive monomer units with respect to the main valence bond direction of the chain (after [83]). Numerical data in the diagram: conformational energies in kJ/mol. o $-CH_2-$ or $>CH_2$; O: CH_3.

Figure 14 shows two energy minima, one corresponding to a right-handed and the other to a left-handed triple helix, which have been detected by X-ray crystallography as well.

If the molecular chains continue parallel to the longer edge of the crystallites and if the disordered chain segments emerge from the shorter edge, fringed crystallites are formed as in native cellulose[84]. On the other hand, if the molecular chains run normal to the longer edge of the crystallites and if they emerge there from the crystalline domain and, either directly or after building a loose loop, enter the same or a neighboring crystallite they are called folded crystallites (see Fig. 15).

The periodic arrangement of crystalline and amorphous domains has been detected by small-angle X-ray scattering. The distance between the centers of gravity of the crystallites (the long period) is found from the position of the reflections. At the same time, these measurements show that the density of the non-crystalline domain is in general exactly the same as that of the purely amorphous polymer[85, 86]. However, this is significant only if we can ignore the dependence of the density of the amorphous and crystalline portions on

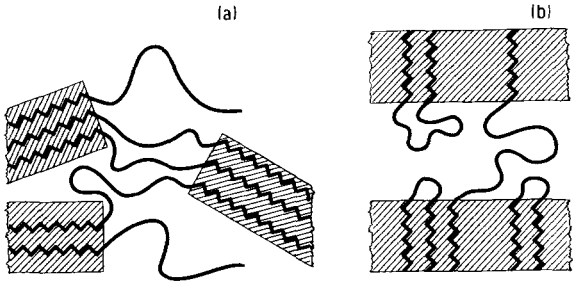


Fig. 15. Chain arrangement in a) fringed and b) folded crystallites (schematic).

the conditions of crystallization, which is difficult in the case of *e.g.* poly(ethylene terephthalate) with the repeating units $-[O-CH_2-CH_2-O-CO-C_6H_4-CO]-$[87]. The surface layer of single crystals of poly(1-butylene) with the repeating unit $-[CH_2-CH(C_2H_5)]-$ has the same glass temperature as the pure amorphous material[88]. Evidently the segmental mobility is frozen in in the cross-loops in the folding regions in the same way as in purely amorphous polymers.

Models for the structure of polymers crystallized from the melt[32] are often based on measurements on single crystals, which are best obtained by subjecting dilute solutions to crystallization. This gives regularly folded lamellar crystals or packets of such crystals; the degree of crystallinity is 80%. The material representing the other 20% goes preferentially to the boundary surfaces, which contain the folds (*i.e.* the loops between leaving and reentering of the chain in the crystallite, see Fig. 15). To elucidate the conformation of the chains in these regions, the sample is subjected to a chemical treatment such as hydrolysis (in the case of polysaccharides) or oxidation with concentrated nitric acid or ozone (in the case of polyethylene), whereupon the chains in the less closely packed folding regions preferentially react first, and the reaction rate falls when the boundaries of the crystalline region have been reached. Chain fragments corresponding to single and multiple traverses across the folding crystallite are obtained. The length of the chain folds in the amorphous domain is obtained in addition if the kinetics of the degradation are studied and the molecular-weight distribution of the decomposition products is determined[89]. This work shows that there is a chain-length distribution, with the greater part of the folds lying in a very narrow region.

The neutron scattering method offers a direct means for investigating the conformation of the chains in partially crystalline polymers. *Schelten et al.*[90, 91] have used this method on melt-crystallized mixtures of non-deuterated and perdeuterated polyethylene, obtained by quenching the melt relatively quickly. This prevents the aggregation of the deuterated material on crystallization and gives a mixture which is still in a state of molecular dispersion. The experimental radii of gyration (scattering mass radii) R_w surprisingly correspond to the conformation of random coils as found in polyethylene melts by *Fischer et al.*[92]. In particular, the dependence of the radius of gyration of the labeled polymer chain on the molecular weight, corresponding to the relationships in a Θ-solvent, cannot be reconciled with the complete insertion into a single folded crystallite. Therefore, *Schelten et al.* assume that the chain molecules crystallize out in their "entirety", with retention both of the coil dimensions of the melt and of the arrangement in which a polymer chain belongs to a number of crystallites and amorphous regions in between. *Yoon* and *Flory* have calculated the angle-dependence of the neutron scattering intensity of perdeuterated polyethylene in a deuterium-free matrix as a function of the proportion of back-folding of the chains into the same crystallite. The best agreement with the experimental values for the scattered intensity, the conformation of chains, and the degree of crystallinity is obtained when a model is used in which it is assumed that 70% of the chains fold back on themselves into the same crystallite[93]. Consequently, quenched melts of crystallizable polymers do not show the adjacent reentry that *Mandelkern*[94] has postulated in general.

If melts of crystallizable polymers are not quenched but are instead cooled slowly under pressure, crystallites with a thickness of up to a few thousand ångstroms are obtained, which thus reach the order of magnitude of fully stretched chain molecules. In recent neutron scattering measurements, *Ballard et al.*[95] have confirmed the stretched conformation in polyethylene crystallized in this way. The lengths of the stretched chains agree with the thickness of crystallites that is determined by the nondeuterated polyethylene matrix and has been found by degradation with nitric acid. The perdeuterated polyethylene molecules aggregate in the deuterium-free matrix, and the number of chain molecules per aggregate can be found from the molecular weight of the latter and that of the perdeuterated polyethylene. The radii of gyration of the aggregates change only slightly with the number of perdeuterated chain molecules in the aggregate. Besides, an increase in the molecular weight of the perdeuterated polyethylene does not lead to a marked increase in the radius of gyration, unlike in the case of the random coil conformation. Clearly, there is again back-folding of the chains into the same crystallite.

There are two models for the conformation and packing in homogeneous melts and solid amorphous polymers. *Flory*'s coil model[96] assumes a random conformation of the chain molecules, similarly to the case of dilute solutions of high polymers. In the unperturbed or Θ-state, the distances of the chain segments from the center of gravity of the coil follow a Gaussian distribution. The scattering mass radius or radius of gyration, which is normally specified, is the mean value of these distances. The coiled conformation leads to penetration of the chain molecules in the condensed state; the network is completely homogeneous. In the bundle models[97–99], on the other hand, it is assumed that the structure is characterized by a nonrandom short-range order, which is due to the parallel alignment of the chain sections and causes inhomogeneity and anisotropy at the molecular level. The situation is analogous either to the back-folding of chains or to the chain bundle in partially crystalline polymers, according to whether the parallel segments belong to the same or to different chain molecules. Because of the assumption of a parallel alignment of the chain sections, the bundle models are expected to give a different value for the radius of inertia from that suggested by the random-coil model. It should therefore be possible to find out which of these models is correct by measuring the radius of gyration as a function of the molecular weight (and in mixtures also of the concentration), as well as by investigating the short-range order at the molecular level to decide whether or not it is anisotropic.

Using the small-angle neutron scattering method, several authors have determined the radii of gyration in the glassy state, for poly(methyl methacrylate)[100, 101] and polystyrene[102–108], and in the melt state, for polyethylene[92, 107] and polypropylene[109], all the samples having been mixed with the corresponding deuterated polymer. Both the glassy state and the fluid state always have radii of gyration that agree with the "unperturbed" values in a Θ-solution. The angle-dependence of the scattered intensity can be described for random coils with the aid of *Debye*'s particle scattering function[92, 110]. Plotting the values in a Zimm diagram shows, with small deviations, a value of zero for the second osmotic virial coefficient, this value being typical of the Θ-state. The

required proportionality is found to exist between the weight-average molecular weight $\bar{M}_w$ and the square of the radius of gyration R_w. Since both the radius of gyration corresponding to the Θ-state and the experimental dependence on the molecular weight can be correctly calculated also for a meandering conformation of the type of a flat disk[111], *Fischer et al.*[92, 112] have tried to detect anisotropy at the molecular level and so to demonstrate the parallel alignment of the chain segments in amorphous polystyrene, poly(methyl methacrylate), and polycarbonate. Electron scattering experiments give a distance distribution for the chain segments in polyethylene melts without any sign of a parallel arrangement. Fluctuations in the density, determined by the small-angle X-ray scattering method, indicate no periodicity whatever. For amorphous polymers above the glass temperature the density fluctuations are fully analogous to those found in high-molecular and also low-molecular melts. The fluctuations at first decrease rapidly with falling temperature, then less rapidly as the temperature drops below the glass point, and finally—after the region of secondary dispersion has been reached—they are completely frozen in. The glassy amorphous state corresponds to a frozen-in melt without any additional order. Measurement of the magnetic birefringence and the scattering of depolarized light has revealed no orientation correlations typical of ordered domains. The anisotropy of the repeating units in the polymer is comparable to that in the monomer, and is a number of orders of magnitude smaller than is expected for parallel bundles of chains. The intermolecular short-range order of the chain segments can be attributed in its entirety to coiling. No additional orientation fluctuations occur in the glassy amorphous polymer. It follows, therefore, that the model predicting a coiled conformation has proven to be the correct one for the amorphous state.

The conformation of the chains in mixtures of various polymers has been determined by the neutron scattering method[26]. In accordance with the exothermal interaction, styrene-acrylonitrile copolymers are expanded with respect to the Θ-state when mixed with poly(methyl methacrylate). The graph obtained by plotting the radii of gyration R_w against the molecular weight (Fig. 16) shows a slope of 0.64 at 110°C and 0.61 at 130°C in the case of low concentrations of the copolymer, as compared to 0.5 for the unperturbed (Θ) state.

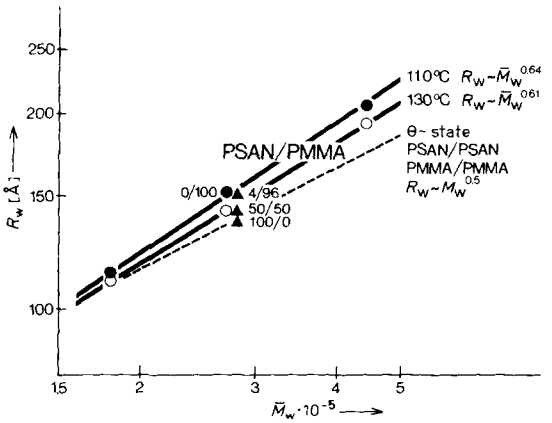


Fig. 16. Radius of gyration R_w of styrene/acrylonitrile copolymers (PSAN containing 19 wt-% acrylonitrile) as a function of the molecular weight $\bar{M}_w$ in blends with poly(methyl methacrylate) (PMMA). ○ = measurements at 130°C; ● and ▲ = measurements at 110°C. Values at points measured: extrapolation values for the composition of PSAN and PMMA in the Zimm plot (Fig. 13).

As the temperature is raised, the coil expansion decreases, and so does the parameter of the R_w *vs.* $\bar{M}_w$ function, indicating that the upper miscibility gap is being approached. The neutron scattering method has also been used to investigate mixtures containing the copolymer in other than very low concentrations[113]. For this purpose both polymers are deuterated with the exception of a small portion of one of the components. The system is then concentrated from the thermodynamic point of view but dilute from the neutron-optical point of view, and the measurements can be again evaluated with the aid of the scattering theory for dilute solutions. As more and more of the "solvent" [poly(methyl methacrylate)] is replaced by styrene-acrylonitrile copolymer the coil expansion decreases in the direction of the unperturbed dimensions of the Θ-state. The radius of gyration for the styrene-acrylonitrile copolymer in its own matrix falls precisely to the R_w *vs.* $\bar{M}_w$ curve for the Θ-state of the amorphous poly(methyl methacrylate).

The aggregation of the chain molecules on incipient phase separation can also be monitored with the aid of the small-angle neutron scattering method, as for example in the case of a mixture of poly(α-methylstyrene) and deuterated poly(methyl methacrylate)[26]. The amount of poly(α-methylstyrene) only has to be raised to above 0.5 wt-% to provoke a drastic increase in the scattered intensity, indicating molecular aggregations. At lower concentrations the mixture is still a molecular dispersion. The evaluation of the measurements in a Zimm diagram (cf. Fig. 11) gives the correct molecular weight and a radius of gyration that is close to the value for the collapsed coil. By analogy with the mixing of polymers with low-molecular compounds, we find that poly(methyl methacrylate) is not a solvent for poly(α-methylstyrene). Its coils are collapsed and tend to aggregate even at low concentrations. The existence of molecular dispersion at low concentrations supports the statement that there is no general incompatibility in the case of amorphous polymers.

5. Supermolecular Structure

The morphology of polyblends is determined by methods that indicate a heterogeneity in the region of supermolecular dimensions. Chemical methods rely on the different reactivities of the phases with special reagents, while physical methods differentiate between the phases on the basis of their different refractive indices, segmental and proton mobilities, polarizabilities, specific heats, and densities. The most frequently used tool is the electron microscope, employed in conjunction with ultrathin sections of the material (for details, see [114–121]).

Electron micrographs are used below to illustrate the effects of the chemical composition of the chain molecules, the temperature, the ratio between the components, and the method of polymerization or mixing on the magnitude, size distribution, and shape of the demixed zones. The system composed of poly(methyl methacrylate) and styrene-acrylonitrile copolymer is used again as an example of mixtures of amorphous polymers with similar freezing-in temperatures for the segmental mobility. The components are miscible at acrylonitrile contents of between 10 and about 30 wt-% in the copolymer, and there are upper miscibility gaps in the system. Figure 17 shows the morphological changes in the melt mixtures

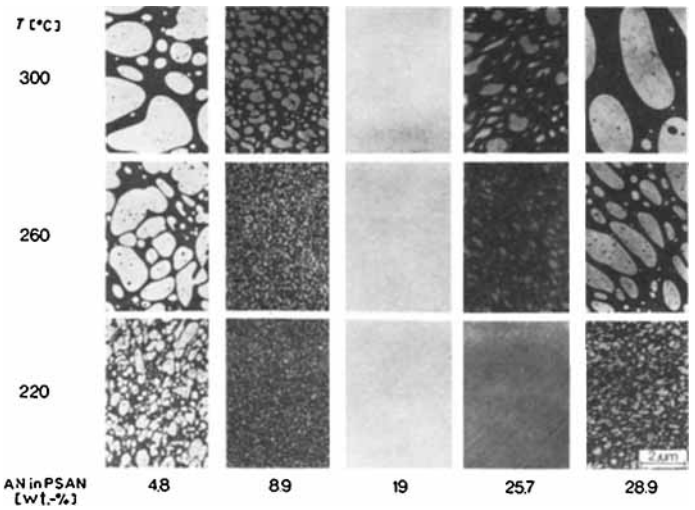


Fig. 17. Electron micrographs for 1 : 1 melt mixtures of poly(methyl methacrylate) and styrene-acrylonitrile copolymers (PSAN) with varying amounts of acrylonitrile (AN). Light areas: phase rich in poly(methyl methacrylate). T = temperature of the melt.

with the composition of the copolymer and the temperature. There are no visible inhomogeneities in the miscibility region[*], and after the miscibility limit has been exceeded the demixed regions become larger and larger and the phase boundaries sharper and sharper. The same occurs when the temperature is raised. The changing contrast of the phases proves that these are not pure substances but are themselves mixtures of the two polymers, with a large amount of poly(methyl methacrylate) (light areas) or of styrene-acrylonitrile copolymer (dark areas).

The combination of styrene-acrylonitrile copolymers with polybutadiene gives ABS polymers, which are important in industry. A characteristic feature of these is the great difference between the glass temperatures of the components. We have here a disperse elastomer phase embedded in a glassy amorphous matrix. Figure 18a shows the morphology of such a material, formed by the simple mixing of the styrene-acrylonitrile copolymer with polybutadiene[**]. The disperse phase is

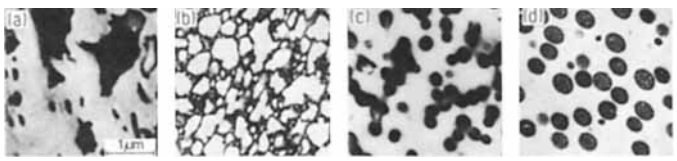


Fig. 18. Acrylonitrile-butadiene-styrene copolymers. a) Melt mixture with disperse elastomer phase, b) melt mixture with continuous elastomer phase, c) latex mixture, with the styrene-acrylonitrile copolymer as the continuous phase, d) emulsion graft copolymer, with the styrene-acrylonitrile copolymer as the continuous phase. Dark areas: elastomer phase.

present in regions of irregular shapes and sizes. The degree of dispersion seems to be fortuitous and depends to a great extent on the shearing forces applied in the mixing. By increasing the amount of the elastomer phase it becomes continuous, and one obtains a reinforced rubber with a morphology such as that shown in Figure 18b, for example.

[*] The globular structure often described in connection with many other amorphous polymers [168] is also absent here.

[**] The elastomer phase is not a butadiene homopolymer here but contains a few percent of acrylonitrile as a comonomer.

In the case of a polybutadiene component that is prepared by emulsion polymerization and is gradually cross-linked, the dispersion is less fortuitous. Figure 18c still shows the original spherical shape of the latex particles. The cross-linking hinders the coalescence of the latex particles, so that the styrene-acrylonitrile copolymer continues to be the continuous phase until its amount in the mixture is much smaller. Graft copolymerization of styrene and acrylonitrile onto preformed polybutadiene latexes gives systems with well-defined morphologies that are largely insensitive to shearing forces and heating to the processing temperature. These systems are stabilized and the latex particles cannot be either fused together or separated. The system shown in Figure 18d is a mixture of a random copolymer and a graft copolymer, illustrated in Figure 1.

The amount of monomers grafted on, the degree of crosslinking, and the particle size are important variables when the required morphology is fixed by emulsion polymerization[11,21]. Figure 19 shows a series of polybutadiene latexes, reacted with increasing quantities of styrene and acrylonitrile and then mixed with more styrene-acrylonitrile copolymer. The

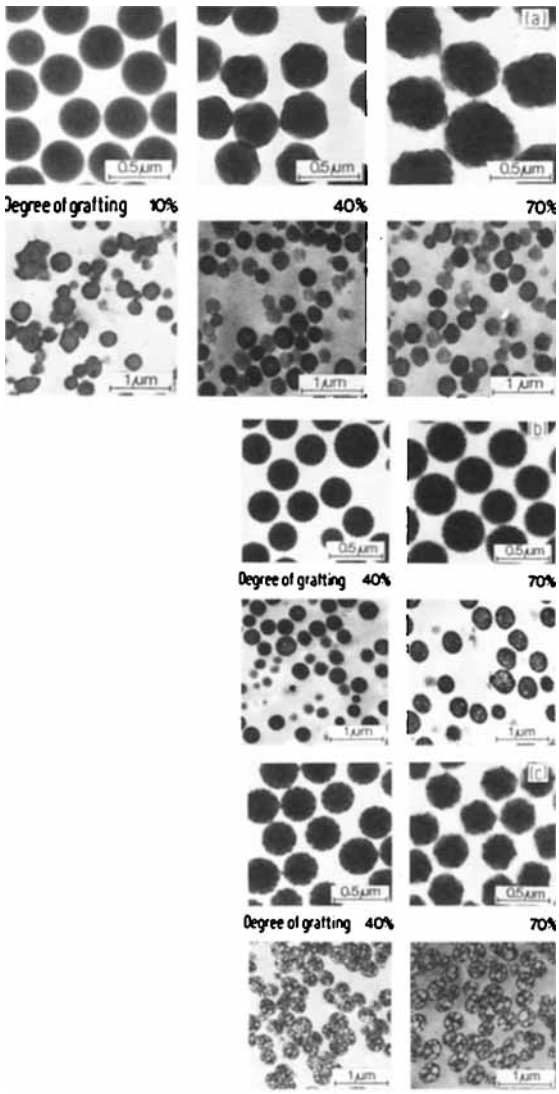


Fig. 19. Acrylonitrile-butadiene-styrene copolymers. Morphology of graft copolymer latexes (above) and of their mixtures with styrene-acrylonitrile copolymer (below), with various amounts of grafted-on monomers and with a) high, b) moderate, and c) slight cross-linking of the polybutadiene base rubber.

grafting monomers cause the latex particles of the basic dispersion to swell and polymerize out on these sites. Since polybutadiene and the graft polymer do not give a homogeneous mixture, a phase separation occurs in the latex particles. Grafted-on monomers can be concentrated in the outer zone of the latex by pre-crosslinking the latex particles (*e.g.* by the addition of a bifunctional comonomer), by introducing the monomers at a rate that is slow in comparison with the rate of polymerization, or by using an initiator that decomposes in an aqueous phase[4]. The result is a stronger envelope, which inhibits the agglomeration of the latex particles when these are mixed with the matrix polymer in the melt. The graft envelope is not visible in the mixture; the dimensions of the polybutadiene-rich phase are about the same as those of the ungrafted rubber particles. As the pre-grafting cross-linking of the latex particles is reduced, the graft envelope becomes less and less complete, even though the amount of the graft monomer remains the same; the graft component is inside the particles. The corresponding electron micrographs in Figure 19 clearly show a domain structure, owing to phase separation inside the particles. The open graft envelope then causes agglomeration of the polybutadiene-rich phase when the components are mixed in the melt. The mechanism and the kinetics of graft polymerization onto elastomeric substrates have been investigated in detail by *Riess* et al.[122–126].

The styrene polymers with a high impact strength, which are produced industrially on a large scale, are also built up of a rigid continuous phase and a soft disperse phase. Monomeric styrene is polymerized in the presence of non-crosslinked dissolved polybutadiene. The formation of homopolystyrene and the grafting of styrene onto polybutadiene proceed here simultaneously, and the result is a mixture of a homopolymer and a graft copolymer. The latter is formed preferentially if polybutadiene with double bonds in side groups is copolymerized with growing styrene chains. Double bonds in the main chain, on the other hand, tend to copolymerize only to a small extent[127] (see Fig. 20). A factor of secondary importance in the case of polybutadiene is the abstraction of allyl hydrogens by a growing polystyrene chain or by a primary radical of the initiator. The radical sites thus transferred to the polybutadiene chain might either become the starting points of a graft branch by the adding-on of further monomer, or they might lose their reactivity by recombination. By contrast, such transfer reactions are responsible for grafting and cross-linking in the case of other base polymers such as polyacrylates.

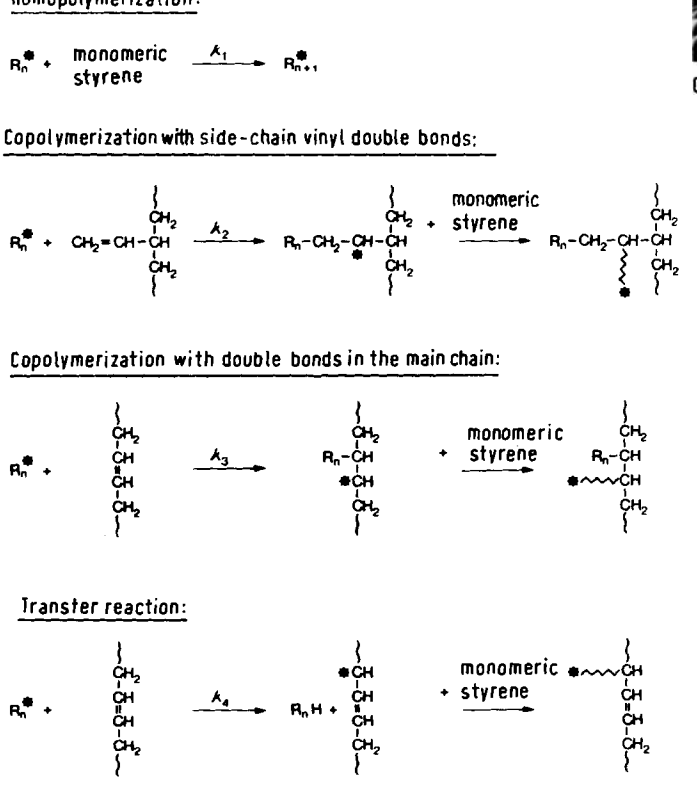


Fig. 20. Graft copolymerization onto polybutadiene (schematic). R_n^*—primary or macroradical, k —rate constant.

Unlike in emulsion polymerization, the attainment of the required morphology of multiphase polymers by grafting and cross-linking is complicated if bulk and suspension polymerization are carried out. If we start the polymerization with a single-phase solution of the base polymer (*e.g.* polybutadiene) in the monomer of the matrix (*e.g.* styrene), a phase separation occurs even at comparatively low conversions; a new disperse phase consisting of the dissolved matrix polymer is formed in the still continuous solution of the rubber in the monomer. The ratio between the volumes of the two phases continuously changes in favor of the matrix polymer until a reversal occurs for geometric reasons, and the phase rich in the matrix polymer coalesces to give a continuous phase (see Fig. 21). After the

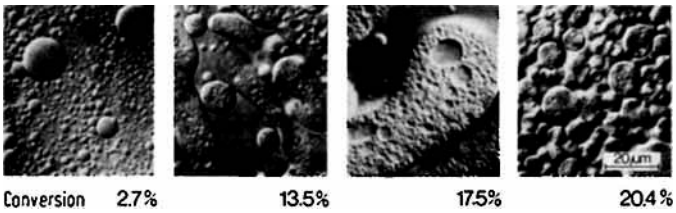


Fig. 21. Interference phase-contrast micrographs for a polymerizing solution of polybutadiene in styrene after a conversion of 2.7, 13.5, 17.5, and 20.4 %.

phase reversal, the graft copolymer formed in the meantime stabilizes the disperse polybutadiene-rich phase, which still contains numerous small polystyrene inclusions. Phenomena of this type were first observed by *Molau*[21,22]. Phase separation and phase reversal depend on the shearing forces in the reaction mixture, the ratio between the viscosities of the disperse and the continuous phase, the molecular weight of the polybutadiene starting material, and the ratio between the amount of styrene grafted on and the total amount of polystyrene formed. Graft copolymers formed before the phase reversal stay in the primary inclusions and do not participate in the phase reversal. Only the graft copolymers formed during or after the phase reversal act as emulsifiers for the disperse phase in the continuous phase[24]. The rheological properties of the reaction mixture largely determine the degree of dispersion and the particle-size distribution of the disperse rubber-phase, whose substructure depends on the chemical composition of the polybutadiene introduced. The substructure changes during the reaction as a result of grafting, and graft copolymers with a block structure are formed. The substructure of the disperse phase can therefore be controlled by adding a styrene-butadiene block copolymers.

Block copolymers form periodically ordered structures at the supermolecular level both in the solid state and in solution, these structures being determined by the ratio between the numbers of repeating units in the blocks (see [115, 128–131]). Figure 22 shows schematically such structures for two-block

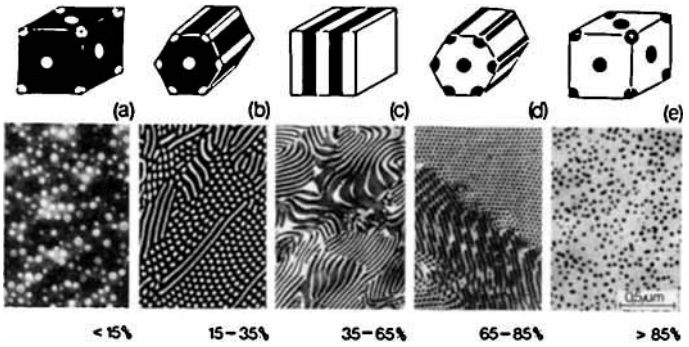


Fig. 22. Morphology of styrene-butadiene two-block copolymers in the solid state as a function of the composition (schematic, after [22]), together with the corresponding electron micrographs a) Polystyrene spheres in a polybutadiene matrix; b) polystyrene cylinders in a polybutadiene matrix; c) polystyrene and polybutadiene lamellae; d) polybutadiene cylinders in polystyrene matrix; and e) polybutadiene spheres in a polystyrene matrix. Dark: polybutadiene. The figures refer to the amount of styrene.

copolymers composed of butadiene and styrene (after *Molau*[22]), together with the corresponding electron micrographs. The polybutadiene-rich and the polystyrene-rich phases separate from each other. In mixtures of styrene-butadiene block copolymers and homopolystyrene, the latter penetrates into the domains of styrene blocks if their molecular weight exceeds that of the homopolymer[132, 133]. As the homopolystyrene portion is increased, the polystyrene-rich domains become larger and finally the morphology abruptly changes into the next type. If the molecular weight of the polystyrene blocks is smaller than that of the homopolymers then they demix to form a separate phase and the morphology of the two-block polymer is not changed but merely perturbed. Increasing the polystyrene content by grafting onto the blocks, on the other hand, always leads, irrespective of the molecular weight of the grafted chains, to a morphological change when the volume of the polystyrene-rich phase exceeds the threshold value to the next type. From the homo- and block-polymers of butadiene a considerable array of morphologies result—on the one hand, by mixing with polystyrene of higher molecular weight, and on the other, *via* the equivalent way of grafting and mixing with low molecular weight polystyrene; the "particle zoo" thus formed is shown in Figure 23.

In the case of block copolymers, the boundaries between the demixed phases do not increase their sharpness indefinitely but are instead characterized by a concentration profile of the repeating units involved, as is shown in Figure 24. Accord-

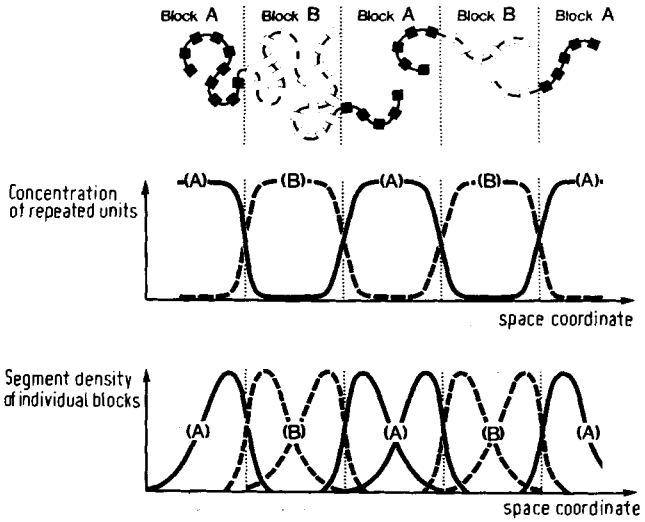


Fig. 24. Domain boundaries and segment-density distribution for two-block copolymers (schematic).

ing to the views on the conformation of the chains in amorphous polymers, a Gaussian curve can be assumed for the variation of the segmental density of the blocks in the area between the site of attachment and the phase boundary lying opposite. The coil dimensions are then fixed for a given molecular weight of the blocks. The size of the phase is limited, because the packing density of the homopolymers involved must be reached in the demixed phases (the temperature-dependent density variations can be neglected here). As a result, the dimensions of the demixed regions are nearly always smaller in block copolymers than in homopolymer mixtures. This readily explains the fact that on mixing a homopolymer in a block copolymer the former is excluded from the block domains when the molecular weight of the homopolymer is higher than that of the block. Homopolymers of lower molecular weight are incorporated in the block domains

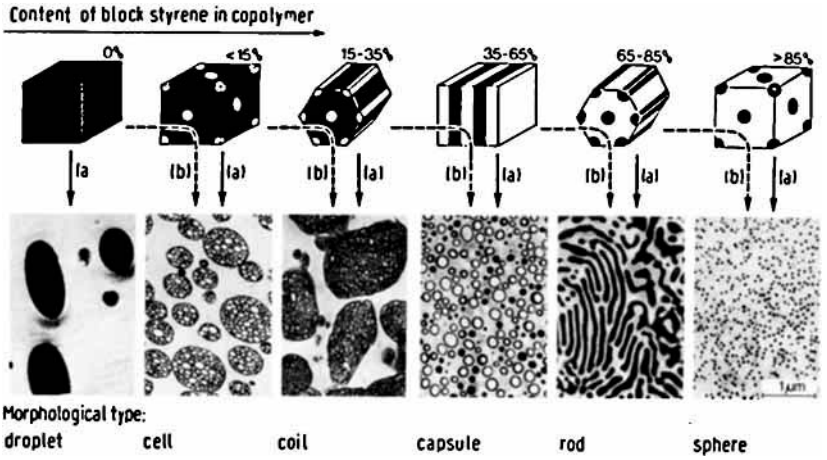
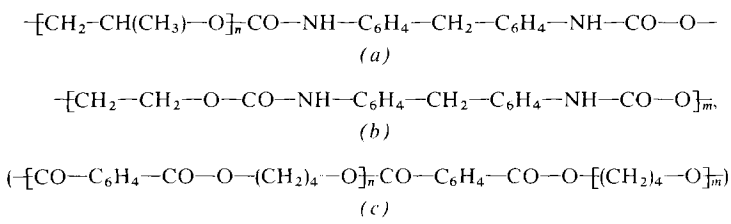


Fig. 23. Manufacture of high-impact polystyrene from ordered precursors (butadiene-styrene block copolymers of varying composition) a) by mixing with fairly high molecular weight polystyrene, b) by grafting in styrene solution.

because of their smaller coil dimensions. Quantitative relationships have been worked out by *Meier*[134–137] and by *Helfand*[138, 139].

As in the case of partially crystalline polymers, the number of possible arrangements of the blocks (and hence their entropy) is smaller in the demixed regions than in the case of free chains in homopolymers. Only the volume of the domains with the same chemical repeating units is available to the blocks, and the site of linkage between the blocks is always near the boundary of the domains. In the case of three-block copolymers there are two coupling sites at the phase boundaries and the entropy is then reduced even more. The diminished entropy of configuration in block copolymers at first opposes the demixing in domains with a high periodicity, but is compensated for by interfacial energies and blurred phase boundaries at the molecular level[140, 170].

Segmental copolymers can be distinguished from copolymers made up of high-molecular blocks, their "blocks" (segments) being much smaller. Polyurethan elastomers are the best known examples; in these, soft and flexible segments *(a)* of aliphatic polyethers or polyesters alternate with hard and stiff segments *(b)* containing the isocyanate linkages. Copolyesters are built up along the same lines; *e. g.* terephthalic acid-diol blocks are connected by soft segments *(c)* formed



(a)

(b)

(c)

by aliphatic polyethers. The hard segments combine to form crystallites, which act as physical cross-linking points. The crystallites melt when the temperature is raised, and re-form on cooling. These materials are therefore described as thermoplastic elastomers. The crystallites connected by soft segments form spherulitic superstructures. Figure 25 shows some typical

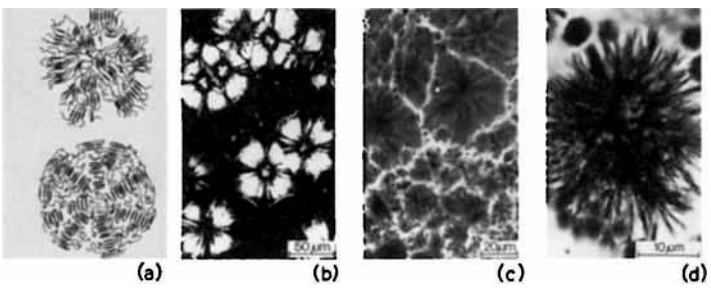


Fig. 25. Morphology of segmental copolymers. a) Schematic (after [141]), b) as seen under a polarization microscope, c) and d) as seen under an electron microscope. Light areas: soft phase.

micrographs, together with a schematic representation of the spherulitic structure after *Seymour*[141], based on light scattering in the small-angle region. The model showing a radial orientation of the crystallites and a tangential direction of the chains (top picture in Fig. 25a) is the more probable one of the two. The low-contrast regions between the spherulites are formed by amorphous material, which largely consists of soft segments and contains only a few short, noncrystallizable hard segments. These do not form a separate phase. In accordance with this morphology, segmental copolymers show, on thermomechanical analysis, a glass transition of the amorphous phase and melting of the crystallites. The dimensions of the crystallites and thus the melting point can be changed by altering the concentration of the hard segments, while the glass temperature and the partial volume of the amorphous phase can be controlled *via* the length of the hard segments[9, 140].

Partially crystalline polyolefin-containing mixed systems must be mentioned as the last example. By a selective reaction between the noncrystalline regions and chlorosulfonic acid, *Kanig* has rendered visible the lamellar crystallites that represent the most important morphological feature of these materials[118, 119]. As Figure 26a shows for linear polyethylene with

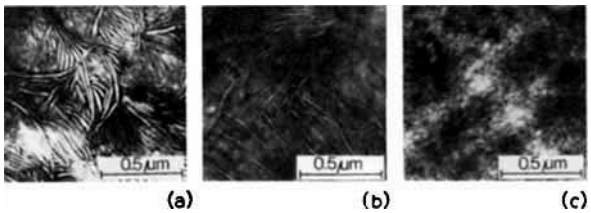


Fig. 26. Morphology of partially crystalline polyolefins (after [119]). a) Linear polyethylene, b) branched polyethylene, c) polypropylene. Dark areas: noncrystalline regions.

the repeating unit $-[CH_2-CH_2]-$, the lamellae are about 15 nm thick, bent, and matted together. As can be seen from Figure 26b, branched polyethylene with the repeating unit $-[CH_2-CH(C_nH_{2n+1})]-$ has thinner lamellae and an altogether less regular structure, somewhat like polypropylene, shown in Figure 26c. According to *Kanig*, this proves that the branching sites are not embedded into the lamellar crystallites but are instead located in the amorphous regions. Up to an ethylene content of about 70%, ethylene-propylene copolymers (possibly mixed with small amounts of nonconjugated dienes) which show a random sequence of the monomer repeating units give noncrystalline flexible thermoplastics that exhibit a high permanent set[169]. When the amount of ethylene is higher, the ethylene sequences form crystallites, which act as physical cross-linking sites and confer elastic properties on the material. The combination of polypropylene with polyethylene or with copolymers of both gives products that are both tough and elastic. Figure 27a shows inclusions in

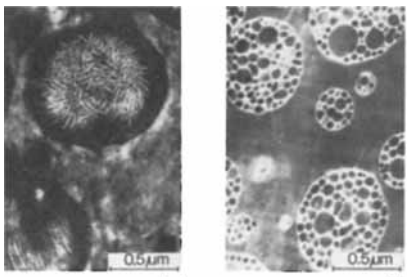


Fig. 27. Morphology of polyolefin copolymers (after [119]). a) Polypropylene with ethylene-propylene copolymer as disperse phase (dark areas: noncrystalline regions), b) polystyrene with cross-linked ethylene-propylene copolymer as the disperse phase (light areas: elastomeric phase).

a polypropylene matrix with small irregular lamellae; these inclusions consist of an outer shell made up of noncrystalline copolymer and of a central core of large polyethylene crystallites. Besides butadiene rubber and acrylate rubber, copolymers of about 30% of propylene, 60% of ethylene, and 10% of a diene are also used to modify the impact strength

of polystyrene. In accordance with this composition, the electron micrograph in Figure 27b shows no lamellar crystallites but instead the well-known picture of impact-resistant polystyrene with an amorphous elastic rubber component.

6. Optical Properties

For multiphase polymers turbidity is the rule and transparency the exception. However, the latter property is needed for certain technical applications. If the dimensions of the demixed phases are comparable to, or larger than, the wavelength of visible light, optically clear mixtures are obtained by equalizing the refractive indices of the various phases. For this, the components with different refractive indices must be mixed homogeneously within the phases. Use is often made of copolymers whose refractive indices are obtained from those of the corresponding homopolymers by linear combination, taking into account the partial volumes of the repeating units. Figure 28 shows the morphology of such copolymers,

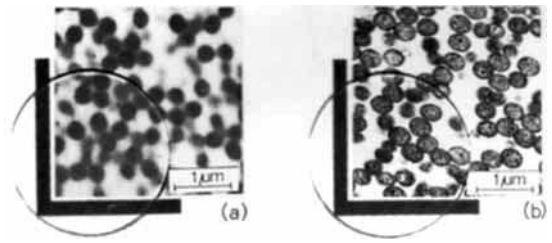


Fig. 28. Transparent elastomer-reinforced thermoplastics. Refractive index equalization between styrene-methyl methacrylate copolymer (continuous phase) and an elastomer phase composed of a) styrene-butyl acrylate copolymer, and b) styrene-butadiene copolymer.

together with disks made from them. Optically clear, elastomer-reinforced thermoplastics are obtained *e.g.* by embedding a random copolymer of butyl acrylate ($n_D = 1.467$[*]) and styrene ($n_D = 1.591$[*]), or by incorporating a copolymer of butadiene ($n_D = 1.515$[*]) and styrene into a styrene-methyl methacrylate matrix. The disperse phase can also contain inclusions of the isorefractive matrix material, as it does here in the second case. The matrix and the elastomer phase are linked by grafting.

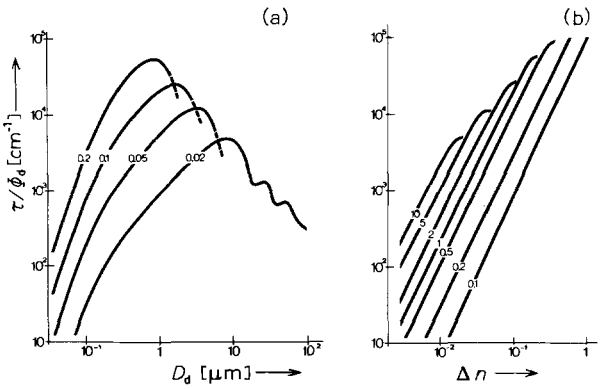


Fig. 29. Turbidity coefficient τ of two-phase mixtures after *Mie*, as a function of a) the diameter d_D of the disperse phase at various values of the refractive index contrast Δn and b) the refractive index contrast, at various values of the particle diameter in [µm]. The refractive index contrast is the difference between the refractive index of the continuous phase and that of the disperse phase, relative to the mean value of the refractive index, and Φ_d is the partial volume of the disperse phase. The curves are calculated at a wavelength of 0.55 nm and a refractive index of $n = 1.55$ for the disperse phase.

[*] These values refer to the homopolymers at 25°C.

The equalization of refractive indices is basically possible only for a single wavelength, and it must be borne in mind that these indices will not coincide if one changes over to other wavelengths. However, polymers with the same refractive index generally show the same wavelength-dependence of the refractive index [poly(vinyl chloride) is an exception], so that the system remains transparent over a wide spectral region. A critical factor is the variation of temperature, which can lead to changes in the phase compositions and thus to turbidity.

Figure 29 shows the turbidity (caused by one-particle scattering of the disperse phase) as a function of the "refractive index contrast" (defined as the difference between the refractive indices of the disperse and the continuous phase) and the magnitude of the phases, after *Mie*. The turbidity coefficient τ relative to the partial volume Φ_D of the disperse phase and defined by eq. (19) is used as a measure of the scattered intensity:

$$I(x)/I_0 = \exp[-(\varepsilon+\tau)x] \tag{19}$$

where I_0 is the intensity of the incident light, $I(x)$ is the transmission, ε is the absorption coefficient, τ is the turbidity coefficient, and x is the layer thickness. The turbidity always increases exponentially with the particle size (at a constant refractive index contrast) and with the refractive index contrast (at a constant particle size). Systems with a low refractive index contrast and small dimensions of the particles in the disperse phase have low turbidity values. For particle diameters of up to one-fifth of the wavelength of light, the refractive index of the disperse phase can be equalized with that of the matrix by grafting. Despite a core envelope structure, it is possible to specify a volume-average refractive index for graft copolymers, according to *Kerker*[142]. If the graft base exhibits a particle-size distribution, the ratio between the volume of the core and that of the envelope is not constant, and smaller particles, which have a larger specific surface area, are more strongly grafted. Thus we have a refractive index distribution after grafting and cannot obtain an accurate coincidence with the refractive index of the matrix polymer. This difficulty is reduced by using a monodisperse graft base. Figure 30 shows, for polybutadiene latexes with a monodisperse and bimodal distribution, the various graft envelopes composed of styrene, the corresponding particle-size distributions, and the transparency obtained after embedding into an isorefractive styrene-methyl methacrylate copolymer. The linking of the elastomeric graft copolymers with the chemically different matrix polymer is achieved by repeated grafting with the monomer of the matrix material. The degree of dispersion of the disperse phase can be controlled in this way.

When the disperse phase is not distributed homogeneously but forms agglomerates, it is particularly the angle-dependence of the scattered light that is modified. Figure 31 shows the scattered intensity I_s as a function of the angle of scattering ϑ in a Guinier plot for two elastomer-modified styrene-methyl methacrylate copolymers of different transparencies. In the case of homogeneous distribution the scatter is drastically reduced. The dimensions of the scattering centers can be found from the gradient of the linear portion of the graph[**]. The

[**] The nonlinear rise in the scattered intensity at small angles is caused by the presence of small amounts of impurities.

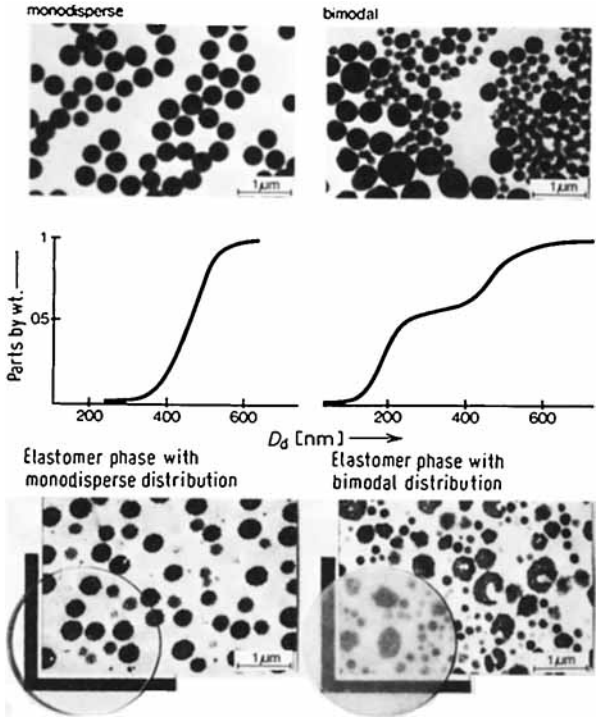


Fig. 30. Particle-size distribution and transparency of elastomer-modified styrene-methyl methacrylate copolymers (elastomer: polybutadiene-styrene graft copolymer). Top: graft dispersion; middle: integral particle-size distribution; bottom: mixture with the copolymer. D_d = particle diameter of the disperse elastomeric phase.

values obtained in the present case (a) are around 1300 nm, so that the scattering centers are not single rubber particles (whose size, found from electron micrographs, is about 100 nm), but larger clusters.

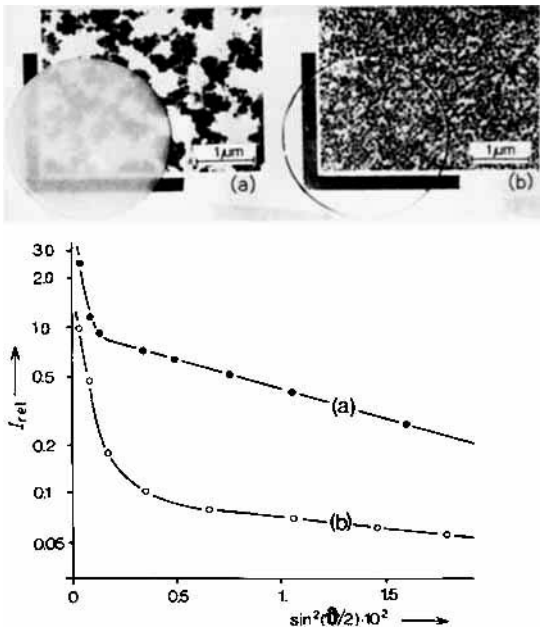


Fig. 31. Transparency and degree of dispersion of the disperse phase in elastomer-modified styrene-methyl methacrylate copolymers. Guinier plot of the relative intensity of the scattered light I_{rel} as a function of the scattering angle ϑ in the case of a) clustering and b) homogeneous dispersion of the elastomer phase. The intensities are relative to the scattering of optically clear samples at the smallest angle. Rubber phase: styrene-butadiene graft copolymer, approximately isorefractive with the continuous phase.

The dependence of the scattered intensity I_s on the angle of scattering ϑ is generally determined by the particle factor P^2 and the lattice factor L^2 in accordance with:

$$I_s(\vartheta) = P^2(\vartheta) \cdot L^2(\vartheta) \tag{20}$$

P^2 describes the scatter caused by single particles, while L^2 describes their superposition. The lattice factor is found from

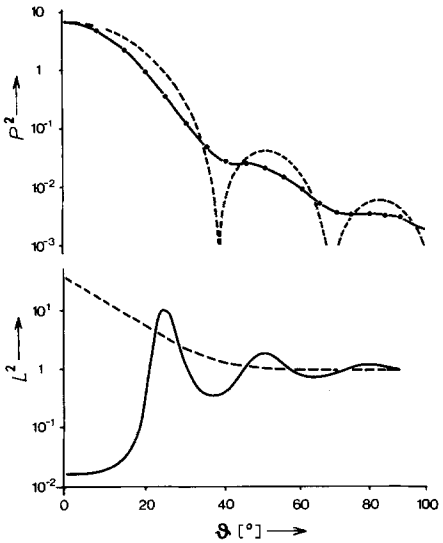


Fig. 32. a) Particle factor P^2 and b) lattice factor L^2 of the scattered intensity as a function of the scattering angle ϑ. a) Scattering centers with a particle-size distribution about the average diameter of 800 nm—experimental values (—); monodisperse scattering centers with a diameter of 800 nm, calculated after *Mie* (----); b) regular short-range order of the scattering centers (—) and Gaussian distribution of the distances (---).

the quotient of the scattered intensities at low and high concentration. Figure 32a shows schematically the variation of P^2 with the scattering angle in the case of particles with a diameter of about 800 nm. At a uniform particle size sharp minima and maxima are obtained, while a particle-size distribution gives a smoothed curve. The distribution of the distances between the scattering centers is represented by the lattice factor L^2 (see Fig. 32b). The variation of L^2 with the angle of scattering is clearly different for Gaussian distribution and for a regular short-range order. Increasing short-range order gives rise to sharp maxima and minima and to particularly low L^2 values in the first region, where P^2 is large. Multiplication of P^2 and L^2 as in eq. (20) gives the angle-dependent scattered light, whose volume integral—the turbidity—decreases with increasing short-range order.

As the distance between the scattering centers decreases, and as the particles become smaller, the curves for P^2 and L^2 shift toward larger angles of scattering. For example, in the case of an arrangement of monodisperse particles that

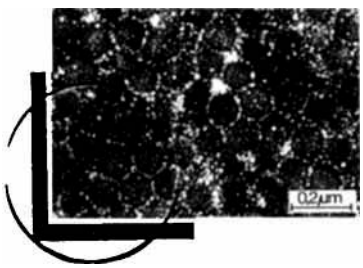


Fig. 33. Morphology and transparency of a polybutadiene latex ($n_D^{20} = 1.515$) and polystyrene ($n_D^{20} = 1.591$).

are in contact with one another and have diameters smaller than 150 nm, the first maximum of the lattice factor leaves the optical region at a scattering angle of 180°. L^2 is then very small in the entire optical region, and fully transparent two-phase systems are obtained (despite the large refractive index contrast), owing to the extinction of the scattered

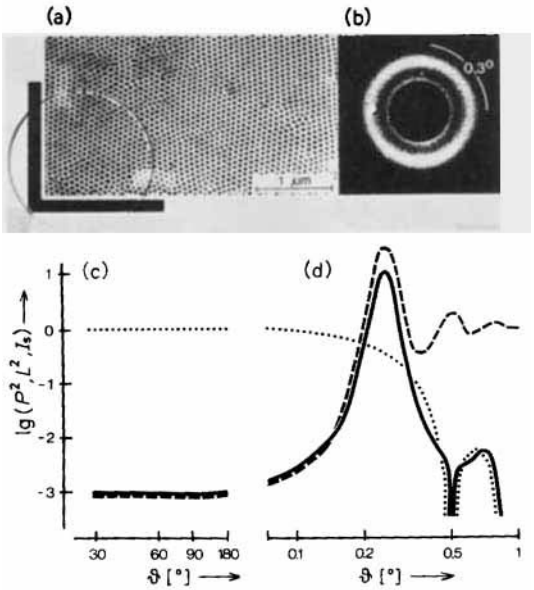


Fig. 34. a) Morphology and transparency of styrene/butadiene/styrene three-block copolymers. b) X-ray scattering of the lattice order in the small-angle region below 0.3°. c) Elucidation of particle scattering by the lattice factor in the light-scattering region ($\lambda = 546$ nm). d) Scattering in the X-ray small-angle region ($\lambda = 0.154$ nm). —— I_s, – – – L^2, ··· P^2. ϑ = scattering angle.

light[143]. Figure 33 shows by way of example a close-packed polybutadiene latex in a polystyrene matrix. Excellent examples of optically clear polymeric multiphase systems with considerable differences in the refractive index of the two phases are the highly ordered anionically polymerized two- or three-block copolymers of styrene and butadiene or isoprene. Demixing of the molecularly uniform blocks leads to domains on uniform size. Figure 34 shows the morphology, the change in the particle factor, the lattice factor, and the scattering intensity for the optical and the small-angle X-ray range. Practically no scattering occurs in the visible region; the copolymers are fully transparent. The high degree of order of the lattice of the demixed phases is made clear from the X-ray picture (Fig. 34b).

7. Mechanical Properties

From the technological point of view, multiphase polymers are of interest mainly because of their ability to withstand impacts without suffering brittle fracture. When a glassy amorphous polymer is subjected to deformation, the stress increases largely in proportion to the elongation and then leads to fracture. Polymers possessing rubber-like elasticity can undergo reversible elongations to several times their original length without fracture. The energy applied is harmlessly stored in the material, and the stresses are restricted. Figure 35 shows some typical tensile stress/elongation curves for glassy styrene-acrylonitrile copolymer, polybutadiene, and two ABS copolymers with different morphologies. Owing to the visco-elasticity of the material, the slope and the shape of

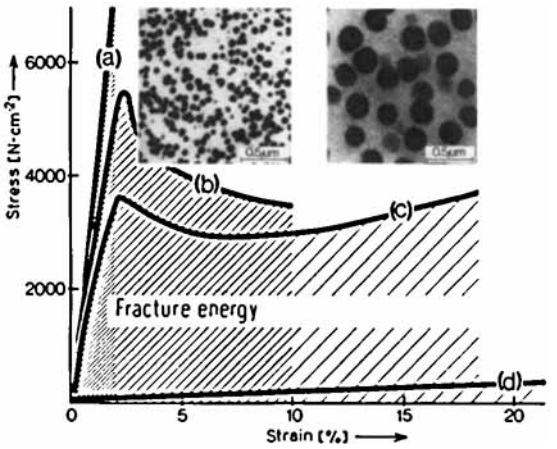


Fig. 35. Stress-elongation diagrams for a) glassy styrene-acrylonitrile copolymer, b) and c) acrylonitrile-butadiene-styrene copolymers with different morphologies, and d) polybutadiene. Electron micrographs: left: blend (b), right: blend (c).

the curves depend on the rate of deformation; as the latter is increased, the slope generally becomes greater and the elongation shorter. The usual impact strength tests correspond to very high rates of deformation. The energy of fracture, which is given by the area under the stress/elongation curve, is a measure of the impact strength. The pure elastomer component has a very low modulus. In contrast, the two-phase ABS polymers have a modulus that is only slightly lower than that of pure styrene-acrylonitrile copolymer and they clearly show the change from reversible elongation to permanent set or yield points.

The mechanical and dynamic properties of multiphase polymers emerge from the use of oscillating loads, the parameters being the shear modulus (a measure of the elastically stored energy of deformation) and the loss modulus (a measure of the dissipated energy). Figure 36 shows the variation of

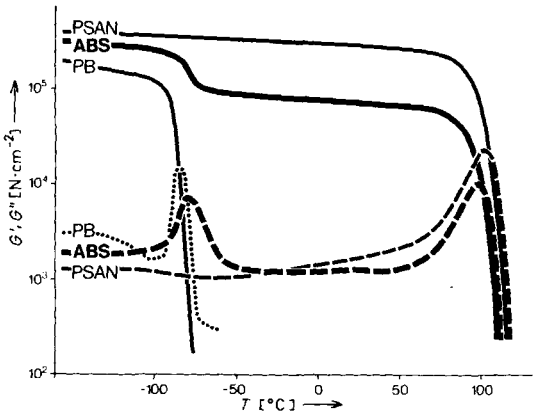


Fig. 36. Thermomechanical measurements on styrene-acrylonitrile copolymer (PSAN), acrylonitrile-butadiene-styrene copolymer (ABS), and polybutadiene (PB). Shear modulus G' (unbroken curve) and loss modulus G'' (dashed curve) as a function of temperature.

both these moduli with the temperature, again in the case of styrene-acrylonitrile copolymer, polybutadiene, and a two-phase ABS polymer. The curves for the first two are typical of the amorphous state: in the region of the glass temperature, the loss modulus G'' reaches a maximum, and the shear modulus G' drops from the value typical of glassy polymers to a value typical of rubber (cf. Fig. 2). Depending on the composition, copolymers with a random arrangement of the

repeating units show a corresponding curve in the region between the glass temperatures of the homopolymers. On the other hand, the curve for the two-phase polymer shows two damping maxima and a stepped fall in the shear modulus at both glass temperatures. The drop occurring at the glass temperature of the elastomer phase depends on the proportion of the latter and is comparatively low up to about 30 wt-%. Good use properties are obtained if the glass temperature of the elastomer phase is well below the temperature of use and the glass temperature of the matrix is well above the temperature of use. The impact strength is linked to the coexistence of a hard phase and an elastomer phase.

Partially crystalline two-phase polymers possess toughness in the sense of a continuous decomposition of the stress in the material without fracture on irreversible deformation. In the lamellar crystallites of these polymers, rearrangements and slip processes occur, which dissipate the energy introduced. Creep also occurs in limited regions in glassy amorphous polymers just before brittle fracture during the deformation process (see Fig. 37). This phenomenon leads either to shear bands (shear yielding) or to crazing. The former are sharply outlined regions of highly ordered chain molecules, with a density unchanged from that of the unoriented material. The chains align in the direction of the load, and the shear bands run at an angle to it, in the direction of the maximum shear stress. Owing to the homogeneous density, shear bands are not visible under the electron micrsocope, but can be observed only by polarization-optical means. The crazed state is characterized by gaps which run normal to the direction in which the load is applied and are filled with fibrils or lamellae, drawn out in the direction of the applied force, with numerous cavities between them. The density is much lower here than in the original material, and there is a volume dilatation, whose quantitative determination enables one to distinguish between shear bands and crazing during deformation[144]. The density fluctuation causes light scattering and is visible to the naked eye as a white fracture.

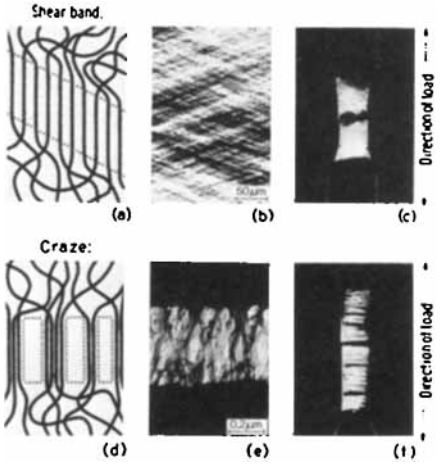


Fig. 37. Shear bands and crazing in glassy amorphous polymers. a) Shear band (schematic), b) under a polarization microscope, c) to the naked eye in polarized light, d) crazing (schematic), e) under an electron microscope [167], f) to the naked eye.

Cold drawing of the polymer chains[*] and the formation of internal surfaces are mechanisms of energy dissipation which decompose the stress and delay the fracture during the application of a load. It is believed that creep is triggered off by inhomogeneities, at which strain peaks cumulate during the application of an external force (for fundamental works see [145–152]). According to generally accepted views, a disperse elastomer phase causes a drastic increase in the initiation of these creep processes by strain peaks in the glassy amorphous matrix at the boundary with the elastomer. Figure 38 shows schematically that a uniaxially applied external force

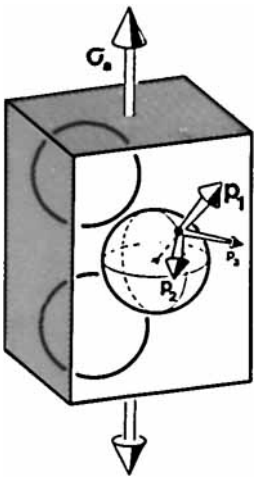


Fig. 38. Resolution of a uniaxial external force σ_a at the elastomer/matrix phase boundary into radial components and tangential components p_1 and p_2 and p_3, respectively.

σ_a produces multiaxial stress states at the boundary with a spherical elastomer phase. Two directions (p_2 and p_3) are tangential and one direction (p_1) is radial to the surface of the sphere. It is decisive for the toughness of the material which of the two types of plastic deformation takes place, which depends on the ratio between the stresses in the various directions; this ratio has different values at different points on the spherical surface. In a simplified model in which the direction of the external force is not taken into account, the total local stress is resolved into a dilatory isotropic component p (hydrostatic tension or hydrostatic pressure) and a shear component s, which causes deformations with a constant volume. The isotropic stress p and the shear stress s are defined by eqs. (21) and (22):

$$p = \frac{1}{3}(p_1 + p_2 + p_3) \tag{21}$$

$$s^2 = \frac{1}{6}[(p_1 - p_2)^2 + (p_2 - p_3)^2 + (p_3 - p_1)^2] \tag{22}$$

Sternstein et al.[153–155] investigated those combinations of the dilatory component and the shear component at which shear-induced creep, crazing, or brittle fracture occurs in the case of a polymethyl methacrylate that was not modified with an elastomer and presumably had a very high molecular weight. Deformation occurs in the form of crazing when the ratio between the dilatory and the shear component of the applied force exceeds 0.2 (at 60 °C). *Matsuo et al.*[156] have applied this result to two-phase systems and calculated the stress distribution in the surroundings of disperse elastomer spheres (for fundamentals, see [157]). With an external force

[*] Shock loads lead to a considerable rise in temperature locally, where the glass temperature is exceeded.

applied in the direction of the poles, the dilatory component of the stress has a maximum positive value at the equator of the sphere, whereas the shear component reaches its maximum at latitudes of 45° (see Fig. 39a). According to *Matsuo*,

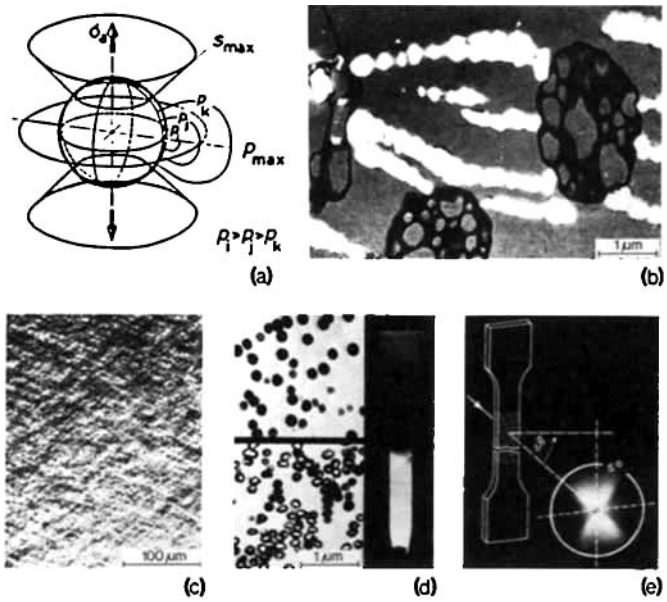


Fig. 39. Deformation mechanisms in rubber-modified thermoplastics. a) Maximum values of the shear component s and the dilatory component p of a uniaxial external force σ_A (schematic); b) crazing in polystyrene with a disperse elastomer phase; c) shear bands in poly(vinyl chloride) with a disperse elastomer phase; d) bursting of the elastomer phase under the influence of an external load; e) light scattering of the burst rubber particles in the small-angle region (ϑ = scattering angle).

the superposition of the force fields between neighboring spheres further increases the dilatory stress component in the equatorial plane. These results are qualitatively supported by the electron micrographs recorded for the deformed rubber-modified material (see Figs. 39b and 39c). Thus the crazing in the equatorial plane is triggered off vertically to the direction of the applied force, and the shear bands run at an angle to it. *Sternstein*'s results cannot be applied quantitatively to the force fields in a rubber modified system, because the experimentally determined craze limits must be assigned exclusively to surface-initiated crazes, and these are not formed at the same stress limits as those found in the bulk of the material[158]. Besides, the side groups of poly(methyl methacrylate) are already mobile at measuring temperatures of over 50 °C.

In Figure 39c, obtained for rubber-modified poly(vinyl chloride), the shear bands can be recognized only indirectly. The corresponding electron micrograph (Fig. 39d) shows cavities in the rubber particles, produced by splitting or bursting under the influence of the applied force. The volume dilatation therefore takes place in the disperse phase and not in the matrix. The light scattered at the cavities leads to a scatter pattern of high orientation, whose preferred directions represent the angle between the shear bands and the direction of the applied force (see Fig. 39e). The burst rubber particles, which act as scattering centers, are concentrated in the shear bands and form a rhomboid network with a lower density than that of the unsheared material[159].

The embedding of disperse rubber particles evidently promotes the creep process, which is also exhibited by the unmodified glassy amorphous matrix. Except for polystyrene, which has a pronounced tendency to crazing, most polymers seem to have a preference for the exclusive or at least the predominant formation of shear bands at high rates of stressing[160, 161]. Thus, practically no crazing can be observed in elastomer-modified poly(methyl methacrylate) whose molecular weight still permits processing *via* the melt; this is in contrast to the numerous published findings, presumably obtained for a high-molecular material.

To obtain a tough material, the disperse elastomer phase must adhere well to the surrounding matrix. The earlier view that the energy of deformation is transferred to the rubber phase *via* an adhesive layer, *e.g.* a graft shell, and is then absorbed there is incorrect, and it is enough to look at the stress-elongation diagram (Fig. 34) to realize that, in the usual elongation, the elastomer phase absorbs only a small proportion of the energy of fracture.

The cooling of a melt with a disperse elastomer phase first leads to the glassy solidification of the continuous phase. On further cooling this phase contracts in accordance with the coefficient of thermal expansion α, which is about 2×10^{-4} K^{-1} for amorphous polymers below the glass temperature. The elastomer phase still has the character of a liquid and contracts about three times as much as specified above. Since the elastomer phase is coupled to the matrix, the result is its unavoidable dilatation and the setting-up of a hydrostatic tension in the rubber[162]. This hypothesis is supported by the observation of the bursting of non-crosslinked polybutadiene inclusions in polystyrene on cooling[163] and on the lowering of the glass temperature of cross-linked polybutadiene graft rubbers below the value of the pure homopolymer[164–166]. This phenomenon is the reverse of the well-known one, where the glass temperature of elastomers rises during isotropic compression (hydrostatic pressure). It is often concluded that the hydrostatic tension of the drawn rubber is transferred to the surrounding matrix as a dilatory stress and promotes *a priori* crazing there. However, as *Breuer* has shown[161], while it is true that the hydrostatic tension in the rubber phase leads to an equal radial counter-stress in the matrix, there are at the same time some "arch stresses" lying tangentially to the boundary surface, as a result of which the sum of all the stresses is zero, and so there is no dilatory stress component in the matrix, according to eq. (21). Since the stress components in the various directions differ in their sign and magnitude, the difference between them gives the matrix a pure shearing stress exerted by the prestressed rubber, in accordance with eq. (22). Independently of this, an external force will then produce a dilatory stress, with a maximum round the equator of the rubber particles.

The author wishes to thank the following persons for their help with the preparation of the present review: Dr. K. Bergmann, Prof. Dr. G. Kanig, and Dr. W. Heckmann (Mess- und Prüflaboratorium der BASF-AG), Dr. J. Stabenow (Ammoniaklaboratorium der BASF-AG), Dr. H. Breuer, Dr. H. Naarmann and Dr. P. Wittmer (Kunststofflaboratorium der BASF-AG), and Prof. Dr. R. G. Kirste (Institut für Physikalische Chemie der Universität Mainz).

Received: June 7, 1978 [A 263 IE]
German version: Angew. Chem. 91, 286 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] *B. Vollmert:* Polymer Chemistry. Springer, Berlin 1973, S. 42, 207.
[2] *B. O. Gesner* in *H. F. Mark, N. S. Gaylord:* Encyclopedia of Polymer Science and Technology. Vol. 10. Wiley-Interscience, New York 1969, p. 694.
[3] *L. Bohn*, Kolloid Z. Z. Polym. *213*, 55 (1966).
[4] *H. Willersinn*, Makromol. Chem. *101*, 296 (1967).
[5] *G. E. Molau*, J. Polym. Sci. Polym. Lett. Ed. *3*, 1007 (1965).
[6] *H. A. Stuart*, Ber. Bunsenges. Phys. Chem. *74*, 739 (1970).
[7] *H. Pohlemann*, Chem.-Ztg. *97*, 165 (1973).
[8] *R. D. Deanin, A. A. Deanin, T. Sjoblom* in *L. H. Sperling:* Recent Advances in Polymer Blends, Grafts and Blocks. Vol. 4. Plenum Press, New York 1974.
[9] *G. Wegner*, Angew. Makromol. Chem. *58/59*, 37 (1977).
[10] *F. Bueche, W. M. Cashin, P. Debye*, J. Phys. Chem. *20*, 1956 (1952).
[11] *F. Bueche*, J. Phys. Chem. *48*, 1410 (1968).
[12] *S. E. Bresler, G. M. Zakharov, S. V. Kisilor*, Vysokomol. Soedon. *3*, 1072 (1961).
[13] *C. C. Lee, W. Rovatti, S. M. Scinner, E. G. Bobalek*, J. Appl. Polym. Sci. *9*, 2047 (1965).
[14] *E. H. Merz, G. C. Claver, M. Baer*, J. Polym. Sci. *22*, 325 (1956).
[15] *Y. Minoura, H. Jino, M. Tsukasa*, J. Appl. Polym. Sci. *9*, 1229 (1965).
[16] *W. Rovatti, E. G. Bobalek*, J. Appl. Polym. Sci. *7*, 2269 (1963).
[17] *D. Z. Angier, W. F. Watson*, J. Polym. Sci. *18*, 129 (1955).
[18] *L. Bohn*, Kolloid Z. Z. Polym. *213*, 55 (1966).
[19] *V. I. Alekseyenko*, Vysokomol. Soedin. *2*, 1449 (1960).
[20] *R. Koningsveld, L. A. Kleintjens, H. M. Schoffeleers*, Pure Appl. Chem. *39*, 1 (1974).
[21] *G. E. Molau*, J. Polym. Sci. Part *A 3*, 1267, 4235 (1965).
[22] *G. E. Molau, H. Keskkula*, J. Polym. Sci. Part *A 1*, *4*, 1595 (1966).
[23] *A. Stein, R. L. Walter*, US-Pat. 2886553 (1957), Monsanto.
[24] *A. Echte*, Angew. Makromol. Chem. *58/59*, 175 (1977).
[25] *R. H. Jung, D. J. Stein*, IUPAC Symposium on Macromolecules, Aberdeen 1973, Preprints G 10, 411.
[26] *W. A. Kruse, R. G. Kirste, J. Haas, B. J. Schmitt, D. J. Stein*, Makromol. Chem. *177*, 1145 (1976).
[27] *L. P. McMaster*, Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. *15*, 254 (1974).
[28] *J. W. Cahn*, J. Chem. Phys. *42*, 93 (1965).
[29] *J. W. Cahn, J. E. Hilliard*, J. Chem. Phys. *23*, 258 (1958).
[30] *J. J. van Aarsten*, Eur. Polym. J. *6*, 919 (1970).
[31] *G. Zachmann*, Kolloid Z. Z. Polym. *231*, 504 (1969).
[32] *B. Wunderlich:* Macromolecular Physics. Vol. 1. Academic Press, New York 1973.
[33] *H. G. Killian*, Makromol. Chem. *116*, 219 (1968).
[34] *J. Jelenic, R. G. Kirste*, unpublished results.
[35] *T. Nishi, T. T. Wang*, Macromolecules *8*, 909 (1975).
[36] *G. D. Patterson, T. Nishi, T. T. Wang*, Macromolecules *9*, 603 (1976).
[37] *H. G. Zachmann*, Angew. Makromol. Chem. *60/61*, 249 (1977).
[38] *H. Goldbach, G. Rehage*, Ber. Bunsenges. Phys. Chem. *70*, 1144 (1966).
[39] *W. Frank, H. A. Stuart*, Kolloid Z. Z. Polym. *225*, 1 (1968).
[40] *V. E. Gul, E. A. Penskaya, V. N. Kuleznev, S. G. Arutyonova*, Dokl. Akad. Nauk SSSR *160*, 154 (1965).
[41] *H. Gerrens*, Chem.-Ing.-Tech. *39*, 1053 (1967).
[42] *R. Koningsveld*, Br. Polym. J. *7*, 435 (1975).
[43] *P. J. Flory:* Principles of Polymer Chemistry. Cornell University Press, Ithaca 1953.
[44] *M. L. Huggins:* Physical Chemistry of High Polymers. Wiley, New York 1958.
[45] *R. L. Scott*, J. Chem. Phys. *17*, 279 (1949).
[46] *P. J. Flory*, Angew. Chem. *87*, 787 (1975).
[47] *P. J. Flory*, Ber. Bunsenges. Phys. Chem. *81*, 885 (1977).
[48] *N. F. Komskaya, G. L. Slonimski*, Zh. Fiz. Khim. *30*, 1529, 1746 (1956).
[49] *G. V. Struminski, G. L. Slonimski*, Zh. Fiz. Khim. *30*, 1941, 2144 (1956).
[50] *T. Nishi, T. K. Kwei*, Polymer *16*, 285 (1975).
[51] *L. P. McMaster*, Am. Chem. Soc., Div. Org. Coat. Plast. Chem. Pap. *35*, 1, 322 (1975).
[52] *B. A. Wolf*, Fortschr. Hochpolym. Forsch. *10*, 109 (1972).
[53] *G. Allen, G. Gee, J. P. Nicholson*, Polymer *2*, 8 (1961).
[54] *B. A. Wolf, G. Blaum*, Coatings and Plastics, Preprints 173. Meeting of the ACS, New Orleans, March 20—25, 1977, p. 11.
[55] *R. L. Scott*, J. Chem. Phys. *13*, 5, 178 (1945).
[56] *R. Koningsveld, A. J. Staverman*, J. Polym. Sci. Part *C 16*, 1775 (1967).
[57] *R. Koningsveld, L. A. Kleintjens, A. R. Schultz*, J. Polym. Sci. Part *A-2*, *8*, 1261 (1970).
[58] *J. H. Hildenbrand, R. L. Scott:* The Solubility of Nonelectrolytes. Reinhold, New York 1950.
[59] *P. A. Small*, J. Appl. Chem. *3*, 75 (1953).
[60] *K. L. Hoy*, J. Paint Technol. *42*, 76 (1970).
[61] *S. Krause*, J. Macromol. Sci. Rev. Macromol. Chem. *67*, 251 (1972).
[62] *R. Casper, L. Morbitzer*, Angew. Makromol. Chem. *58/59*, 1 (1977).
[63] *B. A. Wolf*, Makromol. Chem. *178*, 1869 (1977).
[64] *I. Prigogine:* The Molecular Theory of Solutions. North-Holland, Amsterdam 1957.
[65] *P. J. Flory*, J. Am. Chem. Soc. *87*, 1833 (1965).
[66] *R. A. Orwoll, J. P. Flory*, J. Am. Chem. Soc. *89*, 6814 (1967).
[67] *J. P. Flory, B. E. Eichinger, R. A. Orwoll*, Macromolecules *1*, 287 (1968).
[68] *D. Patterson*, Macromolecules *2*, 672 (1969).
[69] *J. P. Flory*, Discuss. Faraday Soc. *49*, 7 (1970).
[70] *L. P. McMaster*, Macromolecules *6*, 760 (1973).
[71] *D. Patterson, G. Delmas*, Discuss. Faraday Soc. *49*, 98 (1970).
[72] *D. Patterson*, Pure Appl. Chem. *31*, 133 (1972).
[73] *M. L. Huggins*, J. Phys. Chem. *74*, 371 (1970).
[74] *M. L. Huggins*, J. Phys. Chem. *80*, 1317 (1976).
[75] *A. Silberberg*, J. Chem. Phys. *48*, 2835 (1968).
[76] *R. Koningsveld, R. F. T. Stepto*, Macromolecules, in press.
[77] *R. Koningsveld*, Ber. Bunsenges. Phys. Chem. *81*, 959 (1977).
[78] *K. W. Derham, J. Goldsbrough, M. Gordon*, Pure Appl. Chem. *38*, 97 (1974).
[79] *K. W. Derham, J. Goldsbrough, M. Gordon, R. Koningsveld, L. A. Kleintjens*, Makromol. Chem. Suppl. *1*, 401 (1975).
[80] *P. Debye*, J. Appl. Phys. *15*, 338 (1944).
[81] *P. Debye*, J. Phys. Colloid Chem. *51*, 18 (1947).
[82] *B. H. Zimm*, J. Chem. Phys. *16*, 1093, 1099 (1948).
[83] *G. Natta, P. Corradini, P. Ganis*, Makromol. Chem. *39*, 138 (1960).
[84] *O. Gerngross, C. Hermann, W. Abitz*, J. Phys. Chem. *B10*, 371 (1930).
[85] *E. W. Fischer, H. Goddar, G. F. Schmidt*, J. Polym. Sci. *5*, 619 (1967).
[86] *E. W. Fischer, H. Goddar, R. Salovey*, J. Polym. Sci. *7*, 307 (1969).
[87] *S. Fakirow, E. W. Fischer, G. F. Schmidt*, Makromol. Chem. *176*, 2459 (1975).
[88] *E. W. Fischer, F. Kloos, G. Lieser*, J. Polym. Sci. Polym. Lett. Ed. *7*, 845 (1969).
[89] *G. N. Patel, A. Keller*, J. Polym. Sci. Polym. Phys. Ed. *13*, 2259, 2275 (1975).
[90] *J. Schelten, G. D. Wignall, D. G. H. Ballard*, Polymer *15*, 682 (1974).
[91] *J. Schelten, D. G. H. Ballard, G. D. Wignall, G. W. Langmann, W. Schmatz*, Polymer *17*, 751 (1976).
[92] *E. W. Fischer, J. H. Wendorff, M. Dettermaier, G. Lieser, I. Voigt-Martin*, J. Macromol. Sci. Phys. *B12*, 41 (1976).
[93] *D. Y. Yoon, P. J. Flory*, Polymer *18*, 509 (1977).
[94] *L. Mandelkern*, J. Polym. Sci. Part *C 50*, 457 (1975).
[95] *D. G. H. Ballard, A. Cunningham, J. Schelten*, Polymer *18*, 259 (1977).
[96] *P. J. Flory:* Statistical Mechanics of Chain Molecules. Wiley, New York 1969.
[97] *V. A. Kargin*, J. Polym. Sci. *30*, 247 (1958).
[98] *W. Pechhold, S. Blasenbrey*, Kolloid Z. Z. Polym. *241*, 955 (1970).
[99] *G. S. Y. Yeh*, Crit. Rev. Macromol. Sci. *1972*, 173.
[100] *R. G. Kirste, W. A. Kruse, J. Schelten*, Makromol. Chem. *162*, 299 (1972).
[101] *R. G. Kirste, W. A. Kruse, K. Ibel*, Polymer *16*, 120 (1975).
[102] *J. P. Cotton, B. Farnoux, G. Jannink, J. Mous, C. Picot*, C. R. Acad. Sci. Ser. *C 275*, 175 (1972).
[103] *H. Benoit, J. P. Cotton, D. Decker, B. Farnoux, J. S. Higgins, G. Jannink, R. Ober, C. Picot*, Nature *245*, 13 (1973).
[104] *H. Benoit*, J. Macromol. Sci. Phys. *B12*, 27 (1976).
[105] *D. G. H. Ballard, G. D. Wignall, J. Schelten*, Eur. Polym. J. *9*, 965 (1973).
[106] *D. G. H. Ballard, G. D. Wignall, J. Schelten*, Eur. Polym. J. *10*, 861 (1974).
[107] *G. D. Wignall, D. G. H. Ballard, J. Schelten*, J. Macromol. Sci. Phys. B 12, 75 (1976).
[108] *J. P. Cotton, D. Decker, H. Benoit, B. Farnoux, J. Higgins, G. Jannink, R. Ober, C. Picot, J. Cloizeaux*, Macromolecules *7*, 863 (1974).
[109] *E. W. Fischer, J. H. Wendorff, M. Dettenmaier, G. Lieser, I. Voigt-Martin*, Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. *15*, 8 (1974).
[110] *D. Y. Yoon, P. J. Flory*, Polymer *16*, 645 (1975).
[111] *W. Ruhland*, Progr. Colloid Polym. Sci. *57*, 192 (1975).
[112] *M. Dettenmaier, E. W. Fischer*, Makromol. Chem. *177*, 1185 (1976).
[113] *B. J. Schmitt, J. Jelenic, R. G. Kirste*, Makromol. Chem., in press.
[114] *K. Kato*, J. Polym. Sci. Polym. Lett. Ed. *4*, 35 (1966).
[115] *H. Hendus, K. H. Illers, E. Ropte*, Kolloid Z. Z. Polym. *216/217*, 110 (1967).
[116] *M. Matsuo, C. Nozaki, Y. Jyo*, Polym. Eng. Sci. *9*, 197 (1969).
[117] *K. von Bassewitz, G. Menzel*, Angew. Makromol. Chem. *47*, 201 (1975).
[118] *G. Kanig*, Kolloid Z. Z. Polym. *251*, 782 (1973).
[119] *G. Kanig*, Progr. Colloid Polym. Sci. *57*, 176 (1975).
[120] *G. Kanig, H. Neff*, Colloid Polym. Sci. *253*, 29 (1975).
[121] *J. Stabenow, F. Haaf*, Angew. Makromol. Chem. *29/30*, 1 (1973).
[122] *J. Periard, A. Banderet, G. Ries*, Angew. Makromol. Chem. *15*, 37 (1971).
[123] *J. L. Locatelli, G. Ries*, Angew. Makromol. Chem. *28*, 161 (1973).
[124] *J. L. Locatelli, G. Ries*, Angew. Makromol. Chem. *32*, 101, 117 (1973).

[125] J. L. Locatelli, G. Ries, Angew. Makromol. Chem. 35, 57 (1974).
[126] J. L. Locatelli, G. Ries, J. Polym. Sci. Polym. Lett. Ed. 11, 257 (1973).
[127] D. J. Stein, G. Fahrbach, H. J. Adler, Angew. Makromol. Chem. 38, 67 (1974).
[128] M. Matsuo, S. Sagaye in G. E. Molau: Colloidal and Morphological Behaviour of Block and Graft Copolymers. Polym. Colloids Proc. Symp. 1970. Plenum Press, New York 1971, p. 1.
[129] G. Kämpf, M. Hoffmann, H. Krömer, Ber. Bunsenges. 74, 851, 859 (1970).
[130] T. Hashimoto, K. Nagatoshi, A. Todo, H. Hasegawa, H. Kawei, Macromolecules 7, 364 (1974).
[131] B. Gallot, Pure Appl. Chem. 38, 1 (1974).
[132] E. B. Bradford in [128], p. 21.
[133] B. Ptaszynski, J. Terisse, A. Skoulios, Makromol. Chem. 176, 3483 (1975).
[134] D. J. Meier in J. J. Burke, V. Weiss: Block and Graft Copolymers. Syracuse University Press, New York 1973, pp. 105ff.
[135] D. J. Meier, Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. 15, 171 (1974).
[136] D. J. Meier, Appl. Polym. Symp. 24, 67 (1974).
[137] D. J. Meier, Vortragstagung der Fachgruppe Makromolekulare Chemie der GDCh, Bad Nauheim 1975.
[138] E. Helfand in [8].
[139] E. Helfand, Acc. Chem. Res. 8, 295 (1975).
[140] S. L. Aggarwal, Polymer 17, 938 (1976).
[141] R. W. Seymour, J. R. Overton, L. S. Corley, Macromolecules 8, 331 (1975).
[142] M. Kerker, J. Opt. Soc. Am. 65, 376 (1975).
[143] H. Breuer in G. H. Frischat: The Physics of Non-Crystalline Solids. 4th International Conference, Clausthal-Zellerfeld 1977, Trans. Techn. Publ., Rockport, p. 88.
[144] C. B. Bucknall, D. Clayton, Nature Phys. Sci. 231, 107 (1971).
[145] J. P. Berry, J. Polym. Sci. 50, 107, 315 (1961).
[146] J. P. Berry, J. Polym. Sci. A 1, 993 (1963).
[147] J. P. Berry, J. Polym. Sci. A 3, 2027 (1965).
[148] R. P. Kambour, J. Polym. Sci. A 2, 4159, 4165 (1964).
[149] R. P. Kambour, J. Polym. Sci. A-2, 4, 17, 349 (1966).
[150] R. P. Kambour, IUPAC-Symposium Leiden 1970, Preprints II, 977.
[151] R. P. Kambour, J. Polym. Sci. Macromol. Rev. 7, 1 (1973).
[152] J. J. Benbow, Proc. Phys. Soc. London 78, 970 (1961).
[153] L. C. Cessna, S. S. Sternstein, Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. 8, 1516 (1967).
[154] S. S. Sternstein, L. Ongchin, A. Silverman, J. Appl. Polym. Symp. 7, 175 (1968).
[155] S. S. Sternstein, L. Ongchin, Polym. Prepr. Am. Chem. Soc. Div. Polym. Chem. 10, 1117 (1969).
[156] M. Matsuo, T. T. Wang, T. K. Kwei, J. Polym. Sci. A-2, 10, 1085 (1972).
[157] J. N. Goodier, J. Appl. Mech. 55, A 39 (1933).
[158] G. Rehage, G. Goldbach, Angew. Makromol. Chem. 1, 125 (1967).
[159] F. Haaf, H. Breuer, J. Stabenow, Angew. Makromol. Chem. 58/59, 95 (1977).
[160] H. Breuer, F. Haaf, J. Stabenow, J. Macromol. Sci. Phys. B 14, 387 (1977).
[161] H. Breuer, Vortrag auf "Conference Toughening of Plastics", The Plastics and Rubber Institute, London, July 1978.
[162] L. Bohn, Angew. Makromol. Chem. 20, 129 (1971).
[163] J. A. Schmitt, IUPAC-Symposium Toronto 1968, Preprints II, A 9.
[164] M. Matsuo, A. Ueda, Y. Kondo, Polym. Eng. Sci. 10, 253 (1970).
[165] S. S. Sternstein, IUPAC-Symposium Leiden 1970, Preprints II, 973.
[166] D. Kranz, L. Morbitzer, K. H. Ott, R. Casper, Angew. Makromol. Chem. 58/59, 213 (1977).
[167] R. P. Kambour, R. R. Russel, Polymer 12, 237 (1971).
[168] G. Kämpf, Angew. Makromol. Chem. 60/61, 297 (1977).
[169] H. Blümel, Kautsch. Gummi, Kunstst. 24, 517 (1971).
[170] H. A. J. Battaerd, J. Polym. Sci. Polym. Symp. 49, 149 (1975).

Chemical Vapor Deposition of Silicon Carbide and Silicon Nitride—Chemistry's Contribution to Modern Silicon Ceramics

By Erich Fitzer and Dieter Hegen[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Pure silicon carbide and silicon nitride have valuable properties in bulk pore-free form; however, their industrial exploitation has hardly been possible so far. Neither compound can be melted or sintered in pure form; hot pressing or sintering at normal pressure requires the presence of additives; and the reaction-sintering process in which only Si and C or Si and N are employed as additives affords porous materials.—The novel process of chemical vapor deposition has partly overcome the drawbacks of the previous methods. In the new process SiC is produced, *e.g.*, by pyrolysis of CH_3SiCl_3, and Si_3N_4 by reaction of $SiCl_4$ with NH_3. This technique can also be used for pore filling in objects made of SiC and Si_3N_4 (gas phase impregnation) and for producing extremely fine SiC and Si_3N_4 powder and SiC monofilaments suitable as components for SiC composites. Moreover, gas phase impregnation can also give fiber composites.

1. Introduction

The tempestuous advances in the field of physical metallurgy, solid state physics, and fracture mechanics have relegated the chemical basis of materials developments to a background role in modern materials science. It has become apparent, however, that for stringent technical demands greater attention should be focused on chemical aspects in the solution of problems. In the case of the silicon ceramics dealt with in this paper (SiC, Si_3N_4, silicon nitride solid solutions), which are considered for use in the manufacture of components for gas turbines and other topical high-temperature applica-

[*] Prof. Dr. E. Fitzer, Dr. D. Hegen
Institut für Chemische Technik der Universität
Kaiserstr. 12, D-7500 Karlsruhe 1 (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0295 $ 02.50/0

tions[1], chemical vapor deposition could provide new impetus because these materials cannot be produced by fusion methods (see Fig. 1[2-4]); moreover, standard techniques of powder metallurgy or ceramics lead not only to production problems but also to serious restrictions on quality.

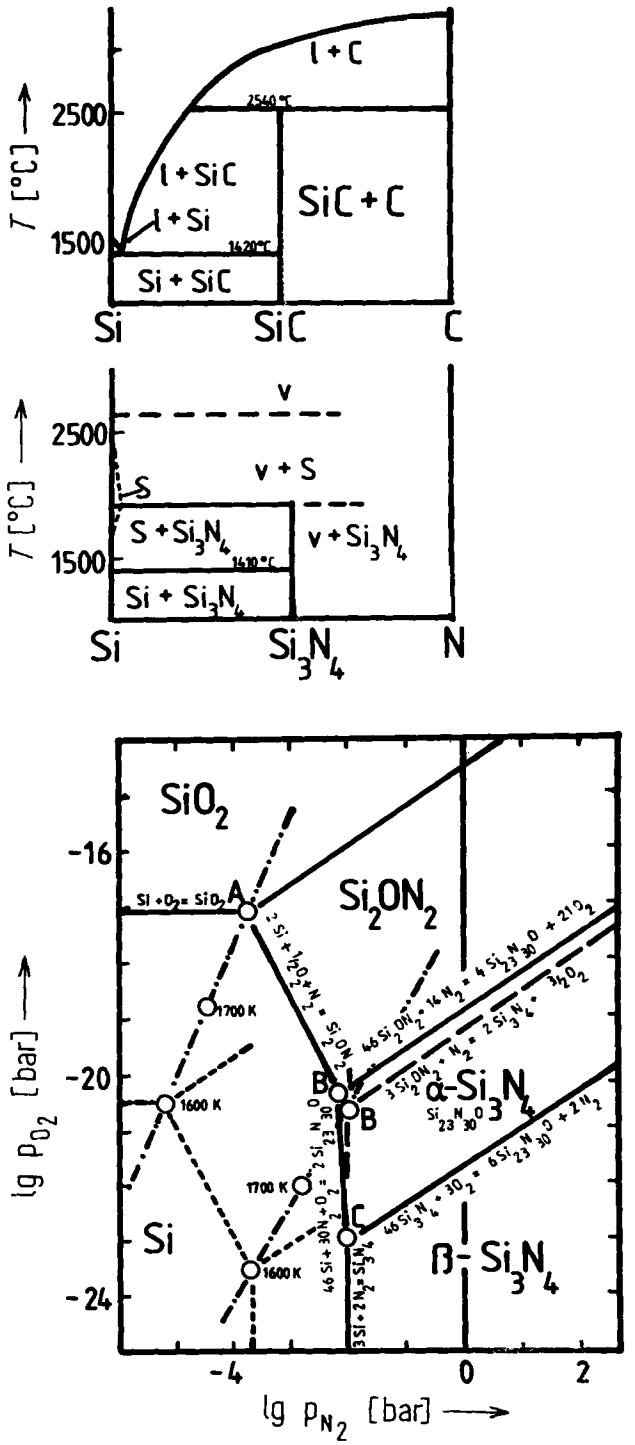


Fig. 1. Phase diagrams of the binary systems silicon/carbon [2] and silicon/nitrogen [3]; equilibrium diagram for the ternary system silicon/oxygen/nitrogen [4]. s = solid, l = liquid, v = vapor. A, B, C = equilibrium points of the phases at 1800 K.

2. Scope and Limitations of Silicon Ceramics

Silicon ceramics do not occur in nature; they are man-made inorganic materials, extending from metallic conductors, *viz.* silicides of transition metals of Group 4 and 5, *via* the stoichiometric covalent compounds SiC and Si_3N_4 having semiconductor properties, to the silicon nitride solid solutions (sialons)[5,6] in which the nitrogen and silicon have been partly substituted by oxygen and aluminum, respectively (see Fig. 1). The structures of the metallic silicides, of which molybdenum disilicide ($MoSi_2$) is the most significant technologically[7], show some resemblance to the interstitial structures of carbides and borides. However, the greater size of the silicon atom leads to lattice widening while still permitting direct Si—Si bonding which will modify the bonding character of the metallic host.

Silicon carbide is strictly stoichiometric and crystallizes, like elemental silicon, in a diamond type structure showing some range of variation of the stacking sequence. The strong covalent Si—C bond leads to a refractory nature, extreme hardness, and a very high theoretical Young's modulus which is indeed realized in industrial SiC monofilaments (up to 450000 MN/m^2). However, dislocation movement is blocked in these compounds, causing high temperature strength but also brittleness. This undesirable brittleness is reduced in silicon nitride and sialons, but at the expense of elasticity and high temperature strength (Table 1).

Table 1. Properties of SiC and Si_3N_4 (α = coefficient of thermal expansion) and strength (σ) of technical products made of these materials. The lower strengths are for reaction-bonded materials and the higher values for hot-pressed materials.

	Bonding strength [kJ/mol]	$\alpha \times 10^{-6}$ [K^{-1}]	$T_{dec.}$ [°C]	σ_{RT} [MN/m^2]	$\sigma_{1200°C}$ [MN/m^2]
SiC	437	5.8	2700	300—800	300—500
Si_3N_4	773	3.5	2200	150—700	150—600

The outstanding property of all of these refractory silicon compounds is their chemical inertness in an oxidizing environ-

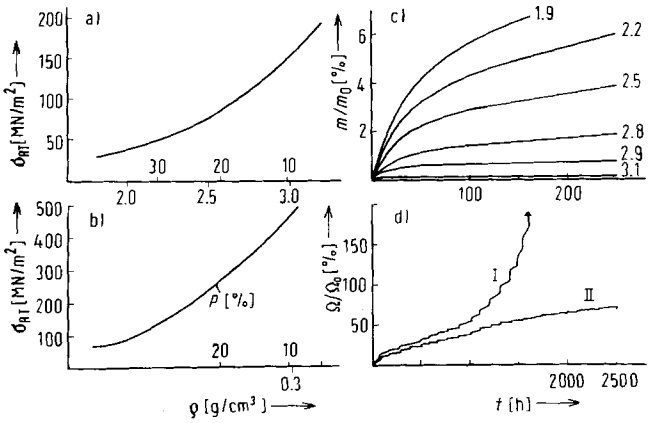


Fig. 2. Flexural strength σ_{RT} of a) reaction-bonded commercial SiC[8] and b) reaction-bonded commercial Si_3N_4 [9] as function of porosity (P) and density (ρ); weight increase (m/m_0) with time on oxidation of SiC at 1500 °C (the numbers next to the curves refer to the density ρ [g/cm^3] [8]); d) change in resistance Ω/Ω_0 of SiC on cycling between 20 °C and 1500 °C (I without glass layer; II with glass layer).

ment which is due to the high affinity of silicon for oxygen. In an aqueous environment, passivity results from reaction between silicon and oxygen. On thermal oxidation, for instance in air, glassy SiO_2 surface layers are formed which strongly suppress further oxidation. Oxidation was found to show a parabolic time dependence (Fig. 2)[8, 9]. Mass transport in such SiO_2 layers is effected solely by non-ionized oxygen, and is additionally hindered by counterdiffusion of volatile by-products of oxidation, such as CO and N_2 respectively.

Comparison of the temperature dependence of the overall oxidation rate of silicon, silicon nitride, silicon carbide, and $MoSi_2$ as well, reveals similar values for the activation energy,

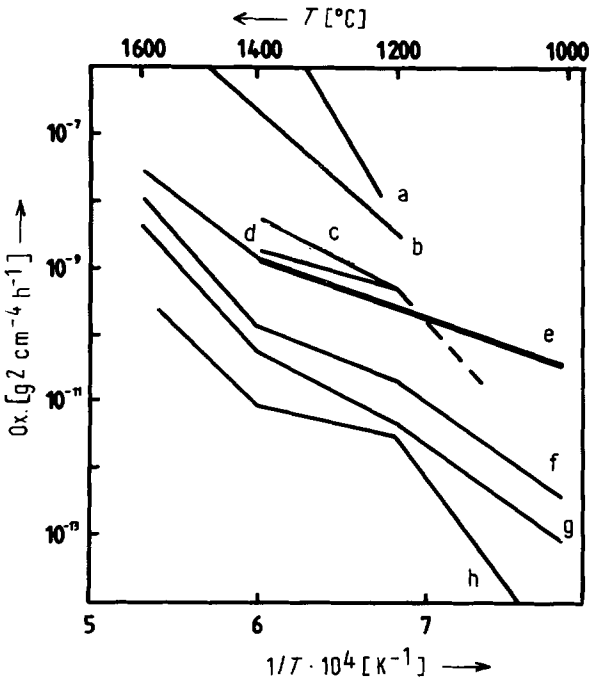


Fig. 3. Temperature dependence of oxidation rate constant (Ox.) of various silicon ceramics [10—12]. a) Si_3N_4 with 30% La_2O_3, air; b) Si_3N_4 with 5% MgO, air; c) sialon with 5—30% Al (air); d) sialon with 50% Al (air); e) $MoSi_2$ (air); f) SiC powder (O_2); g) SiC powder (air); h) Si_3N_4 powder (air).

and shows that the mechanism of the rate-controlling step is always the same (Fig. 3)[4, 5]. The activation energies are also comparable with that of oxygen permeation through SiO_2 glass films.

The blocking efficiency of the SiO_2 surface layers is greatly reduced by small quantities of foreign oxides. For instance, the oxidation rate of $MoSi_2$ is one order of magnitude higher than that of pure silicon carbide, because this compound forms a SiO_2 glass layer with small amounts of MoO_2[11], and does not form counterdiffusing by-products (Fig. 3)[10-12]. Nevertheless, the air oxidation of $MoSi_2$ at 1500°C is one order of magnitude slower than that of 20/80 Cr/Ni alloys at only 1000°C[13]. One can envisage the oxidation resistance of pure silicon carbide as being ten times better at 1400°C than that of today's best "superalloys" at their maximum temperature of application, which is still 1200°C. In such considerations, the superior resistance of silicon ceramics to "hot corrosion" resulting from attack by combustion products has not been taken into account[14].

The problem remains of how to utilize this chemical stability by provision of bulk materials without open porosity. In silicon ceramics having open pores, intercrystalline oxidation will occur, forming SiO_2 glass lamellae between the grains. This causes a deterioration of the material on cooling from the oxidation temperature because of the extremely low thermal expansion coefficient of SiO_2 glass ($\alpha = 0.5 \times 10^{-6}\,K^{-1}$) as compared with that of silicon carbide ($\alpha = 5 \times 10^{-6}\,K^{-1}$). Not only the mechanical properties, mainly impact strength and creep resistance, but also the thermal and electrical conductivity will be considerably impaired. The last mentioned effect is well known to the laboratory chemist from the increase in resistance of commercially available SiC heating elements in intermittently operated high-temperature combustion furnaces.

How can we produce pore-free SiC and Si_3N_4 bulk materials? Pure SiC and Si_3N_4 powders do not sinter in the conventional sense. In contrast, the silicides of the transition metals exhibit similarly high values of surface energy as are known for metals, and such silicides are therefore readily sinterable. Thus wire-wound or tubular $MoSi_2$ heating elements for working temperatures up to 1600°C can be produced by powder

Table 2. Comparison of manufacturing processes for silicon ceramics (RB = reaction bonded, HP = hot pressed, CP = cold pressed).

Process	Reaction sintering SiC	Reaction sintering Si_3N_4	Hot pressing SiC, Si_3N_4, Sialon	Pressureless sintering SiC
Starting materials	SiC powder + pitch binder	Si_3N_4 powder + Si powder	Si ceramic powder + Al_2O_3, MgO, Y_2O_3	Si ceramic powder + B, B_4C, C
Process steps	Molding or extrusion at RT Carbonization at $T = 1000$°C Siliciding at $T = 2000$°C	Molding at RT Nitriding at $T = 1500$°C	Molding at $T > 1500$°C	Molding at RT Sintering at $T = 2000$°C
Product	RB-SiC	Rb-Si_3N_4	HP-SiC, HP-Si_3N_4	CP-SiC
Properties	High porosity Low strength	High porosity Low strength	Low porosity but heterogeneous material High RT strength	Low porosity but heterogeneous material High HT strength
Remarks	Process well controlled Also suitable for complicated shaped sections Inexpensive raw materials	Process controlled Reaction usually incomplete Suitable only for thin-walled sections Inexpensive raw materials	Process difficult to control Suitable only for simple sections Expensive raw materials	Process not yet controlled Suitably only for simple sections Expensive raw materials

metallurgical techniques[15]. In the case of SiC and Si_3N_4 powders, even the finest grain sizes (<0.2 μm diam.) cannot be sintered in the absence of high melting, nonvolatile additives such as B_4C, MgO, Al_2O_3, or Y_2O_3[16-18]. Mechanical pressure is usually also applied during sintering (hot pressing at *ca.* 1600°C), imposing severe restrictions on the shapes and sizes of the products.

The most serious disadvantage introduced by such additives is their influence on oxygen transport within the SiO_2 surface layers (see Fig. 3), and furthermore on the creep behavior of the polygranular bulk material. Intercrystalline oxides will act as plastifiers at high temperatures. The sialons, which partly oxidize to Al_2O_3, exhibit a similar deterioration of their high temperature properties compared with pure silicon carbide and silicon nitride[10].

Silicon ceramics free from additives can be prepared by the reaction bonding (reaction sintering) process. Table 2 compares the process steps with those of other metallurgical processes. Reaction sintering starts with the pure carbide or nitride powder. As in ceramics the material is shaped prior to sintering with the aid of a temporary binder, which consists of one of the components of the silicon material (carbon in the case of SiC and silicon in case of Si_3N_4). This binder is converted into the final silicon compound, which should act as bridge or matrix connecting the primary powdered silicon compounds, at high temperatures (T>1500°C) by chemical reaction (siliciding with molten or vaporized silicon in the case of SiC; nitriding with volatile nitrogen compounds (N_2 or NH_3) in the case of Si_3N_4). This transformation amounts to an impregnation process; the compact must have open pores and a porous final structure is obtained. The pores can subsequently be filled by impregnation with an excess of molten silicon; however, a heterogeneous structure with impaired high temperature properties will result. Furthermore, grain growth is promoted at high temperatures by dissolution-reprecipitation cycles.

The novel process of chemical vapor deposition could at least partly eliminate or compensate the drawbacks of the reaction bonding technique:

1) Subsequent "gas impregnation" treatment densifies porous SiC and Si_3N_4 bulk materials and additionally seals the pore entrances on the surface[19].

2) Direct preparation of finest SiC and Si_3N_4 powder obviates the need for grinding processes for size reduction. Such grinding procedures always lead to surface passivation by oxygen adsorption and thus also inhibit sintering processes.

3) SiC monofilaments exhibiting extremely high Young's modulus and high tensile strength become available for reinforcement purposes.

4) Gas phase impregnation permits fabrication of pore-free, shaped objects, mainly fiber-reinforced composites.

Successful application of chemical vapor deposition requires an accurate knowledge of the kinetics of deposition and of the influence of the various process parameters.

3. Principles of Chemical Vapor Deposition of SiC and Si_3N_4

Chemical vapor deposition (CVD) can be considered as "precipitation" of a solid reaction product from a supersaturated fluid matrix. In contrast to the precipitation processes occurring from solid or liquid solutions, vapor deposition does not occur during cooling but during heating. The thermally activated process steps are mainly pyrolysis reactions having very complicated mechanisms. As in other heterogeneous chemical gas-solids reactions, transport steps can play a very important role during gas phase deposition[20].

With regard to the energy supply, we distinguish between two extreme alternatives: the "hot wall arrangement" in which

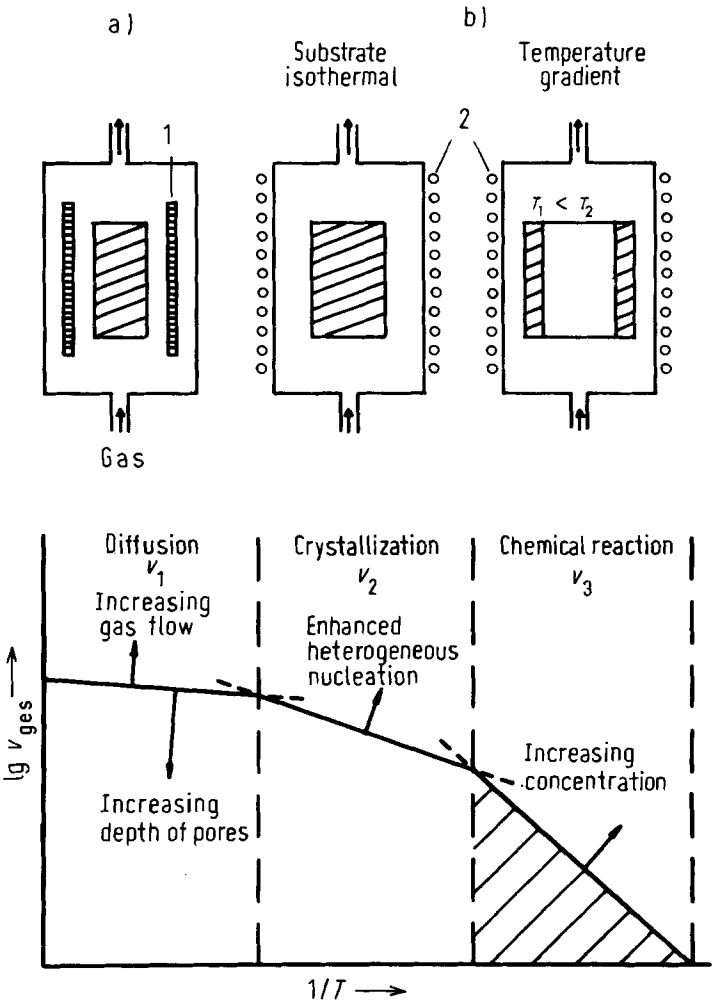


Fig. 4. a) Hot-wall and b) cold wall arrangements for chemical vapor deposition: 1, resistance heating elements; 2, induction coil. c) Rate-determining steps of chemical vapor deposition.

heating of the substrate, where deposition should take place, is performed by radiation from a surrounding heater, and the so-called "cold wall arrangement" with a heat source inside the substrate (Fig. 4a, b).

The mechanism of vapor deposition even on smooth planar surfaces is very complicated. Figure 4 shows a simplified Arrhenius plot from which it is seen that, especially at high temperatures (left-hand side of the diagram), the overall deposition rate will be controlled by mass transport in the outer gaseous surface layer (slowest consecutive step).

These limitations become more critical in case of chemical vapor deposition on inner surfaces because of the long diffusion

paths. Only by means of complicated experimental set-ups (temperature or pressure gradient)[21] is it possible to support diffusion by convective transport (cf. Fig. 4c). In order to achieve good impregnation, the overall deposition rate within the pores must never be controlled by the transport rate but only by the chemical reaction rate. Consequently, deposition must be performed at low temperatures, and low concentrations should be used. Furthermore, gas phase nucleation must be avoided. If finely powdered products are desired, however, high supersaturation is necessary to ensure spontaneous gas phase nucleation and very fast cooling to avoid crystal growth.

The driving force of chemical vapor deposition is the thermodynamic instability of the gaseous compounds used as precursors. Figure 5 shows data on the free energy of formation of some compounds involved in the deposition of SiC and Si_3N_4[22]. Chloro(methyl)silanes are mostly used for SiC deposition because easy control of the Si/C ratio in the feed can thus be achieved. However, cyclic silicon-carbon compounds ("carbosilanes") may be formed as intermediates[23] and deposit as tarry by-products in the cooler areas of the apparatus; on further heating they can initiate gas phase nucleation.

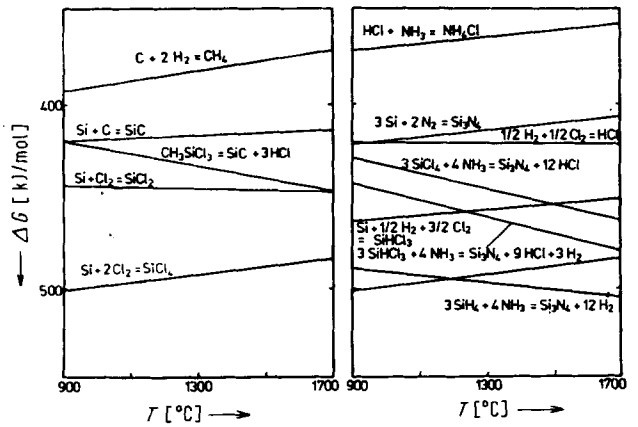
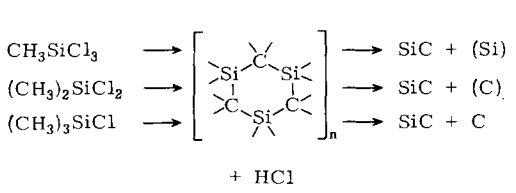


Fig. 5. Gibbs free energy of formation of various compounds arising during vapor phase deposition of SiC and Si_3N_4 [22].



The question whether a stoichiometric deposit or a deposit with an excess of silicon or carbon is obtained depends on the type of precursor. As SiC has practically no solubility for free silicon or carbon (Fig. 1), an excess of silicon or carbon can impart a heterogeneous structure to the deposit (see Fig. 7)[27]. However, the conditions during deposition will also influence the chemical composition of the deposit.

Figure 6[24] shows the yields of SiC and excess carbon deposited on a cold wall on decomposition of chloromethylsilanes. As can be seen, deposition of free carbon does not occur below 1000 °C whereas free silicon is often found even on use of CH_3SiCl_3, *i.e.* the compound with a 1:1 ratio of carbon and silicon[16, 26].

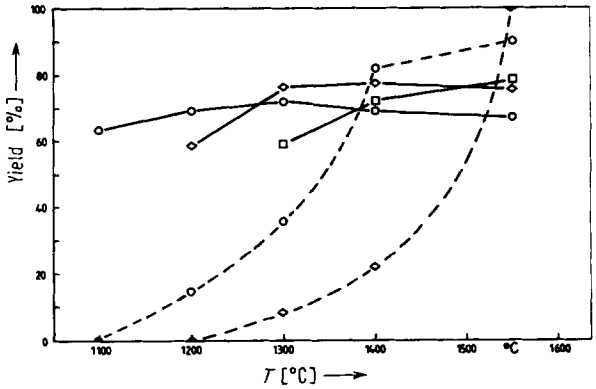


Fig. 6. Yield of SiC (—) and free carbon (---) during pyrolysis of various chloro(methyl)silanes CH_3SiCl_3 (□), $(CH_3)_2SiCl_2$ (◇), and $(CH_3)_3SiCl$ (○) [24].



Fig. 7. Alternating deposition of SiC and carbon caused by oscillating reaction [25]. The layers are about 0.5—1 μm thick.

In general, $SiCl_4$ and NH_3 are used as precursor compounds for the deposition of Si_3N_4 because they are inexpensive and easy to handle. As shown in Figure 5, however, NH_4Cl may be formed from the feed and the by-product HCl if backmixing of the reaction gases in not avoided.

Low deposition temperatures, which are necessary for reaction rate control of the overall kinetics, have the additional advantage of ensuring fine-grained and even amorphous structure of the deposits[20]. Scanning micrographs (Fig. 8) show the influence of deposition temperature on the morphology of chemical vapor-deposited SiC and Si_3N_4 for some typical examples[28].

The key to successful chemical vapor impregnation lies in a thorough comprehension of the deposition kinetics under various conditions. Figure 9a shows overall deposition rates of silicon carbide from trichloro(methyl)silane and of silicon nitride from tri- or tetra-chlorosilane and ammonia[28, 29] as a function of deposition temperature and gas concentration. These data were obtained with a hot wall arrangement. This is also the reason why we have found a maximum in the case of silicon nitride deposition; the fall in the deposition rate with further temperature increase is caused by gas phase nucleation which consumes the precursor before the gas flow

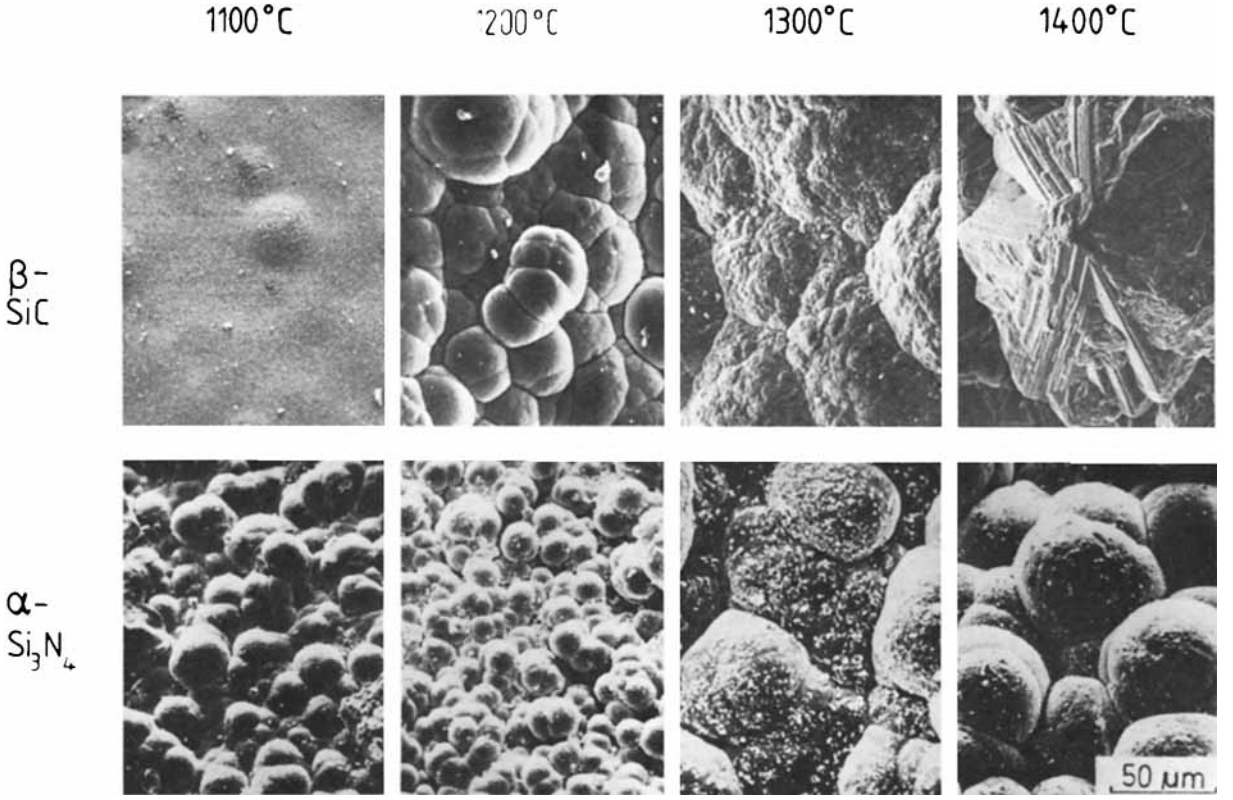


Fig. 8. Morphology of SiC and Si_3N_4 layers (secondary electron image) [28].

185510

reaches the surface of the substrate. The flattening of the rate of growth of SiC layers at high temperatures indicates mass transport control of the overall deposition rate, even on plane surfaces. This transition from reaction control to diffusion control is better recognized in the Arrhenius plot from the break in the curve. For cold wall silicon carbide deposition on plane substrate surfaces, this diffusion control starts at deposition temperatures above 1050 °C. The situation in a fluidized bed, *i.e.* a hot wall arrangement, is also shown for sake of comparison; diffusion control is then observed only above 1250 °C.

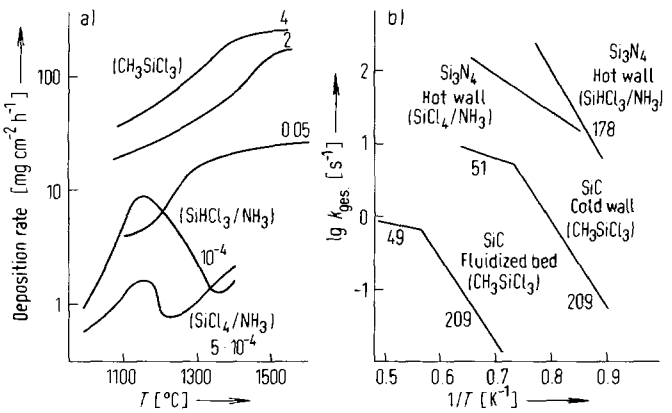


Fig. 9. Growth rates of SiC and Si_3N_4 layers deposited from the gas phase [28, 29]. a) The numbers next to the curves refer to the concentrations of the precursor compounds in the gas phase (in mol/l); b) the numbers next to the curves refer to the activation energies for decomposition (in kJ/mol).

The specific reaction rate for Si_3N_4 deposition is much higher than that for SiC. This is why very low concentrations are necessary in order to avoid gas phase nucleation.

4. Gas-Phase Impregnation of Porous SiC and Si_3N_4 Objects

If information is available about mass transport and reaction rates at various temperatures, the maximum impregnation depth can be predicted. In reaction kinetics, dimensionless numbers like the second Damköhler number Da_{II} and the Thiele number ϕ are used for calculations on diffusion in porous catalysts. Figure 10[30] shows the ratio η of the deposition rate in the pores to the deposition rate on the surface. In the interest of maximum possible impregnation, η should

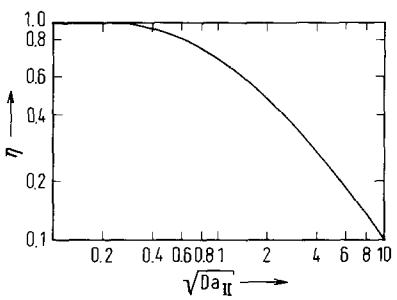


Fig. 10. Ratio η of the rate of deposition in the pores and on the surface as a function of the second Damköhler group Da_{II} [30]. $Da_{II} = k l^2/D$; k = rate constant, D = diffusion coefficient, l = depth of pores to be impregnated.

lie near the maximum value. l stands for the depth of the pores, which are assumed to be cylindrical.

We have precalculated such theoretical impregnation depths using the deposition rate as a measure of the reaction rate in the reaction rate-control regime (Fig. 9). The diffusion coefficients were calculated with data shown in Table 3.

Table 3. Diffusion coefficients in hydrogen of some gaseous species formed on chemical vapor deposition of SiC and Si_3N_4.

Cpd.	D [cm²/s] at T=			
	900 °C	1000 °C	1100 °C	1200 °C
CH_3SiCl_3	0.50	0.51	0.54	0.56
$(CH_3)_2SiCl_2$	0.49	0.50	0.52	0.54
$SiCl_4$	0.63	0.64	0.65	0.67
NH_3	0.95	0.96	0.97	0.98
CH_4	0.93	0.94	0.96	0.97
HCl	1.32	1.33	1.34	1.36

Attempts were made to test the results by model experiments on graphite samples with drilled holes as large model pores (Fig. 11)[28] and with polygranular graphite having a defined pore spectrum[31] (Fig. 12a) as substrate. At 1500 °C closing of the pore entrances is observed, even at very large diameters, owing to preferential surface deposition. In practical work, successful impregnation of substrates with smaller pore entrances requires much lower impregnation temperatures, *i.e.* about 800—900 °C.

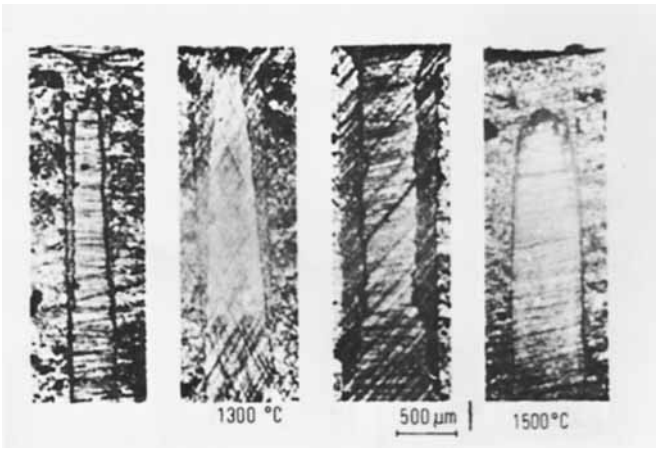


Fig. 11. Deposition of SiC in cylindrical model pores in graphite [28]. From left to right: d=400, 600, 800, 600 µm.

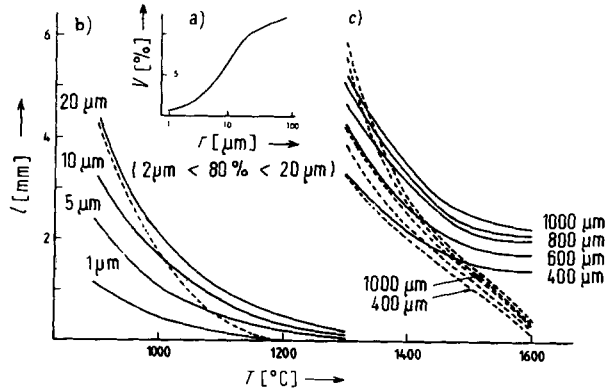


Fig. 12. a) Pore size distribution of porous graphite (V=pore volume, r=pore radius); b) calculated (—) and experimental (---) depth of impregnation l in porous graphite (see Fig. 12a), and c) in model pores. The pore radius is given next to the curves. Impregnation was with CH_3SiCl_3.

These predicted values were compared with experimentally observed impregnation depths in Figures 12b and 12c. The results confirm the applicability of such kinetic data for a precalculation of impregnation depths. The deviation of the experimental curves in the direction of lower impregnation depths is caused by a rapid narrowing of the pore entrances at the higher temperatures. However, there is an ever-present danger of merely converting open porosity into closed porosity by preferred deposition at the pore entrances. Thus, pore filling of originally open porosity can only be achieved in part.

We used five different types of reaction-bonded SiC and Si_3N_4 in our experiments on densification by SiC chemical vapor impregnation (CVI) (Fig. 13)[32,33]. They differed considerably in grain size and pore characteristics.

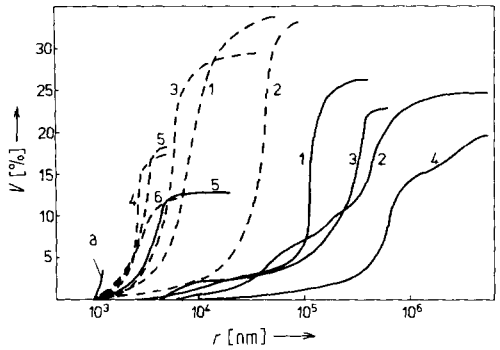


Fig. 13. Pore size distribution of reaction-bonded SiC (—) and Si_3N_4 (---) samples used as substrates [32, 33] (V= pore volume [vol. %], r = pore radius), a = experimental values after impregnation of SiC sample no. 2.

The results of CVI treatment with CH_3SiCl_3 are shown in Figure 14 for SiC sample no. 2. All open pores with radii larger than 1 µm are completely filled after 40 h. The volume fraction of open pores which can be filled by CVI depends strongly on the original pore spectrum. Impregnation yields up to 70 % have been achieved in the most favorable cases. Sample no. 5, the finest-grained sample of the series with only 12 % open porosity, was much more difficult to impregnate.

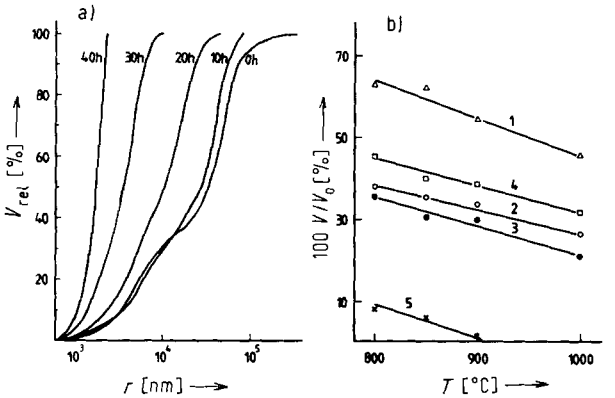


Fig. 14. Results of gas-phase impregnation of SiC with CH_3SiCl_3 at 800 °C. a) Pore size distribution of sample no. 2 (see Fig. 13) after impregnation for various periods; b) maximum degree of pore filling accomplished by impregnation (samples 1—5, see Fig. 13).

Table 4 shows that the strength of all samples, except no. 5, can be increased by densification. However, even in this last case, the surface properties are improved to the same

extent as with the other samples. The resistance to oxidation became the same as that of smooth SiC single crystal surfaces in all cases.

Table 4. Results of gas phase impregnation of five reaction-bonded SiC materials of various porosities. Samples 1—5, see Fig. 13. a is before, b after, impregnation. The values in the columns headed "Si" and "C" refer to wt.-% of free Si and C, respectively.

Sample	Si	C	Bulk density [g/cm³]		Flexural strength [MN/m²]		Oxidation constant [cm/h$^{1/2}$]	
			a	b	a	b	a	b
1	3.0	0.7	2.10	2.45	47	80	4.9×10^{-1}	8×10^{-5}
2	0.5	2.7	2.22	2.47	40	87	4.4×10^{-1}	8×10^{-5}
3	—	0.8	2.47	2.67	90	113	2×10^{-1}	8×10^{-5}
4	—	0.3	2.44	2.64	82	143	3×10^{-1}	8×10^{-5}
5	—	6.5	2.33	2.34	100	100	9×10^{-1}	8×10^{-5}

It was interesting to test how densification affects the high temperature strength. Figure 15 shows the improvement of the short time flexural strength and its variation with increasing testing temperature. It is not influenced up to 1400°C, but drops sharply with further increase of the testing temperature. Most striking is the effect of chemical vapor impregnation of RB-SiC on creep resistance (see Fig. 16).

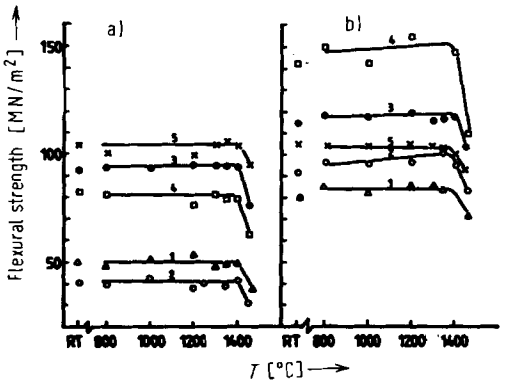


Fig. 15. High temperature flexural strength (short-time HT strength) of reaction-bonded SiC a) before and b) after impregnation with CH_3SiCl_3 (samples 1—5; see Fig. 13).

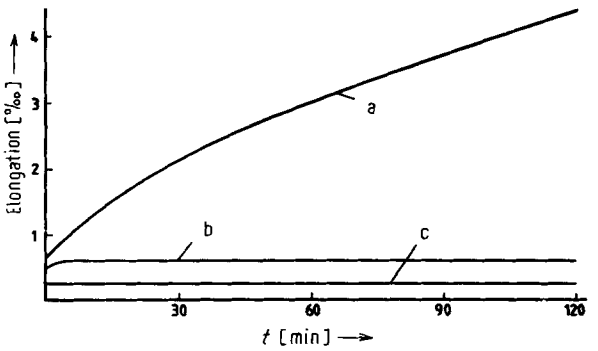


Fig. 16. Creep behavior of reaction-bonded SiC at 1350°C: a, before impregnation (load 30 MN/m²); b and c, after impregnation (load 50 and 30 MN/m², respectively). Sample no. 1, see Fig. 13.

The CVD of Si_3N_4 in general and the densification of porous RB-Si_3N_4 samples by CVI in particular are much more difficult. Not only does the reaction gas consist of two components but the reaction rate is also much higher. As the overall kinetics for CVI must be controlled by the reaction step, practical execution of in-pore deposition becomes very difficult. Furthermore, in the case of silicon nitride there is a high tendency for gas phase nucleation. The conditions for the gas-phase impregnation therefore have to be shifted not only to low temperatures (about 900°C—1000°C), but also to low gas concentrations. However, the latter condition increases the risk of diffusion control.

We selected a cold wall arrangement mainly in order to avoid gas phase reactions. We further used indirect heating with the aim of achieving a thermal gradient (see Fig. 4b)[33]. Finally, both reactive gases were introduced through separate tubes, and the flow of the gases was directed to the surface site from where impregnation should start[28]. In spite of all these preventive measures, we were unable to avoid preferential densification of the surface layers due to the very high deposition rate even at 1000°C. The maximum degree of impregnation was 20% on complete transformation of closed pores into sealed ones[33]. There is no increase in strength on Si_3N_4 gas-phase impregnation but the surface properties are decisively improved[34].

5. Preparation of SiC and Si_3N_4 Powders

Böcker and *Hausner*[35] recently described the preparation of sinter-active SiC powders with grain sizes in the submicron range by pyrolysis of CH_3SiH_3 in argon carrier gas at temperatures between 1000 and 1800°C but did not report the results of sinter experiments.

Previously described processes for the production of SiC powder by reaction of silicon halides[36] or silicon monoxide[37] with hydrocarbons do not give well-defined products. The transformation of amorphous into crystalline SiC by subsequent heat treatment (1800—2000°C) of the product obtained from pyrolysis of methylsilanes or chlorosilanes at 600—1100°C is described by *Enk* and *Nickl*[38].

Apart from the preparation of SiC powder by chemical vapor deposition, the plasma process can be used for the same purpose. *Neuenschwander*[39] described the reaction between $SiCl_4$ and hydrocarbon compounds in a direct current torch. *Kuhn*[40] used reactive anodes consisting of SiO_2 and carbon. *Fyans*[41] reported the reaction of solid SiO_2 with hydrocarbons. Only *Salinger*[42] used chloro(methyl)silanes as reactive compounds for cracking in a high frequency plasma.

The SiC powder used by *Prochazka*[43] in his first sintering experiments without applying mechanical pressure was apparently a powder prepared by the plasma process. The excess of carbon needed in these sintering experiments was probably necessary to reduce the oxides introduced by the plasma process.

Several methods of producing Si_3N_4 powder have already been described. *Mazdiyasni*[44] reported the pyrolysis of $Si(NH)_2$. *Morgan*[45] studied the reaction of $SiCl_4$ with NH_3. Inclusions of HCl were found to be unavoidable. *Prochazka et al.*[46] prepared Si_3N_4 powder from SiH_4 and NH_3 in a tubular reactor at temperatures above 1450°C. *Kijima*[47] introduced hydrogen into the same reaction gas. The resulting powder is finer than 0.1 μm.

Most interesting with respect to the sintering behavior of CVD Si_3N_4 powder is the work of *Thümmler et al.*[48]. The idea was to deposit β-Si_3N_4[28] and to utilize the β→α transformation occurring during sintering heat treatment to initiate and assist the sintering process. It is hoped to achieve products of high density without using high melting additives.

6. SiC Fibers and Fiber-Reinforced Composites

The first experiments on the preparation of SiC monofilaments were performed with W fibers as substrate using a technique already described for B fibers[49, 50, 51]. *Diefendorff*[52] reported tensile strengths up to 3500 MN/m² for fibers deposited from CH_3SiCl_3.

Our own studies were performed with carbon monofilaments as substrates[31, 53, 54]. The strength and flexibility of the monofilaments depend strongly on the deposition temperature. Coarse-grained products must be avoided. The tensile strength varies between 2500 and 3500 MN/m². A Young's modulus of up to 400×10^3 MN/m² can be reached[55, 56].

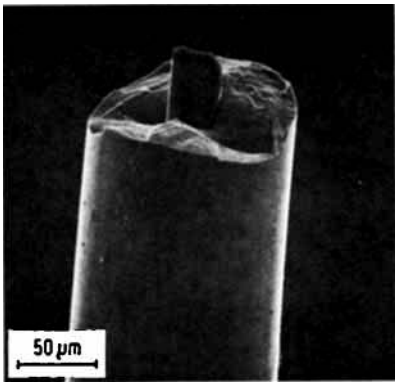


Fig. 17. SiC monofilament with carbon core.

SiC monofilaments with carbon cores (see Fig. 17) have superior high temperature properties to those with W cores because tungsten reacts with silicon carbide above 600°C. Similar results are described by *De Bolt*[57] and *McHenry*[58].

No literature is available on the formation of Si_3N_4 monofilaments. However, preliminary experiments have shown that it should be possible to coat carbon fiber yarn with Si_3N_4 by CVD[28].

Production of monolithic silicon ceramic objects from the gas phase is precluded by frozen-in stresses. However, CVD can be used for preparation of SiC-fiber and C-fiber reinforced composites with a SiC matrix. The steps involved are shown schematically in Figure 18. Such composites have a final closed porosity of 15—20%. The SiC matrix preferentially grows epitactically and thus increases the diameter of the core fiber (Fig. 19, left). Alternatively, a carbon fiber yarn may be impregnated from the gas phase with SiC (Fig. 19, right).

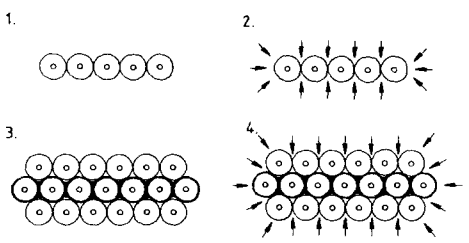


Fig. 18. Stepwise production of unidirectionally reinforced SiC composites (fiber-reinforced composites) by gas-phase impregnation.

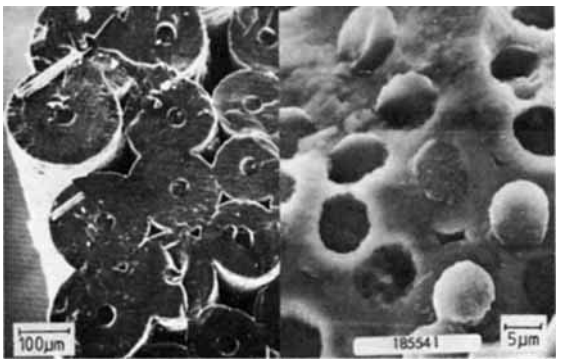


Fig. 19. Fracture of unidirectionally reinforced SiC/SiC (left) and C/SiC composites (right).

As shown in Figure 19, such unidirectionally reinforced composites are stronger than all other SiC materials, with flexural strengths up to 1000 MN/m². However, this strength is limited to the direction parallel to the fibers. Nevertheless, these composites are interesting and show promise for special future applications.

7. Outlook

Chemical vapor deposition promises improvements in the production and quality of silicon ceramics. For instance, comparison of the high temperature strength properties shows that chemical vapor impregnation of reaction-bonded silicon carbide materials (Fig. 20, e) with pure silicon carbide (Fig. 20, d) gives product having strengths formerly only achievable by liquid silicon impregnation (Fig. 20, c) which leads to silicon excess and attendant low creep resistance. In contrast, oxidation and creep resistance of vapor impregnated silicon carbide is enormously improved.

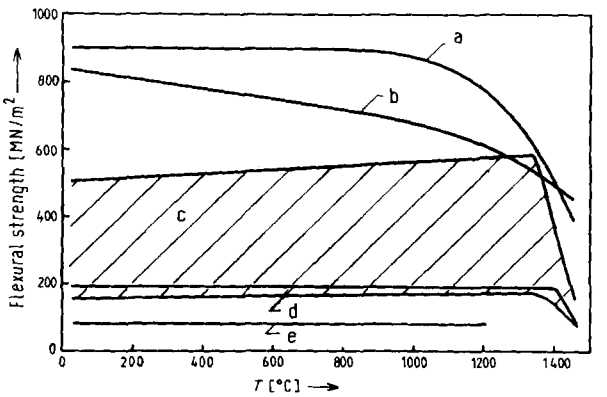


Fig. 20. High-temperature flexural strength of unidirectionally reinforced SiC/SiC and C/SiC composites (a) and gas-phase impregnated reaction-bonded SiC (d) compared with commercially available hot-pressed SiC (b) and reaction-bonded SiC with 5—15% excess of Si (c) and untreated reaction-bonded SiC (e).

Fiber-reinforced SiC composites (Fig. 20, a) exhibit high temperature strength data at 1400°C, superior to those of all today's leading hot pressed materials (Fig. 20, b).

The production of ultrafine powders by chemical vapor deposition could lead to a breakthrough of cold pressing techniques without mechanical pressure for high quality SiC and for Si_3N_4.

Received: January 18, 1979 [A 268 IE]
German version: Angew. Chem. 91, 316 (1979)

[1] *W. Bunk, M. Böhmer:* Keramische Komponenten für Fahrzeug-Gasturbinen. Springer, Berlin 1978.
[2] *C. E. Lowell:* The Silicon-Carbon Phase Diagram. National Research Laboratories, TM-436, 1959.
[3] *M. Nowotny, E. Partme, R. Kieffer, F. Benesovsky*, Monatsh. Chem. *85*, 255 (1954).
[4] *K. Blegen* in *P. Popper:* Special Ceramics 6. Brit. Ceram. Res. Assoc., Penkhull 1973.
[5] *L. J. Gauckler, H. L. Lukas, G. Petzow*, J. Am. Ceram. Soc. *58*, 46 (1975).
[6] *K. H. Jack*, J. Mater. Sci. *1976*, 1135.
[7] *J. Schlichting*, High Temp. High Pressures *1978*, 3.
[8] *O. Rubisch, R. Schmidtt*, Ber. Dtsch. Keram. Ges. *43*, 173 (1966).
[9] *J. W. Edington, D. J. Rowcliffe, J. L. Henshall*, Powder Metall. Int. 7, 82 (1975).
[10] *J. Schlichting, L. J. Gauckler*, Powder Metall. Int. 9, 36 (1977).
[11] *E. Fitzer, K. Reinmuth* in *F. Benesovsky:* Hochtemperaturwerkstoffe. 6th Plansee Seminar, Reutte 1968. Springer, Vienna 1969.
[12] *E. Fitzer, R. Ebi* in *R. C. Marshall, J. W. Faust, C. E. Ryan:* Silicon Carbide. University of South Carolina Press, Columbia 1973.
[13] *E. Fitzer, H. Herbst, J. Schlichting*, Werkst. Korros. *24*, 274 (1973).
[14] *J. Schlichting* in *P. Popper:* Special Ceramics 6. Brit. Ceram. Res. Assoc., Penkhull 1973.
[15] *E. Fitzer, O. Rubisch*, Elektrowärme *5*, 163 (1958).
[16] *R. A. Allieqro, L. B. Coffin, J. R. Trinklepaugh*, J. Am. Ceram. Soc. *39*, 386 (1956).
[17] *S. Prochazka, R. J. Charles*, Am. Ceram. Soc. Bull. *52*, 885 (1973).
[18] *R. F. Coe, R. J. Lumby, J. F. Pawson* in *P. Popper:* Special Ceramics 5. Brit. Ceram. Res. Assoc., Penkhull *1972*, p. 361.
[19] *E. Fitzer:* International Symposium of Factors in Densification and Sintering of Oxides and Non-Oxide Ceramics. Hakone (Japan), Oct. 1978.
[20] *E. Fitzer, W. Fritz, D. Kehr*, VDI-Z. *114*, 1221 (1972).
[21] *W. V. Kotlensky* in *P. L. Walker:* Chemistry and Physics of Carbon. Vol. 9. Marcel Dekker, New York 1973, pp. 173ff.
[22] JANAF, Thermochemical Tables of the Elements. Washington 1965.
[23] *G. Fritz, J. Grobe*, Z. Anorg. Allg. Chem. *229*, 302 (1959).
[24] *M. Bonnke*, Dissertation, Universität Karlsruhe 1965.
[25] *M. Bonnke, E. Fitzer*, Ber. Dtsch. Keram. Ges. *41*, 180 (1966).
[26] *J. E. Spruiell:* Fundamentals of Chemical Vapour Deposition. 2nd International Conference. The Electrochemical Society. New York 1970, p. 279.
[27] *E. Fitzer*, Chem.-Ing.-Tech. *41*, 331 (1969).
[28] *H. J. Bühler*, Dissertation, Universität Karlsruhe 1976.
[29] *L. Aggor, W. Fritz*, Chem.-Ing.-Tech. *43*, 472 (1971).
[30] *E. Fitzer, D. Kehr, M. Sahebkar*, Chem.-Ing.-Tech. *45*, 1244 (1973).
[31] *M. Sahebkar*, Dissertation, Universität Karlsruhe 1973.
[32] *D. Hegen*, Dissertation, Universität Karlsruhe, projected for 1979.
[33] *H. Strohmeier*, projected dissertation, Universität Karlsruhe.
[34] *F. Thümmler et al.*, Sci. Ceram. *8*, 133 (1975).
[35] *W. Böcker, H. Hausner*, Ber. Dtsch. Keram. Ges. 55, 233 (1978).
[36] British Titan Products, Brit. Pat. 1174859 (1967).
[37] Degussa, Brit. Pat. 960537 (1962).
[38] *E. Enk, J. Nickl*, DBP 1047180 (1958).
[39] *E. Neuenschwander*, DBP 1250796 (1964).
[40] *W. E. Kuhn*, Can. Pat. 695133 (1962).
[41] *A. W. Fyans*, Can. Pat. 812157 (1966).
[42] *R. M. Salinger*, Ind. Eng. Chem. Prod. Res. Dev. *11*, 230 (1972).
[43] *S. Prochazka* in *J. J. Burke, A. E. Gorum, R. N. Katz:* Ceramics for High Performance Applications. Brook Hill Publ. Co., Chestnut Hill, Mass. 1974, p. 239.
[44] *K. S. Mazdyasni, C. M. Cooke*, J. Am. Ceram. Soc. *56*, 628 (1973).
[45] *P. E. D. Morgan*, Final Reports NTIS-AD-778-373, Franklin Institute Res. Lab., Philadelphia 1973.
[46] *S. Prochazka, C. D. Greskovich*, General Electric Company, Technical Information Series No. 77 CRD 104 (1977).
[47] *K. Kijima:* International Symposium of Factors in Densification and Sintering, Hakone (Japan), Oct. 1978.
[48] *F. Thümmler, E. Porz, G. Gratwohl*, personal communication.
[49] *L. G. Davies, J. C. Withers, D. F. Bazarre*, Final Report, Contract NOW 64-0176 C, Bureau of Naval Weapons, Washington 1965.
[50] *J. C. Withers, C. L. McCamdless, R. Schwarz* in: Advanced Fibrous Reinforced Composites. Society of Aerospace and Process Engineers, New York D 33 (1966).
[51] *J. A. Herzog*, Metall *1967*, 525.
[52] *R. J. Diefendorff*, personal communication.
[53] *H. D. Eichhorn*, Diplomarbeit, Universität Karlsruhe 1976.
[54] *J. Horn*, Diplomarbeit, Universität Karlsruhe 1977.
[55] *E. Fitzer, D. Kehr, M. Sahebkar* in *R. C. Marshall, J. W. Faust, C. E. Ryan:* Silicon Carbide. University of South Carolina Press, Columbia 1973, p. 33.
[56] *E. Fitzer, D. Kehr, D. Morin, M. Sahebkar*, Chemical Vapour Deposition Conference. London 1975, p. 589.
[57] *H. Debolt, V. Krukonis*, Arco Systems Division, Lowell, Mass., AFML-TR-73-140 (1972).
[58] *K. D. McHenry, R. E. Tressler*, J. Compos. Mater. *9*, 73 (1975).

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 New Entry to Naphthalene Oxides[**]

By *Richard R. Schmidt* and *Rolf Angerbauer*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Arene oxides and dihydroarenediols are of considerable interest as metabolites of aromatic hydrocarbons[1]. The discovery of the pronounced carcinogenic nature of epoxytetrahydroarenediols[2] has prompted several recent syntheses[3].

In our work on the *de novo* synthesis of sugars *via* cycloaddition[4], we have now found a facile and productive method

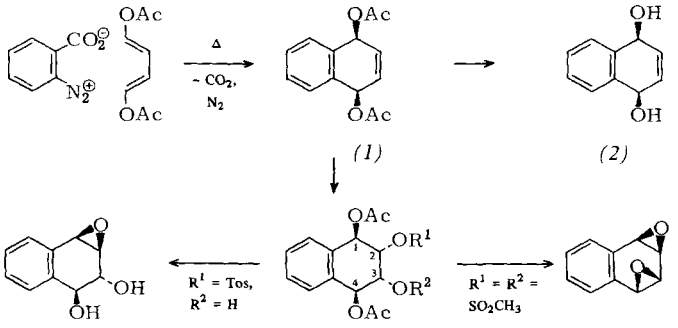
[*] Prof. Dr. R. R. Schmidt, Dipl.-Chem. R. Angerbauer
Fachbereich Chemie der Universität
Postfach 7733, D-7750 Konstanz (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to BASF AG for a gift of cyclooctatetraene.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0304 $ 02.50/0*

for the synthesis of 1,4-dihydronaphthalene-*cis*-1,4-diol *(2)*[5], racemic epoxytetrahydronaphthalenediol *(4)*[6], and *syn*-naphthalene 1,2:3,4-dioxide *(5)*[7], which should also be applicable to other systems.

The Diels-Alder reaction of *trans,trans*-1,4-butadienylene diacetate with benzyne (from *o*-benzenediazoniumcarboxylate) gives *(1)* (53%, m.p. 88°C) (see Table 1 for NMR data). Compound *(1)* is readily deacetylated to *(2)*[5] (88%, m.p. 105°C) with Na_2CO_3 in methanol. *cis*-Hydroxylation of *(1)* with hydrogen peroxide and catalytic amounts of osmium tetroxide leads stereospecifically to *(3a)* (60%, m.p. 156°C) which undergoes facile transformation into the racemic monotosylate *(3b)* (75%, m.p. 141°C) with tosyl chloride in dry pyridine. On stirring with Na_2CO_3 in methanol, *(3b)* affords the racemic epoxy-diol *(4)*[6] (90%, viscous oil) almost quantitatively. This product has the stereochemistry characteristic for carcinogens of this type. The dimesylate *(3c)* (82%, m.p. 157°C) also readily accessible from *(3a)* specifically forms the *syn*-dioxide *(5)*[7] (90%, m.p. 170°C) on treatment with Na_2CO_3 in methanol. Unlike the *anti*-dioxide, the *syn* isomer cannot be prepared by direct oxidation of naphthalene[8].



(a), $R^1 = R^2 = H$
(b), R^1 = Tos, $R^2 = H$
(c), $R^1 = R^2 = SO_2CH_3$

Table 1. ^{1}H-NMR data [a] of the compounds *(1)*, *(3a)*, *(3b)*, and *(3c)* [b].

(1):	6.19 (s; 2H, H-1, H-4), 6.08 (s; 2H, H-2, H-3), 2.10 (s; 6H, OAc), 7.22 (s; 4H, arom.)
(3a):	5.99 (d; 2H, H-1, H-4), 4.16 (d; 2H, H-2, H-3), 2.10 (s; 6H, OAc), 7.20 (s; 4H, arom.), 3.45 (br. s; 2H, OH), $J_{1,2}=6$
(3b):	6.28 (d; 1H, H-1), 6.05 (d; 1H, H-4), 5.08 (dd; 1H, H-2), 4.32 (m; 1H, H-3), 2.70 (d; 1H, OH), 2.20 (s; 3H, CH_3), 2.12 (s; 3H, OAc), 2.00 (s; 3H, OAc), 7.20–7.90 (m; 8H, arom.), $J_{1,2}=7$, $J_{2,3}=2$, $J_{3,4}=5$, $J_{3,OH}=5$
(3c):	6.28 (d; 2H, H-1, H-4), 5.32 (d; 2H, H-2, H-3), 3.12 (s; 6H, CH_3), 2.17 (s; 6H, OAc), 7.37 (m; 4H, arom.), $J_{1,2}=5$

[a] 80-MHz spectra in $CDCl_3$ with TMS as internal standard; δ values, coupling constants in Hz.
[b] The NMR spectra of *(2)* [5], *(4)* [6], and *(5)* [7] agree with those reported in the literature. All new compounds gave correct elemental analyses.

Procedure

Synthesis of *(1)*: 1,3-Butadienylene diacetate (10 g, 58 mmol) and *o*-benzenediazoniumcarboxylate (10 g, 67 mmol) are heated to 60°C for 2 h with stirring in dry $CHCl_3$ (160 ml). After stripping off the solvent the residue is filtered on a short silica gel column and recrystallized from ethanol; yield 7.7 g (53%), m.p. 88°C.

Received: December 18, 1978 [Z 168 IE]
German version: Angew. Chem. *91*, 325 (1979)

CAS Registry numbers:
(1), 69532-84-9; *(2)*, 51096-10-7; *(3a)*, 69532-85-0; *(3b)*, 69532-86-1; *(3c)*, 69532-87-2; *(4)*, 58116-21-5; *(5)*, 58692-14-1; 1,3-butadienylene diacetate, 15910-11-9; *o*-benzenediazoniumcarboxylate, 1608-42-0

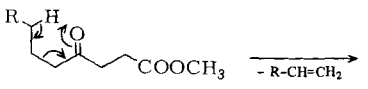
[1] *J. W. Daly, D. M. Jerina, B. Witkop*, Experientia *28*, 1129 (1972); *D. M. Jerina, J. W. Daly*, Science *185*, 573 (1974); *Th. C. Bruice, P. Y. Bruice*, Acc. Chem. Res. 9, 378 (1976), and references cited therein; cf. *M. Schäfer-Ridder*, Nachr. Chem. Tech. Lab. 27, 4 (1979), and references cited therein.
[2] *P. Sims, P. L. Grover, A. Swaisland, K. Pal, A. Hewer*, Nature *252*, 326 (1974); *J. Kapitulnik, P. G. Wislocki, M. Levin, H. Yagi, D. M. Jerina, A. H. Conney*, Cancer Res. *38*, 354 (1978), and references cited therein.
[3] *H. Yagi, D. R. Thakker, O. Hernandez, M. Koreda, D. M. Jerina*, J. Am. Chem. Soc. 99, 1604 (1977); *R. E. Lehr, M. Schäfer-Ridder, D. M. Jerina*, Tetrahedron Lett. *1977*, 539; *P. P. Fu, R. G. Harvey, ibid. 1977*, 2059; *P. P. Fu, H. M. Lee, R. G. Harvey, ibid. 1978*, 551; *R. E. Lehr, C. W. Taylor, S. Kumar, H. D. Mah, D. M. Jerina*, J. Org. Chem. *43*, 3462 (1978), and references cited therein.
[4] *R. R. Schmidt, R. Angerbauer*, Angew. Chem. *89*, 822 (1977); Angew. Chem. Int. Ed. Engl. *16*, 783 (1977); *R. R. Schmidt, A. Lieberknecht, ibid. 90*, 821 (1978) and *17*, 769 (1978); *R. R. Schmidt, R. Angerbauer*, Carbohydr. Res., and references cited therein.
[5] *A. M. Jeffrey, H. J. C. Yeh, D. M. Jerina*, J. Org. Chem. *39*, 1405 (1974); *M. Schäfer-Ridder, U. Brocker, E. Vogel*, Angew. Chem. *88*, 262 (1976); Angew. Chem. Int. Ed. Engl. *15*, 228 (1976).
[6] *H. Yagi, O. Hernandez, D. M. Jerina*, J. Am. Chem. Soc. 97, 6881 (1975).
[7] *E. Vogel, H.-H. Klug, M. Schäfer-Ridder*, Angew. Chem. *88*, 268 (1976); Angew. Chem. Int. Ed. Engl. *15*, 229 (1976).
[8] *K. Ishikawa, G. W. Griffin*, Angew. Chem. *89*, 181 (1977); Angew. Chem. Int. Ed. Engl. *16*, 171 (1977). *S. Krishnan, D. G. Kuhn, G. A. Hamilton*, J. Am. Chem. Soc. 99, 8121 (1977).

ω-Formyl- and 4-Oxocarboxylic Acids in Blood Plasma

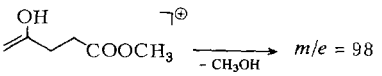
By *Jürgen Pfordt* and *Gerhard Spiteller*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

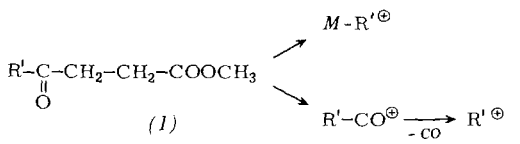
During workup of blood plasma with the aim of concentrating any dicarboxylic acids present, a fraction that was obtained after esterification with diazomethane was analyzed by combined glass-capillary chromatography and mass spectrometry. Besides the mono- and dicarboxylic esters already known to occur in plasma this fraction contained a series of homologous compounds whose mass spectra are characterized by key ions of mass 130 and 98. The key ions are formed by McLafferty rearrangement and subsequent elimination of methanol from the methyl 4-oxocarboxylates *(1)*.



(1)



Although molecular ions are absent the molecular weight can still be determined, *i.e.* from the $M-31$ ($M-OCH_3$) fragment. Further typical fragments are formed by rupture of the bonds in the neighborhood of the carbonyl group.



(1)

[*] Prof. Dr. G. Spiteller, Dipl.-Chem. J. Pfordt
Lehrstuhl für Organische Chemie I der Universität
Postfach 3008, D-8580 Bayreuth (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979
0570-0833/79/0404-0305 $ 02.50/0

The structures derived from spectra for a 4-oxooctanoic, a 4-oxononanoic, and a 4-oxodecanoic methyl ester were confirmed by synthesis and subsequent comparative measurements of mass spectra and retention indices (Table 1).

Table 1. 4-Oxo- and ω-formylcarboxylic methyl esters.

Name	Retention index [a]	Key ions in mass spectrum
4-Oxooctanoic methyl ester ($M=172$)	1236	29 (47 %), 41 (42 %), 55 (60 %), 57 (100 %), 59 (28 %), 71 (5 %), 85 (67 %), 87 (16 %), 98 (50 %), 111 (9 %), 115 (61 %), 130 (36 %), 141 (23 %)
4-Oxononanoic methyl ester ($M=186$)	1336	41 (32 %), 43 (100 %), 55 (56 %), 59 (26 %), 71 (50 %), 87 (16 %), 98 (73 %), 99 (48 %), 111 (10 %), 115 (58 %), 130 (41 %), 155 (19 %)
4-Oxodecanoic methyl ester ($M=200$)	1436	41 (34 %), 43 (100 %), 55 (46 %), 57 (36 %), 59 (18 %), 71 (10 %), 85 (22 %), 87 (24 %), 98 (59 %), 113 (25 %), 115 (45 %), 130 (34 %), 169 (11 %)
7-Formyl-heptanoic methyl ester ($M=172$)	1288	41 (100 %), 43 (81 %), 55 (76 %), 57 (51 %), 59 (45 %), 69 (72 %), 74 (89 %), 81 (31 %), 87 (88 %), 97 (39 %), 101 (17 %), 111 (16 %), 129 (44 %), 141 (23 %), 144 (10 %)
8-Formyl-*octanoic* methyl ester ($M=186$)	1387	29 (42 %), 41 (74 %), 43 (63 %), 55 (81 %), 59 (37 %), 69 (33 %), 74 (100 %), 83 (43 %), 87 (64 %), 97 (10 %), 111 (21 %), 115 (7 %), 136 (5 %), 143 (29 %), 155 (19 %), 158 (11 %)

[a] Stationary phase OV-101, temperature program 2°C/min, initial temperature 80°C.

Two further compounds in the chromatogram were identified as acid aldehydes (ω-formylcarboxylic acids). Their mass spectra, like those of the long-chain fatty acid methyl esters, are characterized by key ions of mass 74 and 87. The molecular weight can be determined from an $M-31$ ($M-OCH_3$) fragment and an $M-28$ ion. These ions, as well as an $M-43$ fragment, are typical for methyl ω-formylcarboxylates[1, 2]. The structures of both the C_8 and the C_9 acid aldehydes were likewise confirmed by synthesis and comparative measurements (Table 1).

Isolation and workup

Blood plasma (5 ml) was diluted with five times its volume of physiological saline solution, and the resulting solution adjusted to pH = 1 with 6 N hydrochloric acid and extracted with 3 × 25 ml diethyl ether. The organic phase was concentrated to 1 ml and esterified with ethereal diazomethane solution. The dicarboxylic methyl ester fraction, which also contains the ω-formyl- and 4-oxocarboxylic methyl esters, can be isolated by chromatography on a silica gel column with petroleum ether/diethyl ether as eluent[3]. After separation in a coupled glass-capillary gas chromatograph/mass spectrometer, the compounds listed in Table 1 were identified by retention indices and mass spectra.

Received: January 8, 1979 [Z 171 IE]
German version: Angew. Chem. 91, 321 (1979)

CAS Registry numbers:
Table 1, from top to bottom: 4316-48-7; 33566-57-3; 7011-82-7; 3884-92-2; 1931-63-1

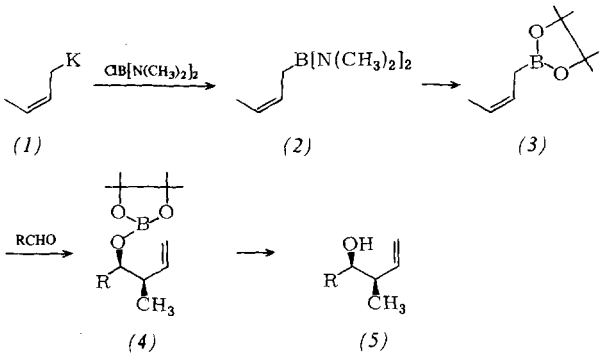
[1] *A. C. Noble, W. W. Nawar*, J. Agric. Food Chem. *19*, 1039 (1971).
[2] *W. Gärtner, G. Spiteller*, unpublished.
[3] *S. Lindstedt, K. Norberg, G. Steen, E. Wahl*, Clin. Chem. *22*, 1330 (1976).

Diastereoselective Synthesis of β-Methyl Homoallyl Alcohols

By *Reinhard W. Hoffmann* and *Hans-Joachim Zeiss*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

The diastereoselective synthesis of the β-methyl alcohol units of macrolide antibiotics represents a similar challenge[1] to preparative organic chemistry today as did the stereoselective synthesis of carotenoids twenty years ago[2]. Significant achievements have been the *threo*-selective addition of (*E*)-2-butenyl-metal derivatives[3] and the *erythro*-selective addition of (*Z*)-metal enolates[4] to aldehydes. Starting from the effective addition of allylboronates to aldehydes[5, 6] we have found an *erythro*-selective addition of (*Z*)-2-butenylboronates *(3)* to aldehydes.



	R	*erythro*:*threo*
a	CH_3	97:3
b	C_2H_5	97:3
c	$(CH_3)_2CH$	94:6
d	C_6H_5	96:4

Only in the absence of Lewis acids do 2-butenylboronates prove to be *E*/*Z*-stable on heating[6a]. This is presumably the reason why direct reaction of (*Z*)-2-butenylpotassium *(1)*[6b] with chloro(dialkoxy)boranes led to *E*/*Z* mixtures of the 2-butenylboronates. We therefore used the weaker Lewis acid chlorobis(dimethylamino)borane[7] in tetrahydrofuran/hexane (−120 to 0°C) to convert *(1)* into 2-butenylbis(dimethylamino)borane *(2)*, which was shown by ^{13}C-NMR to be more than 95 % *Z*-configurated. *(2)* could be separated from minor amounts of the methylallylborane derivative also formed by distillation (70°C/15 torr) over a Spaltrohr® column. Reaction of *(2)* with pinacol followed by removal of dimethylamine led almost quantitatively to *(3)* (>95% *Z*), which was used immediately for the conversion[5b] of aldehydes *via (4)* into the β-methyl homoallyl alcohols *(5)* in crude yields of up to 92 %. The *erythro*/*threo* ratio[8] of the alcohols *(5)* has been determined by gas chromatography.

The reaction of *E*/*Z* mixtures of 2-butenyl(dimethoxy)borane with acetaldehyde or benzaldehyde gave β-methyl homoallyl alcohols in *erythro*/*threo* ratios[8] corresponding exactly to the *Z*/*E* ratios of the boronates used. It can therefore be concluded that not only the (*Z*)-2-butenylboronate but also the (*E*) isomer reacts diastereospecifically.

Received: December 27, 1978 [Z 170 IE]
German version: Angew. Chem. 91, 329 (1979)
Publication delayed at authors' request

[*] Prof. Dr. R. W. Hoffmann, Dipl.-Chem. H. J. Zeiss
Fachbereich Chemie der Universität
Postfach 1929, D-3550 Marburg 1 (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0306 $ 02.50/0

CAS Registry numbers:
(Z)-(1), 59304-72-2; *(E)-(1)*, 60647-48-5; *(Z)-(2)*, 69610-99-7; *(E)-(2)*, 69611-00-3; *(Z)-(3)*, 69611-01-4; *(E)-(3)*, 69611-02-5; *(R*,R*)-(4a)*, 69611-03-6; *(R*,S*)-(4a)*, 69611-04-7; *(R*,R*)-(4b)*, 69611-05-8; *(R*,S*)-(4b)*, 69611-06-9; *(R*,R*)-(4c)*, 69611-07-0; *(R*,S*)-(4c)*, 69611-08-1; *(R*,R*)-(4d)*, 69611-09-2; *(R*,S*)-(4d)*, 69611-10-5; *(R*,R*)-(5a)*, 1538-23-4; *(R*,S*)-(5a)*, 1538-22-3; *(R*,R*)-(5b)*, 1538-21-2; *(R*,S*)-(5b)*, 1589-07-7; *(R*,R*)-(5c)*, 1502-91-6; *(R*,S*)-(5c)*, 1502-90-5; *(R*,R*)-(5d)*, 52922-10-8; *(R*,S*)-(5d)*, 52922-19-7; chlorobis(dimethylamino)borane, 6562-41-0; acetaldehyde, 75-07-0; benzaldehyde, 100-52-7; propanal, 123-38-6; 2-methylpropanal, 78-84-2; pinacol, 76-09-5

[1] *S. Masamune, G. S. Bates, J. W. Corcoran*, Angew. Chem. *89*, 602 (1977); Angew. Chem. Int. Ed. Engl. *16*, 585 (1977).

[2] *H. Pommer*, Angew. Chem. *72*, 811, 911 (1960).

[3] *Y. Okude, S. Hirano, T. Hiyama, H. Nozaki*, J. Am. Chem. Soc. *99*, 3179 (1977); *C. T. Buse, C. H. Heathcock*, Tetrahedron Lett. *1978*, 1685; cf. also *C. Servens, M. Pereyre*, J. Organomet. Chem. *35*, C20 (1972).

[4] *W. A. Kleschick, C. T. Buse, C. H. Heathcock*, J. Am. Chem. Soc. *99*, 247 (1977); *C. T. Buse, C. H. Heathcock, ibid. 99*, 8109 (1977); *W. Fenzl, R. Köster, H. J. Zimmermann*, Justus Liebigs Ann. Chem. *1975*, 2201; *E. A. Jeffery, A. Meisters, T. Mole*, J. Organomet. Chem. *74*, 373 (1974); *H. O. House, D. S. Crumrine, A. Y. Teranishi, H. D. Olmstead*, J. Am. Chem. Soc. *95*, 3310 (1973).

[5] a) Cf. *B. M. Mikhailov*, Organomet. Chem. Rev. *A8*, 1 (1972); b) *T. Herold, R. W. Hoffmann*, Angew. Chem. *90*, 822 (1978); Angew. Chem. Int. Ed. Engl. *17*, 768 (1978).

[6] a) *J. Blais, A. L'Honore, J. Soulie, P. Cadiot*, J. Organomet. Chem. *78*, 323 (1974); cf. *H. C. Brown, N. R. De Lue, Y. Yamamoto, K. Maruyama, T. Kasahara, S. Murahashi, A. Sonoda*, J. Org. Chem. *42*, 4089 (1977); *M. Schlosser, G. Rauchschwalbe*, J. Am. Chem. Soc. *100*, 3258 (1978); b) cf. *G. Rauchschwalbe, M. Schlosser*, Helv. Chim. Acta *58*, 1094 (1975).

[7] *H. Nöth, P. Fritz*, Z. Anorg. Allg. Chem. *322*, 297 (1963).

[8] Our assignment is based on the rule (*H. Felkin, Y. Gault, G. Roussi*, Tetrahedron *26*, 3761 (1970)), that the *threo*-isomer shows the shorter retention time on gas chromatography. This has been secured by further transformations in the case of *(5)*, R = CH_3: *P. A. Bartlett, K. J. Jernstedt*, J. Am. Chem. Soc. *99*, 4829 (1977); *P. A. Bartlett*, personal communication 1977.

Economic Synthesis of Activated *N-tert*-Butyloxycarbonyl Amino Acid Esters[1]

By *Gerd Schnorrenberg* and *Wolfgang Steglich*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

We have found that 4,6-diphenylthieno[3,4-*d*][1,3]dioxol-2-one 5,5-dioxide *(1)*[2] permits an economic synthesis of activated Boc-amino acid esters *(5a)* if the reagent is used not only for activation of the Boc-amino acid *(3a)*[2] but also for introduction of the Boc group. To this end, activated *tert*-butyl carbonate *(2a)*[1] is heated with the amino acid and one equivalent of 1,1,3,3-tetramethylguanidine[3] in tetrahydrofuran (THF) until the amino acid has dissolved (variant A).

In the case of sparingly soluble amino acids, the components are stirred in dioxane/water at room temperature (variant B). After removal of the base with aqueous citric acid the Boc-amino acid *(3a)*, together with the sulfone *(4)*, is again treated with equimolar amounts of *(1)* and pyridine[5]. The sulfone *(4)* can be readily removed, and the crystalline activated ester *(5a)* (Table 1) is usually obtained analytically pure.

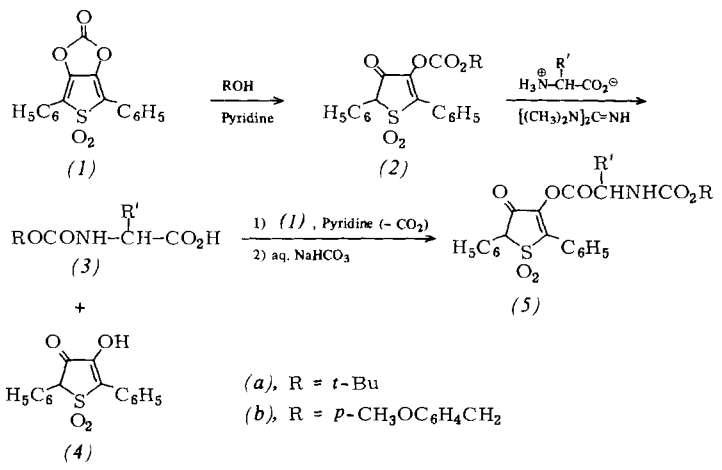


Table 1. Activated Boc- *(5a)* and Z(OMe) amino acid ester *(5b)* [a].

Activated ester *(5)* of	*t* [h] [b]	Variant	Yield [%] [c]	M.p. [°C] [d]
Boc-Ala	24	B	82	95
Boc-Cys(*S*-Bzl)	12	A	90	153
Boc-Gly	48	B	72	138
Boc-Leu	7	A	83	158
Boc-Phe	12	A	84	178
Boc-Pro	3	A	92	166
Boc-Ser(*O*-Bzl)	4	A	87	145
Boc-Trp	12	A	72	147
Boc-Val	18	A	87	160
Z(OMe)-Leu	4	A	85	138
Z(OMe)-Pro	3	A	76	146

[a] All compounds gave correct elemental analyses. [b] For reaction of the amino acids with *(2a)* or *(2b)*. [c] Based on amino acid. [d] Diastereomeric mixtures except for Boc-glycine derivative.

Unlike similar one-pot preparations of activated Boc-amino acid esters[4], our method avoids activation with dicyclohexylcarbodiimide and hence the difficulties of removing dicyclohexylurea. The yields are often higher than for conventional introduction of the Boc group. The activated esters *(5a)* are well suited for peptide syntheses[2].

Preparation of the esters *(5a)* was shown by gas chromatography[5] and polarimetry to proceed without racemization.

Reaction of *(1)* with *p*-methoxybenzyl alcohol gives the activated carbonate *(2b)* (m.p. 226°C after prior sintering with red coloration above 85°C) in 82% yield. Like *(2a)*, *(2b)* can be used for preparing the activated Z(OMe)-amino acid esters *(5b)*. Highly acid-labile alcohols such as triphenylmethanol or α,α-dimethyl-3,5-dimethoxybenzyl alcohol[6] cannot be converted into carbonates of *(2)*.

Procedure

Synthesis of *(2a)*: Compound *(1)*[2] (3.26 g, 10 mmol), dry *tert*-butanol (0.89 g, 12 mmol), and pyridine (0.81 ml, 10 mmol) are stirred together at 20°C for 1.5 h in dry dichloromethane (80 ml). The mixture is then washed twice with saturated $NaHCO_3$ solution, once with 20% citric acid solution, and once with water, dried over $MgSO_4$, and evaporated to dryness *in vacuo*; yield 3.60 g (90%), m.p. 158°C (dec.).

Synthesis of *(5a)*: variant A: Compound *(2a)* (4.00 g, 10 mmol), finely powdered amino acid (10 mmol), and 1,1,3,3-tetramethylguanidine (1.85 ml, 15 mmol) are heated under reflux in dry THF (100 ml) until the amino acid has dissolved. After evaporation *in vacuo*, the residue is taken up in dichloromethane, extracted four times with saturated $NaHCO_3$ solution; the pH of the aqueous extracts is then adjusted to 3 with solid citric acid or cold 1 N HCl before extracting three times with ethyl acetate. After washing with H_2O, drying over $MgSO_4$, and evaporation *in vacuo* the mixture is stirred with *(1)* (3.26 g, 10 mmol) and pyridine (0.81 ml, 10 mmol) in dry CH_2Cl_2 (80 ml) at 20°C for 30 min. The mixture is shaken three times each with 20% citric acid solution and saturated

[*] Prof. Dr. W. Steglich, Dipl.-Chem. G. Schnorrenberg
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979*

0570-0833/79/0404-0307 $ 02.50/0

$NaHCO_3$ solution, washed once more with citric acid solution and water, dried over $MgSO_4$, and evaporated. The esters *(5a)* can be used without further purification for peptide synthesis. For analysis, the product can be crystallized, if necessary, from ethyl acetate/light petroleum.—Variant B: The components are stirred in dioxane/water (2:1) (150 ml) at 20 °C for 1—2 days, the mixture evaporated down and treated as for variant A.

Received: January 31, 1979 [Z 173 IE]
German version: Angew. Chem. *91*, 326 (1979)

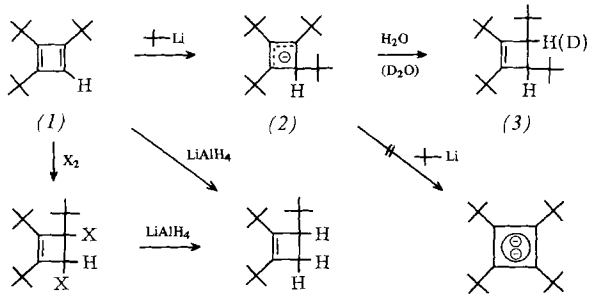
[1] Activated Carboxylic Acid Derivatives, Part 4.—Part 3: *H. Schmidt, O. Hollitzer, A. Seewald, W. Steglich*, Chem. Ber., in press.
[2] *O. Hollitzer, A. Seewald, W. Steglich*, Angew. Chem. *88*, 480 (1976); Angew. Chem. Int. Ed. Engl. *15*, 444 (1976).
[3] Cf. *A. Ali, B. Weinstein*, J. Org. Chem. *36*, 3022 (1971); *A. Ali, F. Fahrenholz, B. Weinstein*, Angew. Chem. *84*, 259 (1972); Angew. Chem. Int. Ed. Engl. *11*, 289 (1972); *U. Ragnarson, S. M. Karlsson, B. E. Sandberg*, Acta Chem. Scand. *26*, 2550 (1972); *W. Steglich, S. Hinze*, Synthesis *1976*, 399.
[4] Examples: *M. Frankel, D. Ladkany, C. Gillon, Y. Wolman*, Tetrahedron Lett. *1966*, 4765; *Y. Wolman, D. Ladkany, M. Frankel*, J. Chem. Soc. *C 1967*, 689; *W. Broadbent, J. S. Morley, B. E. Stone, ibid. 1967*, 2632.
[5] *F. Weygand, A. Prox, L. Schmidhammer, W. König*, Angew. Chem. *75*, 282 (1963); Angew. Chem. Int. Ed. Engl. *2*, 183 (1963).
[6] *C. Birr, W. Lochinger, G. Stahnke, P. Lang*, Justus Liebigs Ann. Chem. *763*, 162 (1972).

Electrophilic Behavior of Tri-*tert*-butylcyclobutadiene[1]

By *Günther Maier* and *Fritz Köhler*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

The cyclobutadiene *(1)*, which is readily accessible from 2,3,4-tri-*tert*-butylcyclopentadienone *via* the corresponding "housenone"[2], is extremely versatile in its reactions. It behaves both as a diene and as a dienophile[3a], as a nucleophile and as a base[3b], and as a potential diradical[3c]. No evidence of electrophilic properties has yet been reported for *(1)*, but our latest studies now close this gap. This chemical omnipotence of the cyclobutadiene 4π-system confirms its exceptional nature.



Reaction of *(1)* with *tert*-butyllithium in diethyl ether in the presence of *N,N,N',N'*-tetramethylethylenediamine at −78 °C smoothly affords the adduct *(2)*. Aqueous work-up gives a high yield (94 % based on the cyclopentadienone reactant) of 1,2,3,4-tetra-*tert*-butylcyclobutene *(3)*[4]. Treatment with D_2O gives only the monodeuterated derivative D_1-*(3)*. This means that addition does not proceed beyond the monoanion *(2)*; no deprotonation to give the "aromatic" dianion *(6)* occurs. The H/D NMR coupling constant in D_1-*(3)* proves the *trans* configuration[5].

A hydride ion is also added to *(1)*[6]. Both the direct action of lithium aluminum hydride on *(1)* and the circuitous route *via* the halogen adducts *(4a)*[4, 7] or *(4b)* [^{1}H-NMR ($CDCl_3$): $\delta = 1.18$ (9H), 1.20 (9H), 1.36 (9H), 5.13 (1H); ^{13}C-NMR ($CDCl_3$): $\delta = 28.24, 30.04, 31.10, 33.62, 34.31, 40.48, 58.60, 85.53, 149.89, 155.79$] lead to 1,2,3-tri-*tert*-butylcyclobutene *(5)*[4].

Nucleophilicity and basicity of *(1)* parallel the excellent donor properties of unsubstituted cyclobutadiene and its alkyl derivatives[8]. It is therefore all the more surprising that *(1)* should also show pronounced electrophilic character. The reason for this dualism is to be found in the pseudo-Jahn-Teller effect[9a] which gives rise to a low-lying LUMO and a high-energy HOMO, and thus endows *(1)* with the properties of a nucleophile and of an electrophile[9b]. The addition of *tert*-butyllithium—also known in the case of open-chain butadiene[10]—is even able to overcome the kinetic hindrance of three *tert*-butyl groups as a result of the energetic destabilization of the π-system.

Received: January 19, 1979 [Z 175 IE]
German version: Angew. Chem. *91*, 327 (1979)

CAS Registry numbers:
(1), 51067-53-9; *(2)*, 69631-78-3; *(3)*, 69631-79-4; *(4a)*, 69631-80-7; *(4b)*, 69631-81-8; *(5)*, 37715-08-5

[1] Small Rings, Part 26. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 25: *G. Maier, S. Pfriem, U. Schäfer, R. Matusch*, Angew. Chem. *90*, 552 (1978); Angew. Chem. Int. Ed. Engl. *17*, 520 (1978).
[2] *G. Maier, U. Schäfer, W. Sauer, H. Hartan, R. Matusch, J. F. M. Oth*, Tetrahedron Lett. *1978*, 1837.
[3] a) Review: *G. Maier*, Angew. Chem. *86*, 491 (1974); Angew. Chem. Int. Ed. Engl. *13*, 425 (1974); b) *G. Maier, W. Sauer, ibid. 87*, 675 (1975) and *14*, 648 (1975); c) *ibid. 89*, 49 (1977) and *16*, 51 (1977).
[4] *A. E. Feiring, J. Ciabattoni*, J. Am. Chem. Soc. *95*, 5266 (1973).
[5] J_{HD} is *ca.* 0.4 Hz for D_1-*(3)*. This gives $J_{HH} \approx 2.5$ Hz, which corresponds more closely to the *trans* coupling (1.7 Hz) typical of allylic cyclobutene protons than to *cis* coupling (4.9 Hz). We are grateful to Dr. *H.-O. Kalinowski* for this configurational assignment.
[6] This reaction is not very clear-cut; gas chromatography shows the crude product to contain about 18 % of *(5)*.
[7] Presumably, the halogen adducts are also *trans*-configurated. In the compound 3,4-dichlorotetramethylcyclobutene formerly[4] used as reference substance the chlorine atoms are also *trans*-oriented contrary to the original assumption: *R. Criegee*, Angew. Chem. *80*, 585 (1968); Angew. Chem. Int. Ed. Engl. *7*, 559 (1968).
[8] *G. Maier, H. P. Reisenauer*, Tetrahedron Lett. *1976*, 3591; *G. Maier, W. Mayer, C. Haacke, R. Askani*, Angew. Chem. *85*, 1057 (1973); Angew. Chem. Int. Ed. Engl. *12*, 1016 (1973).
[9] a) *L. Salem:* The Molecular Orbital Theory of Conjugated Systems. Benjamin, Reading 1966, pp. 486ff.; b) *I. Fleming:* Frontier Orbitals and Organic Chemical Reactions. Wiley, New York 1976.
[10] *W. H. Glaze, D. J. Berry, D. R. Duncan*, J. Organomet. Chem. *52*, 233 (1973).

Ester and Lactone Formation with the Reagent 1,2-Dihydro-4,6-dimethyl-2-thioxo-3-pyridinecarbonitrile

By *Ulrich Schmidt* and *Dieter Heermann*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Several synthetic routes affording entry to macrolactones have been described in recent years[1-4]. So far, however, no single method has proven universally satisfactory for the synthesis of complex macrolides.

We report here on the formation of esters with the readily accessible reagent 1,2-dihydro-4,6-dimethyl-2-thioxo-3-pyri-

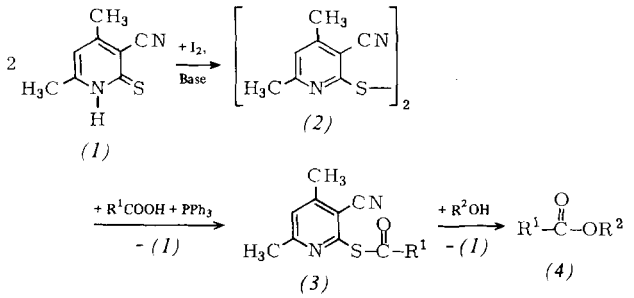
[*] Prof. Dr. G. Maier, F. Köhler
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Lahn-Giessen 1 (Germany)

[*] Prof. Dr. U. Schmidt, Dr. D. Heermann
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0308 $ 02.50/0

dinecarbonitrile *(1)*[5], whose thiol esters *(3)* react with alcohols much more rapidly than the thiol esters of 2-thiopyridone, thus circumventing any necessary activation with silver ions[3].

The thiol esters *(3)* are formed within a few minutes on reaction of the disulfide *(2)*[6] with carboxylic acids and triphenylphosphane in toluene (concentration: 1 mol/l) at room temperature according to the method of *Mukaiyama*[7]. After addition of alcohol and 20 hours' heating at 100 °C, the esters *(4)* are formed in almost quantitative yields (isopropyl valerate >90 %)[8a].



Ring closure to the macrolactone was investigated in the case of 15-hydroxypentadecanoic acid. The acid was esterified with *(2)* and the thiol ester *(3)* (0.01 M in toluene) heated for 2 h; pentadecanolide[8a] was formed in 60 % yield together with *ca.* 10 % of dimeric lactone[8b]. Under moderate dilution conditions (dropwise addition of *(3)* in boiling toluene over 3 h) the yield of pentadecanolide was increased to 70 %[8a, c], under high dilution conditions (dropwise addition over 48 h) to 80 %[8a]. The yields do not alter if *(3)* is generated and lactonized in dilute solution (slow dropwise addition of *(2)* to a mixture of carboxylic acid and triphenylphosphane in toluene).

Owing to the sparing solubility of the thiopyridone *(1)*, the disulfide *(2)* and the thiol ester *(3)* are appreciably more reactive than the unsubstituted analogues. The thiol esters *(3)* react at rates comparable with the reaction rate of the thiol esters of 4-*tert*-butyl-1-isopropylimidazoline-2-thione[2], but they are less expensive and easier to obtain than the latter.

Received: February 9, 1979 [Z 176 IE]
German version: Angew. Chem. *91*, 330 (1979)

CAS Registry number:
(1), 54585-47-6

[1] *E. J. Corey, K. C. Nicolaou*, J. Am. Chem. Soc. *96*, 5614 (1974).
[2] *E. J. Corey, D. J. Brunelle*, Tetrahedron Lett. *1976*, 3409.
[3] *H. Gerlach, A. Thalmann*, Helv. Chim. Acta *57*, 2661 (1974).
[4] *T. Mukaiyama, M. Usui, K. Saigo*, Chem. Lett. *1976*, 49.
[5] *U. Schmidt, H. Kubitzek*, Chem. Ber. *93*, 1559 (1960).
[6] Preparative data for *(1)* → *(2)*: *U. Schmidt, G. Giesselmann*, Chem. Ber. *93*, 1590 (1960).
[7] *T. Mukaiyama, T. Matsueda, M. Suzuki*, Tetrahedron Lett. *1970*, 1901.
[8] a) Determined gas chromatographically; b) identified mass spectrometrically; c) isolated chromatographically.

Directed Synthesis of Acyl Ortho Esters

By *Günter Wulff, Ulrich Schröder*, and *Wolfram Schmidt*[*]

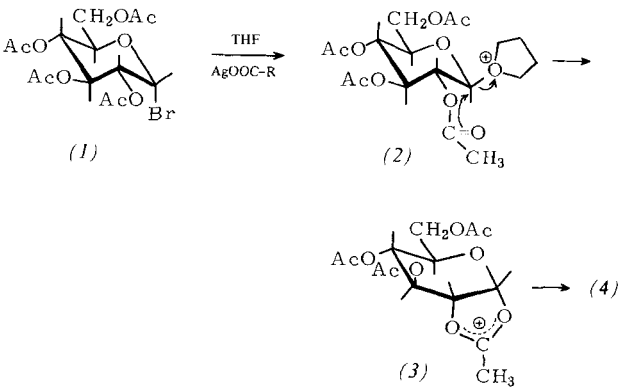
Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

The *trans*-glycosides [*e.g. (7)*] obtained from alcohols and peracetylated 1-halo sugars in the Koenigs-Knorr glycoside synthesis are usually accompanied by many undesired products, the main contaminants generally being 1-hydroxy sugars, *e.g. (9)*[2–4]. The formation of these hydroxy sugars has been attributed to reaction between the water entrained in or produced by condensation with the haloses[3]. However, it is doubtful that this should be solely responsible for their formation, since drying agents fail to suppress the reaction.

In order to investigate the mode of formation of the 1-hydroxy sugars we treated the halose *(1)* with cholesterol (as alcohol component) in the presence of silver propionate as acid acceptor since, unlike Ag_2O, Ag_2CO_3, or silver salts of hydroxy carboxylic acids, no water is formed in its reaction. Nevertheless, reaction in diethyl ether gave some 40 % of the monohydroxy sugars in addition to the expected 1-acyl sugars *(5a)* and the β-glycoside *(7c)* on conventional workup. Hydroxy sugars were also found to accompany *(5a)* in the absence of cholesterol.

It therefore appeared likely that the hydroxy sugars result from a reactive intermediate during workup. Direct ^{1}H-NMR examination of the anhydrous reaction mixture suggested the presence of the acyl ortho ester *(4a)* whose hydrolysis would lead to hydroxy sugars[5]. All attempts to isolate *(4a)* were thwarted by its ready decomposition. We therefore undertook the directed synthesis of this class of compounds.

The very first synthesis of an acyl ortho ester and the study of its properties were of interest for yet another reason. In their work on 1,2-disubstituted cyclohexane derivatives, *Winstein et al.*[6] examined the influence of neighboring acyl groups on the stereochemistry of substitution reactions and ascribed an essential role to intermediate acyl ortho esters; yet they were unable to synthesize or detect them directly[6, 7].

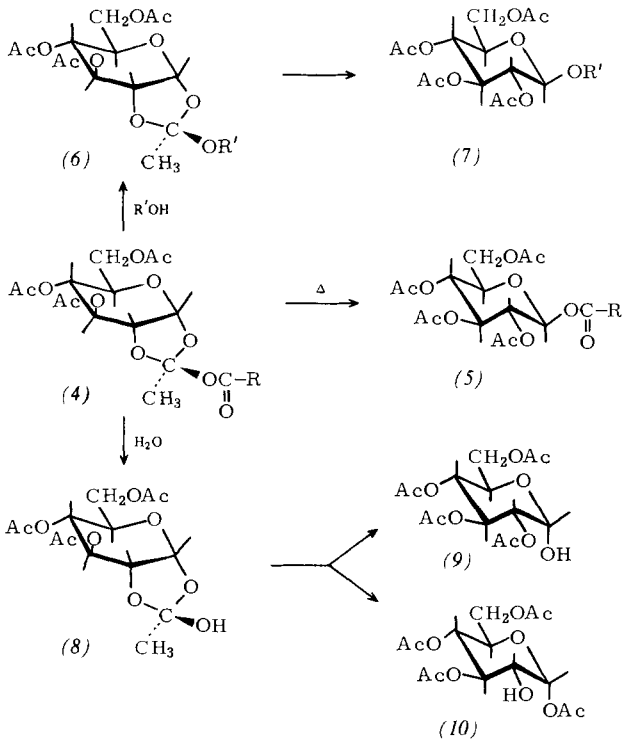


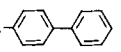
Since acylated haloses *(1)* are transformed almost quantitatively into acetoxonium ions *(3)* *via* the oxonium compound *(2)* in the presence of tetrahydrofuran[4], we treated *(1)* with silver propionate in tetrahydrofuran. This afforded the acyl ortho ester *(4a)* in some 70% yield; it could not be isolated pure owing to its reluctance to crystallize. Acyl ortho esters *(4)* of aromatic carboxylic acids are far more reactive and decompose faster. 4-(4-Biphenylyl)butyric acid proved more suitable; its derivatives crystallize readily. Reaction of its silver salt with *(1)* in tetrahydrofuran gave about 80 % of 3,4,6-tri-*O*-acetyl-1,2-*O*-{1-[4-(4-biphenylyl)butyryloxy]ethylidene}-α-D-glucopyranose *(4b)*[8], of which 67 % could be isolated in pure crystalline form. Crystalline *(4b)* is rather stable; m. p. 85—90 °C (dec.), $[\alpha]_D^{22} = +13.4°$ ($c = 3.5$, CH_2Cl_2). The structure follows unequivocally from its ^{1}H-NMR spectrum. The signals of H-1 ($\delta = 5.83$, $J_{1,2} = 5.6$ Hz), of H-2 ($\delta = 4.46$, $J_{2,3} = 2.8$ Hz; $J_{2,4} = 1.0$ Hz) and the protons of the methyl group attached to the dioxolane ring ($\delta = 1.97$) are expectedly shifted relative to the corresponding signals of other 1,2-ortho acetyl derivatives of glucose. However, the

[*] Prof. Dr. G. Wulff, Dipl.-Chem. U. Schröder, Dr. W. Schmidt
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0309 S 02.50/0*

chemical shifts and the coupling constants of the other signals are nearly identical to those of alkyl ortho esters [*e.g. (6)*]. We found no signals corresponding to the *endo* form of *(4b)* in the ^{1}H-NMR spectrum.



(a), R = C_2H_5; *(b)*, R = $(CH_2)_3$- 

(c), R' = 3-Cholesteryl

The structure of *(4b)* also follows from its reactions. On heating to above its melting point or even on heating to over 60 °C in solution in the presence of 2,6-lutidine, *trans* cleavage of the dioxolane ring occurs, giving the *trans*-1,2-diacyl derivative *(5b)* almost quantitatively. The second conceivable *trans*-cleavage product of the mannose series could not be detected.

The reaction of *(4b)* with D_2O in [D_6]acetone in the presence of 2,6-lutidine was monitored by ^{1}H-NMR spectroscopy. It proceeds rather slowly (*ca.* 75 min until the signals of *(4b)* disappear) and affords (again followed by ^{1}H-NMR spectroscopy after trifluoroacetylation) about 60 % of the 1-hydroxy sugar *(9)* and 40 % of the 2-hydroxy sugar *(10)* *via* exclusive *cis* cleavage of the dioxolane ring. Thus both possible ring opening products are formed. The acidic ortho ester *(8)* has not yet been detected.

Reaction of *(4b)* with alcohols at room temperature for several hours gives the ortho ester *(6)*. Small amounts of trityl bromide considerably accelerate the reaction; the ortho esters of complex alcohols such as cholesterol are thus formed in goods yields. The trityl bromide probably transforms *(4b)* into the far more reactive acetoxonium ion *(3)*.

The acyl ortho ester *(4b)* also appeared suitable for 1,2-*trans*-glucoside synthesis by analogy with the use of 1,2-ortho esters according to *Kochetkov*[2]. Preliminary experiments using various kinds of Lewis acids gave modest yields of the 1,2-*trans*-glucoside *(7c)* from cholesterol and *(4b)*; the reaction proceeds preferentially *via* the ortho ester *(6c)*.

The mode of reaction of the acyl ortho ester is essentially in accord with the proposals of *Winstein et al.*[6].

It is seen that, in glycoside syntheses in the presence of silver salts, numerous side products, and especially an appreciable amount of hydroxy sugars, are formed *via* acyl ortho esters *(4)*. Similar intermediates must also be expected in the presence of other metal salts, as demonstrated by the occurrence of 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose in the presence of $Hg(CN)_2$[9].

Procedure

Compound *(1)* (15 g, 36.5 mmol) was stirred with silver 4-(4-biphenylyl)butyrate in anhydrous tetrahydrofuran (under N_2) at room temperature for 7.5 h. After removal of silver salt on a reverse frit, the solution was evaporated to dryness *in vacuo* at room temperature and anhydrous diethyl ether (200 ml) was added. After a short time *(4b)* crystallized, and was collected on a reverse frit and dried at room temperature and 10^{-2} torr. Yield 13.9 g (67 %) of *(4b)*, shown to be homogeneous by analysis and spectroscopy.

Received: December 28, 1978 [Z 178 IE]
German version: Angew. Chem. *91*, 337 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(1), 572-09-8; *(4a)*, 69668-77-5; *(4b)*, 69653-25-4; *(5b)*, 69653-26-5; *(6c)*, 58769-34-9; *(7c)*, 6907-84-2; *(8)*, 69686-94-8; *(9)*, 6207-76-7; *(10)*, 4692-12-0; silver propionate, 5489-14-5; 4-(4-biphenylyl)butyric acid, 6057-60-9

[1] Studies on Glycoside Synthesis, Part 10. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 9: *G. Wulff, J. Wichelhaus*, Chem. Ber., in press.
[2] Review: *G. Wulff, G. Röhle*, Angew. Chem. *86*, 173 (1974); Angew. Chem. Int. Ed. Engl. *13*, 157 (1977).
[3] *H. E. Goldschmid, A. S. Perlin*, Can. J. Chem. *39*, 2025 (1961).
[4] *G. Wulff, W. Schmidt*, Carbohydr. Res. *53*, 33 (1977).
[5] *G. Wulff, W. Schmidt*, VI. Internat. Symposium on Carbohydrate Chemistry, Madison, USA, August 1972, Abstracts p. 57.
[6] *C. B. Anderson, E. C. Friedrich, S. Winstein*, Tetrahedron Lett. *1963*, 2037, and earlier papers.
[7] See also *S. Jacobson, B. Nielsen, C. Pederson*, Acta Chem. Scand. *B31*, 359 (1977).
[8] The ortho ester type products are shown in a twisted boat form [9] although the conformation has not been determined in our case.
[9] *B. Coxon, L. D. Hall*, Tetrahedron *20*, 1685 (1964).

Lactide Contraction—A Method for the Synthesis of α,α'-Dihydroxy Ketones from α-Hydroxy Carboxylic Acids

By *Ulrich Schöllkopf, Wolfgang Hartwig, Uwe Sprotte*, and *Werner Jung*[*]

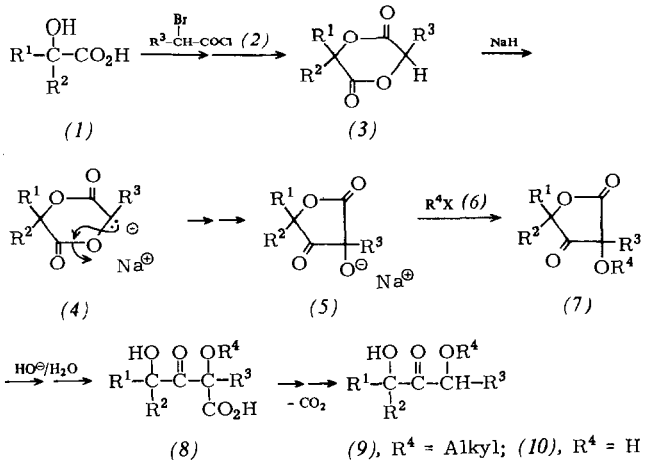
Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

α,α'-Dihydroxy ketones *(10)* and their derivatives *(9)* are of interest as versatile synthons and on account of their established or possible biological activity[1]. We now wish to report a method of synthesizing them from α-hydroxy carboxylic acids *(1)*. Compounds *(1)* react with a 2-bromoalkanoyl chloride *(2)* to give the lactides *(3)*, which afford the α-alkoxytetronic acids *(7)* on treatment with sodium hydride in the presence of an alkyl halide *(6)*. The sodium compounds *(4)* are intermediates; they form the sodium alkoxides *(5)* by lactide contraction. Since tetronic acids also exhibit biological activity[2], the α-alkoxytetronic acids *(7)* also warrant attention. Their basic hydrolysis, coupled with decarboxylation of the β-oxo acids *(8)*, yields the α-alkoxy-α'-hydroxy ketones *(9)*. Compounds *(9)*, $R^4 = C_2H_5OCH_2$ or CH_3OCH_2,

[*] Prof. Dr. U. Schöllkopf, Dr. W. Hartwig, Dipl.-Chem. U. Sprotte, Dr. W. Jung
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0310 $ 02.50/0

undergo acid-catalyzed hydrolysis to give the α,α'-dihydroxy ketones *(10)* (Table 1).



(1) *(3)* *(4)* *(5)* *(7)* *(8)* *(9)*, R^4 = Alkyl; *(10)*, R^4 = H

stable[3] ketones *(9)*) (6 mmol) in water/methanol (1:1 v/v; 10 ml) are stirred together for 4 h (in some cases for 2 h at 60 °C). Removal of methanol and extraction with ether are followed by drying over $MgSO_4$. The crude ketones *(9)* are purified by bulb-to-bulb distillation (b.p. 80 °C/0.05 torr).—IR: $\tilde{\nu}$ = 1710—1750 (C=O); 3400, 3500 cm^{-1} (OH).

α,α'-Dihydroxy ketones *(10)*: Compound *(9)*, $R^4 = C_2H_5OCH_2$ or CH_3OCH_2 (*ca.* 1 g) is dissolved in methanol (*ca.* 20 ml), 2 N HCl (*ca.* 20 ml) is added and the mixture stirred at 50 °C for 2 h (or at room temperature for *ca.* 20 h). After thorough extraction with ether and drying over $MgSO_4$, the solution is concentrated and the residual solvent removed at room temperature *in vacuo*. Compounds *(10)* are thermolabile and cannot be distilled.—^{1}H-NMR ($CDCl_3$): δ = 2.8 (OH); 4.8 (*CH*—CH_3, *CH*—C_2H_5).—IR: $\tilde{\nu}$ = 1700 (C=O), 3400 cm^{-1} (OH).

Received: January 9, 1979 [Z 172 IE]
German version: Angew. Chem. *91*, 329 (1979)

Table 1. Lactides *(3)*, α-alkoxytetronic acids *(7)*, and ketones *(9)* and *(10)* prepared.

R^1	R^2	R^3	*(3)* Yield [%]	M.p. [°C]	R^4X	Yield [%] *(7)*	*(9)*	*(10)*
H	CH_3	CH_3	60	126—127	CH_3I	73	48	
CH_3	C_2H_5	CH_3	67 [a]	78—80	CH_3I	63	57	
CH_3	CH_3	C_2H_5	62	61—62	CH_3I	75	61	
CH_3	CH_3	C_2H_5	62	61—62	$C_2H_5OCH_2Cl$	68	73	43
CH_3	C_2H_5	n-C_4H_9	61 [a]	(b.p. 97 °C/0.05 torr)	CH_3OCH_2Cl	71	72	66
CH_3	$CH_2C_6H_5$	CH_3	85 [a]	60—65	CH_3I	91	90	
CH_3	$CH_2C_6H_5$	CH_3			$C_6H_5CH_2Br$	76	90	
—$(CH_2)_4$—		CH_3	72	71—72	CH_3I	62	70	
—$(CH_2)_4$—		CH_3	72	71—72	$C_2H_5OCH_2Cl$	40	79	
—$(CH_2)_4$—		C_2H_5	70	92—93	CH_3OCH_2Cl	82	65	
—$(CH_2)_5$—		CH_3	75	76—77	$C_2H_5OCH_2Cl$	81	75	85
—$(CH_2)_5$—		C_2H_5	85	73—74	CH_3OCH_2Cl	82	82	80
—$(CH_2)_4$—CH(CH_3)—		CH_3	73 [a]	(b.p. 80 °C/0.05 torr)	CH_3OCH_2Cl	74	74	87
—$(CH_2)_6$—		CH_3	66	64—66	$C_2H_5OCH_2Cl$	42	72	80
—$(CH_2)_6$—		C_2H_5	80	≈70	CH_3OCH_2Cl	90	69	86

[a] The crude product is a mixture of diastereomers; m.p. may be that of only one diastereomer.

Procedure

Lactides *(3)*: A stirred equimolar mixture of (vacuum-dried) *(1)* and *(2)* is heated to 80 °C for 0.5—2 h (until evolution of HCl has ceased). The melt is allowed to cool and then dissolved in (P_4O_{10}-dried) acetone [150 ml for 0.2 mol of *(1)*], triethylamine (2 equiv.) is added portionwise, and the mixture stirred at 50—60 °C for 1 h. The solvent is removed in a rotary evaporator (4—6 torr), the residue extracted with aqueous $NaHCO_3$ and ether (or dichloromethane), the phases separated, and the aqueous phase extracted several times with ether (or dichloromethane). After drying over $MgSO_4$, work-up is as usual. The crude lactides *(3)* are purified by distillation or crystallization (from ether/light petroleum).—IR: $\tilde{\nu}$ = 1720—1740 cm^{-1} (C=O).

α-Alkoxytetronic acids *(7)*: A solution of *(3)* (20 mmol) and *(6)* (20 mmol) in dimethylformamide (DMF) (40 ml) is added dropwise over 5—10 min to a suspension of NaH (0.52 g, *ca.* 20 mmol) in DMF (40 ml, dried over 4-Å molecular sieve) and stirring is continued for 2—5 h. After removal of solvent at 4—6 torr (bath temp. 80—100 °C), the residue is dissolved in a small volume of ether and filtered over silica gel (20 g; ether as eluant). The tetronic acids *(7)* are purified by bulb-to-bulb distillation (b.p. ≈110 °C/0.05 torr).—IR (film): $\tilde{\nu}$ = 1740—1755 (C=O), 1770—1790 cm^{-1} (O—C=O).

α-Alkoxy-α'-hydroxy ketones *(9)*: Compound *(7)* (3 mmol) and a solution of Na_2CO_3 (NaOH or KOH with alkali-

[1] Cf. cortisone or cortisol.

[2] *C. T. Calam, A. R. Todd, W. S. Waring*, Biochem. J. *45*, 520 (1949); *A. W. Nineham, R. A. Raphael*, J. Chem. Soc. *1949*, 118; *W. N. Cannon, R. G. Jones*, J. Org. Chem. *23*, 126 (1958).

[3] Concerning the base-induced rearrangement of ketols, see *I. Elphimoff-Felkin, G. LeNy, B. Tchoubar*, Bull. Soc. Chim. Fr. *73*, 522 (1958).

Crown Ethers with Fluctuating Ring Size ("Breathing Crown Ethers")[**]

By *Gerhard Schröder* and *Walter Witt*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

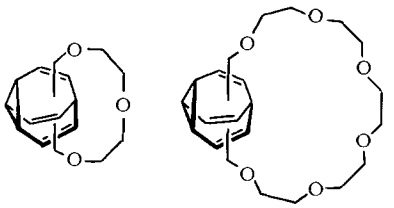
The ring size of a cyclic system is generally determined by the number of ring members. We present here the first two examples of a class of compounds in which a supply of energy (E_a < 20 kcal/mol) suffices to vary the ring size reversibly. The bullvalene principle conceived by *Doering*[1] led us to the idea of fluctuating or "breathing" rings and inspired us to synthesize the bullvaleno[11—13]crown-3 *(1)* and bullvaleno[20—22]crown-6 *(2)*[2]. *(1)* and *(2)* are disubstituted

[*] Prof. Dr. G. Schröder, Dipl.-Chem. W. Witt
Institut für Organische Chemie der Universität
Richard-Willstätter-Allee 2, D-7500 Karlsruhe 1 (Germany)

[**] This work was supported by BASF AG, Ludwigshafen

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0311 $ 02.50/0*

bullvalenes with two equal substituents. For such bullvalenes one can formulate twelve positional isomers, *i.e.* four each of the 1,2-, 1,3-, and 1,4-isomers[2, 3]. The ring size in the macrocyclic moiety of the "breathing" crown ethers *(1)* and *(2)* varies between the limiting values 11 and 13 and 20 and 22, respectively.



(1)

(2)



(3), R = Br
(4), R = CN
(5), R = CHO
(6), R = CH_2OH

The syntheses of *(1)* and *(2)* follow the conventional routes used for the preparation of crown ethers[4]. The key compound is bullvalenedimethanol *(6)*. Reaction of dibromobullvalene *(3)*[5] with sodium dicyanocuprate[6] in dimethylformamide in the molar ratio 1:2.4, followed by extraction with ether and chromatography on silica gel (ether/pentane 3:2) afforded the dinitrile *(4)*. Reduction of *(4)* with 2.2 equivalents of diisobutylaluminum hydride in toluene at 40°C led to formation of *(5)* in almost quantitative yield. Reduction of *(5)* with a suspension of 0.56 equivalents of $LiAlH_4$ in ether at −40°C, hydrolysis at −25°C and chromatography on silica gel (ether) generated bullvalenedimethanol *(6)*.

(6) is allowed to react with 1.0 equivalent of diethylene glycol ditosylate and 2.2 equivalents of NaH in dimethyl sulfoxide (DMSO) (4 days at 40°C). Extraction with dichloromethane and chromatography on silica gel (ethyl acetate) led to *(1)*. The crown ether *(2)* was obtained analogously by reaction of *(6)* with pentaethylene glycol ditosylate.

Table 1. Physical data of compounds *(1)*, *(2)*, *(4)*, *(5)*, and *(6)*.

(1): colorless crystals, m.p. 84°C (from ether/pentane); yield 9%; ^{1}H-NMR (160°C, [D$_6$]-DMSO): δ=4.18 (br. s, 8H, bullvalene-H), 3.91 (s, 4H, methylene-H), 3.60 (m, 8H, ethylene-H); ^{1}H-NMR (−40°C, CD_2Cl_2): δ=5.85 (narrow m, 4.3H, olef. H), 4.35—2.92 (m of many narrow bands of differing intensity, 12H, methylene- and ethylene-H), 2.78 (m, 0.9H, aliph. bullvalene-H), 2.19 (m, 2.8H, aliph. bullvalene-H); IR (KBr): 3030, 2940—2840, 1650 cm^{-1}; UV (methanol): λ=230 nm (ε=3800)

(2): colorless, highly viscous oil, b.p. 110°C/10^{-3} torr; yield 20%; ^{1}H-NMR (120°C, [D$_6$]-DMSO): δ=4.18 (br. s, 8H, bullvalene-H), 3.83 (s, 4H, methylene-H), 3.58 (s, 20H, ethylene-H); ^{1}H-NMR (−40°C, CD_2Cl_2): δ=5.85 (m, 4.5H, olef. H), 4.40—3.80 (m, 4H, methylene-H), 3.58 (m, 20H, ethylene-H), 2.65 (m, 0.8H, aliph. bullvalene-H), 2.20 (m, 2.7H, aliph. bullvalene-H); IR (film): 3020, 2860, 1630 cm^{-1}; UV (methanol): λ=230 nm (ε=3500)

(4): colorless needles, m.p. 134°C (from ether); yield 45%; ^{1}H-NMR (120°C, [D$_6$]-DMSO): δ=4.68 (br. s); ^{1}H-NMR (−30°C, CD_2Cl_2): δ=7.20—6.65 (m, 2H, olef. H), 6.35—5.70 (m, 2H, olef. H), 3.05—2.40 (m, 4H, aliph. H); IR (KBr): 2200, 1615 cm^{-1}; UV (methanol): λ_{max}=245 (ε=6300), 255 sh nm (5600)

(5): colorless crystals, m.p. 119°C (from toluene); ^{1}H-NMR (120°C, [D$_6$]-DMSO): δ=9.13 (s, 2H, aldehyde-H), 4.80 (br. s, 8H, bullvalene-H); ^{1}H-NMR (−30°C, CD_2Cl_2): δ=9.30 (s, 0.3H, aldehyde-H), 9.10 (s, 1.7H, aldehyde-H), 7.02—6.68 (m, 2H, olef. H), 6.15—5.55 (m, 2H, olef. H), 4.16 (split d, J=8 Hz, 0.6H, aliph. H), 3.50 (m, 0.6H, aliph. H), 2.95—2.50 (m, 2.8H, aliph. H); IR (KBr): 3010, 1670, 1625 cm^{-1}

(6): colorless oil, b.p. 100°C/10^{-3} torr; yield 92% based on *(4)*: ^{1}H-NMR (120°C, [D$_6$]-DMSO): δ=4.25 (s, 10H, bullvalene-H and OH), 3.78 (s, 4H, methylene-H); ^{1}H-NMR (−40°C, CD_2Cl_2): δ=5.83 (m, 4.5H, olef. H), 4.82 (br. s, 2H, OH), 4.25—3.56 (5 overlapping pseudo-s of differing intensity, 4H, methylene-H), 2.65—1.90 (m, 3.5H, aliph. bullvalene-H); IR (film): 3300, 3010, 2900, 2850, 1630 cm^{-1}; UV (methanol): λ=230 nm (ε=3200).

Like precursors *(3)* to *(6)*, the crown ethers *(1)* and *(2)* show temperature-dependent ^{1}H-NMR spectra (Table 1). Particularly strongly dependent upon temperature are the resonance signals of the bullvalene protons and, in the case of *(1)*, *(2)*, and *(6)*, also those of the protons of the methylene groups attached to the bullvalene system. In contrast to all other substituents the CH_2OH-, CH_2OCH_3-, and CH_2OAc-groups display no pronounced preference for definite positions at the bullvalene skeleton[7]. This finding, together with the ring size (which, according to model considerations, is sufficiently large for the macrocyclic moiety in *(1)* and *(2)*), and the temperature-dependence of the ^{1}H-NMR spectra are convincing enough reasons for us to describe *(1)* and *(2)* as "breathing" crown ethers[8].

A study of the temperature-dependent ^{1}H-NMR spectra of *(1)* and *(2)* in the presence of alkali-metal ions would be interesting. We presume that *(2)*, in particular, is capable of adapting itself to cations of various sizes.

Received: December 29, 1978 [Z 180a IE]
German version: Angew. Chem. *91*, 331 (1979)

[1] *W. von E. Doering, W. R. Roth*, Tetrahedron *19*, 715 (1963).
[2] First indications on the expected properties of macrocycles with annelated bullvalene groups, see *J. F. M. Oth, R. Merényi, H. Röttele, G. Schröder*, Chem. Ber. *100*, 3538 (1967).
[3] *G. Schröder, J. F. M. Oth*, Angew. Chem. *79*, 458 (1967); Angew. Chem. Int. Ed. Engl. *6*, 414 (1967).
[4] *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 2495 (1967); see *e.g. D. J. Cram, J. M. Cram*, Acc. Chem. Res. *11*, 8 (1978); *D. A. Laidler, J. F. Stoddart*, J. Chem. Soc. Chem. Commun. *1977*, 481; *W. Hain, R. Lehnert, H. Röttele, G. Schröder*, Tetrahedron Lett. *1978*, 625.
[5] *J. F. M. Oth, R. Merényi, G. Engel, G. Schröder*, Tetrahedron Lett. *1966*, 3377.
[6] *L. A. Paquette, G. H. Birnberg*, J. Org. Chem. *40*, 1709 (1975).
[7] *G. Schröder, H. Focke, J. F. M. Oth*, Tetrahedron Lett. *1975*, 2403. Our argument is as follows: the inductive effect of these three groups is virtually zero and therefore similar to the case of hydrogen.
[8] In this connection, the relatively rapid mixing process of the proton resonance signals of the bullvalenedicarboxylic anhydride should be mentioned. Because of the size of the anhydride ring the exchange process can only involve 1,2- and no 1,3- or 1,4-positional isomers; *E. Vogel, W. Grimme, W. Meckel, H. J. Riebel, J. F. M. Oth*, Angew. Chem. *78*, 599 (1966); Angew. Chem. Int. Ed. Engl. *5*, 590 (1966).

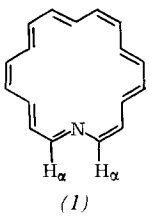
Aza[18]annulenes[**]

By *Walter Gilb* and *Gerhard Schröder*[*]

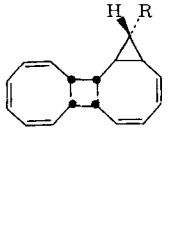
Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Higher membered *monocyclic* vinylogs of pyridine with $(4n+2)$ π-electrons were hitherto unknown. It may, however, be expected—as previously assumed[1]—that the range of validity of the Hückel rule in these compounds and in the carbocyclic annulenes is very similar.

Vogel et al.[2] and *Muchowski et al.*[3] recently described bridged aza[10]annulenes. We now report on the synthesis and properties of the aza[18]annulene *(1)*. The key step is the photolysis of the tetracyclic azide *(8)*.



(1)



(2), R = $COOC_2H_5$
(3), R = COOH
(4), R = CON_3
(5), R = N=C=O
(6), R = NH—C(=O)—NH_2
(7), R = N(NO)—C(=O)—NH_2
(8), R = N_3

[*] Prof. Dr. G. Schröder, Dipl.-Chem. W. Gilb
Institut für Organische Chemie der Universität
Richard-Willstätter-Allee 2, D-7500 Karlsruhe 1 (Germany)

[**] This work was supported by BASF AG, Ludwigshafen.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* 0570-0833/79/0404-0312 $ 02.50/0

Reaction of the 2:2 dimer of cyclooctatetraene with diazoacetic ester in the presence of copper powder furnishes four isomeric monoadducts, of which *(2)* is the major product[4]. The carboxylic acid *(3)*[4] is allowed to react firstly with triethylamine and ethyl chloroformate and then with aqueous sodium azide solution to give the acid azide *(4)* (95%). Its transformation into the azide *(8)* proceeds analogously to the synthesis of cyclopropyl azide from cyclopropanecarbonyl azide[5]. Heating of *(4)* in benzene for 2h leads to the isocyanate *(5)* (96%), which is converted *via* the urea derivative *(6)* (94%, ether solution and NH_3) into the *N*-nitrosourea *(7)* (not isolated; with N_2O_4 in ether). Reaction of *(7)* with lithium azide in methanol, followed by column chromatography (SiO_2, pentane/ether = 19:1) affords *(8)* as a colorless oil [25% based on *(6)*].

Irradiation of *(8)* at −80°C in pentane (5×10^{-4} M) with a mercury low-pressure lamp yields, after concentration of the pentane phase and column chromatography (SiO_2, pentane/ether = 19:1) of the liquid residue, dark-green crystalline aza[18]annulene *(1)* (28%) (see Table 1).

Table 1. Physical data of the compounds *(1)*, *(4)*, *(5)*, *(6)*, *(8)*, *(9)*⇌*(10)*.

(1): black-green needles, m. p. ≥200°C (dec., from pentane); ^{1}H-NMR (28°C, $CDCl_3$): $\delta = -1.84$ (m, 5 H_i), 8.86 (m, 10 H_o), 10.05 (d, $J = 5.2$ Hz, 2 H_o = 2 H_α); UV (dioxane): $\lambda_{max} \approx 276$ ($\varepsilon = 7400$), 329 (sh, 20200), 349 (sh, 43000), 374 (140000), 410 (sh, 11400), 467 (11400), 611 (720), 682 nm (580); IR ($CHCl_3$): 3005, 1310, 950 cm^{-1}

(4): m. p. 74°C (dec.); ^{1}H-NMR ($CDCl_3$): $\delta = 1.25$ (m, 1H), 2.20 (m, 3H), 3.40 (m, 3H), 5.20—6.30 (m, 10H); UV (dioxane): $\lambda = 227$ nm (sh, $\varepsilon = 1600$); IR ($CHCl_3$): 2140, 1690 cm^{-1}

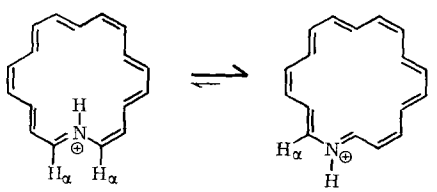
(5): yellowish oil, ^{1}H-NMR ($CDCl_3$): $\delta = 1.73$ (m, 2H), 2.28 (m, 1H), 3.38 (m, 4H), 5.12—6.16 (m, 10H); UV (dioxane): $\lambda = 260$ nm (sh, $\varepsilon = 3250$); IR (CCl_4): 2255 cm^{-1}

(6): m. p. 213°C (dec., from dioxane); ^{1}H-NMR ($CDCl_3$): $\delta = 1.78$ (m, 2H), 2.25 (d of a t, $J = 4.2$ and 1.0 Hz, 1H), 3.46 (m, 4H), 4.62 (br. s, 2H, NH_2), 4.77 (br. s, 1H, NH), 5.45—6.05 (m, 10H); UV (dioxane): $\lambda = 249$ nm (sh, $\varepsilon = 2100$); IR (KBr): 3480, 3180, 1674 cm^{-1}

(8): colorless oil, ^{1}H-NMR ($CDCl_3$): $\delta = 1.69$ (m, 2H), 2.56 (m, 2H), 3.42 (m, 3H), 5.13—6.40 (m, 10H); UV (methanol): $\lambda = 251$ nm (sh, $\varepsilon = 4000$); IR ($CHCl_3$): 2090 cm^{-1}

(9)⇌*(10)*: violet-black crystals, m.p. ≥180°C (dec.); ^{1}H-NMR ([D]$_7$-dimethylformamide, −50°C): $\delta = -4.24$ (m, 5 H_i), −3.60 (pseudo-t, $J = 12$ Hz, 0.8 H_i), −0.81 (br. s, 0.1—0.2 H, inner NH), 9.76—10.71 (m, 10 H_o), 10.90 (dd, $J = 12.6$ and 5.5 Hz, 0.8 H_o = 0.8 H_α), 11.49 (dd, $J = 13.5$ and 6.5 Hz, 0.4 H_o = 0.4 H_α), 19.0 (br. s, *ca.* 0.8 H, exterior NH)

The ^{1}H-NMR spectrum confirms the structure of *(1)*. The difference between the resonance signals for the 5 inner (H_i) and 12 outer protons (H_o) is *ca.* 11 ppm. Like [18]annulene[6] the molecule is strongly diatropic. The doublet of the two outer protons arises from the protons in the α-position to the nitrogen. The coupling constant proves the *cis* arrangement of H_α and H_β; the nitrogen thus occupies an internal position in the aza[18]annulene. The ^{1}H-NMR spectrum of *(1)* is practically temperature-independent. *(1)* thus behaves like 1,2-disubstituted [18]annulenes[7].



(9) *(10)*

Feeding dry hydrogen chloride into an etheral solution of *(1)* leads to precipitation of a black-violet crystalline hydrogen chloride derivative which is stable at room temperature in the absence of moisture (see Table 1).

The lower the temperature the more structured are the two broad singlets around $\delta = -0.81$ and 19.0 in the ^{1}H-NMR spectrum of the hydrogen chloride derivative. On irradiation at the frequency of these signals the double doublets at $\delta = 11.49$ and 10.90 each change to one doublet with $J = 6.5$ and 12.6 Hz, respectively. D_2O addition leads to the same result; in addition the two broad singlets disappear. The coupling constant $J = 6.5$ Hz corresponds to a *cis*-, that of $J = 12.6$ Hz to a *trans*-relationship between H_α and H_β. The ^{1}H-NMR spectrum thus provides proof of the structure of the aza[18]annulenium ions *(9)* and *(10)*, which presumably are present in equilibrium with each other (1:4 mixture). Addition of NH_3 at −50°C leads to deprotonation. A ^{1}H-NMR spectrum recorded immediately thereafter at this temperature revealed the presence of only *(1)*. Apparently the conjugate base of *(10)* rapidly isomerizes to the more stable *(1)*.

Received: December 29, 1978 [Z 180b IE]
German version: Angew. Chem. *91*, 332 (1979)

CAS Registry numbers:
(1), 69622-60-2; *(2)*, 42339-87-7; *(3)*, 42339-91-3; *(4)*, 69622-61-3; *(5)*, 69622-62-4; *(6)*, 69622-63-5; *(7)*, 69622-64-6; *(8)* (isomer A), 69622-65-7; *(8)* (isomer B), 69684-56-6; *(9)*, 69622-66-8

[1] *G. Schröder*, Pure Appl. Chem. *44*, 925 (1975).
[2] *M. Schäfer-Ridder, A. Wagner, M. Schwamborn, H. Schreiner, E. Devrout, E. Vogel*, Angew. Chem. *90*, 894 (1978); Angew. Chem. Int. Ed. Engl. *17*, 853 (1978).
[3] *H.-J. Gölz, J. M. Muchowski, M. L. Maddox*, Angew. Chem. *90*, 896 (1978); Angew. Chem. Int. Ed. Engl. *17*, 855 (1978); *Note added in proof*: see also *W. J. Lipa, H. T. Crawford, P. C. Radlick, G. K. Helmkamp*, J. Org. Chem. *43*, 3813 (1978).
[4] *P. Hildenbrand, G. Plinke, J. F. M. Oth, G. Schröder*, Chem. Ber. *111*, 107 (1978).
[5] *W. Kirmse, H. Schütte*, Chem. Ber. *101*, 1674 (1968).
[6] *R. Wolovsky, E. P. Woo, F. Sondheimer*, Tetrahedron *26*, 2133 (1970).
[7] *R. Neuberg, J. F. M. Oth, G. Schröder*, Justus Liebigs Ann. Chem. *1978*, 1368.

The Double Salt $Na_2S_2O_5 \cdot NaOOCH$ as Intermediate in the Formation of Sodium Dithionite by Reduction of SO_2 with Sodium Formate

By *Gert Ertl, Volker Kiener, Werner Ostertag*, and *Gerd Wunsch*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Sodium dithionite is of importance in vat dyeing and in bleaching. One method of industrial production consists in the reduction of sulfur dioxide by formate in aqueous methanol[1-3]:

$$NaOH + 2SO_2 + NaOOCH \rightarrow Na_2S_2O_4 + CO_2 + H_2O$$

Little has been reported on the mechanism of this reaction which proceeds in a three-phase system (solid, liquid, gaseous). *Yoshio et al.* assumed the intermediacy of $Na_2S_2O_5 \cdot HCOOH$ in the dithionite formation process[2]. We were unable to detect this compound, but found instead that the reaction proceeds *via* the isolable double salt $Na_2S_2O_5 \cdot NaOOCH$.

Our experiments were conducted in the following way: all the NaOH and half the amount of NaOOCH required

[*] Dr. G. Ertl, Dr. V. Kiener, Dr. W. Ostertag, Dr. G. Wunsch
Hauptlaboratorium der BASF AG
D-6700 Ludwigshafen (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0313 $ 02.50/0

were suspended in aqueous methanol and a solution of SO_2 in methanol was added simultaneously with the rest of the sodium formate solution. The solid phases present were isolated from different experiments at various reaction periods and the content of Na_2SO_3, $Na_2S_2O_3$, $Na_2S_2O_4$, $Na_2S_2O_5$ and NaOOCH was determined. Figure 1 shows the composition of the solid samples as a function of reaction time.

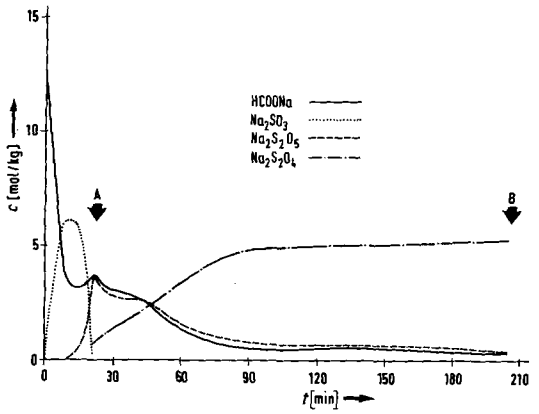


Fig. 1. Composition of solid material [mol/kg] as a function of the reaction time.

On progressive addition of SO_2, Na_2SO_3 is instantaneously formed and undergoes fast further reaction to give the disulfite at a rate depending on the decrease in pH:

$$2\,NaOH + SO_2 \rightarrow Na_2SO_3 + 2\,H_2O$$
$$Na_2SO_3 + SO_2 + H_2O \rightarrow 2\,NaHSO_3$$
$$2\,NaHSO_3 \rightarrow Na_2S_2O_5 + H_2O$$

The molar ratio of $Na_2S_2O_5$ to NaOOCH amounts to 1:1 within the limits of experimental accuracy once the reaction time exceeds 22.5 min (Fig. 1, sample A).

Our presumption that $Na_2S_2O_5$ might be present in the form of a double salt $Na_2S_2O_5 \cdot NaOOCH$ was confirmed by comparison of the X-ray diffraction diagrams[4] of the solid samples with that of the double salt obtained from an aqueous solution of $Na_2S_2O_5$ and NaOOCH (Table 1). An X-ray structure analysis[5] showed that the double salt forms monoclinic crystals with $a = 11.79_6$, $b = 5.47_6$, $c = 12.47_0$ Å, $\beta = 108.29°$.

Table 1. Characteristic d values of the double salt $Na_2S_2O_5 \cdot HCOONa$.

d [Å]	$I_{exp.}$	hkl
5.5865	5	200
4.7599	5	$11\bar{1}$
4.3182	8	111
3.5309	10	202
3.1783	4	$20\bar{4}$
2.8755	7	113
2.7987	10	$31\bar{3}$
2.0256	4	$22\bar{4}$
1.9463	3	420
1.6001	5	133

With the aid of the powder diagrams it was possible to trace the time dependence of the concentration of the double salt, with a maximum at 22.5 min (corresponding to sample A). As seen from Figure 1, dithionite formation only begins when significant amounts of the double salt are present; its concentration decreases at about the same rate as that of the dithionite increases. This also applies under the reaction conditions reported by *Yoshio et al.*[2]. The question whether dithionite formation takes place in the liquid phase or at the solid/liquid interface cannot be answered unequivocally. Evidence in favor of reaction at the interface is, however, provided by the following observations:

- The yield of dithionite decreases as the solubility of the intermediate compounds increases with increasing water concentration.
  Soluble dithionite is not stable under the above reaction conditions.
- Viewed under the microscope, the initially transparent crystals of the double salt become significantly cloudy with increasing conversion into the dithionite (Fig. 2a, b).
- Dithionite obtained from the "formate process" differs from that produced by the "zinc dust process" (crystallization from aqueous solutions) in its crystal habit (Fig. 2b, c) and is also shown by its X-ray diffraction pattern to exist in a different crystal modification.

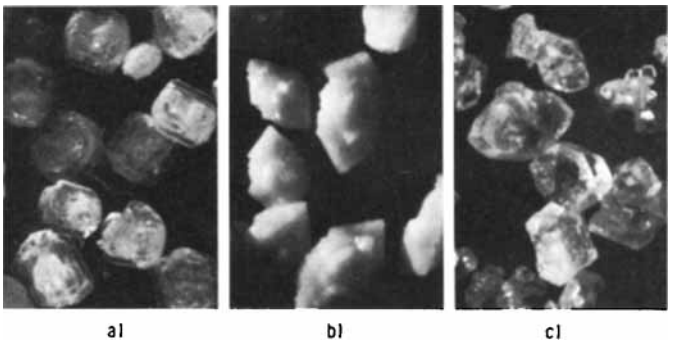


Fig. 2. Crystals of a) the double salt $Na_2S_2O_5 \cdot NaOOCH$ (solid sample obtained on stopping the reaction after 22.5 min, composition: $Na_2S_2O_5 \cdot NaOOCH$ 94.5 %, $Na_2S_2O_4$ 2.3 %, Na_2SO_3 3.0 %, $Na_2S_2O_3$ 0.2 %); b) sodium dithionite (formate process, corresponding to sample B, composition: $Na_2S_2O_5 \cdot NaOOCH$ 7.4 %, $Na_2S_2O_4$ 92.3 %, $Na_2S_2O_3$ 0.3 %); c) sodium dithionite (zinc dust process, from aqueous alkaline solution, precipitated with NaCl, composition: $Na_2S_2O_4$ 97.3 %, Na_2SO_3 1.9 %, $Na_2S_2O_3$ 0.4 %, NaCl 0.4 %).

Experimental

A solution of SO_2 (212 g) in methanol (636 g) and a solution of sodium formate (120 g) in water (106 g) are simultaneously added (50 % of each solution in 15 min and the rest within 7.5 min) to a suspension of sodium formate (120 g), NaOH(solid) (90 g), water (182 g), and methanol (402 g) in a 2-l glass flask fitted with a stirrer and two entry tubes; the temperature is kept at 67 °C during the addition. After cooling to 60 °C, the solid material is filtered off, washed with methanol, and dried. In this way, 211 g of a crystalline product is obtained which consists of $Na_2S_2O_5 \cdot NaOOCH$ (94.5 %), $Na_2S_2O_4$ (2.3 %), Na_2SO_3 (3.0 %), and $Na_2S_2O_3$ (0.2 %); the yield of $Na_2S_2O_5 \cdot NaOOCH$ is 46.7 % based on SO_2.

Received: January 30, 1979 [Z 189 IE]
German version: Angew. Chem. 91, 333 (1979)

[1] *S. Kapff*, DRP 175582 (Feb. 10, 1905); Kinzelberger & Co., Austrian Pat. 65225 (June 10, 1914); DRP 343791 (Nov. 10, 1921); *B. M. Vanderbilt, H. Adler*, US Pat. 2010615 (July 7, 1933); *M. N. Merlis* USSR Pat. 52052 (Oct. 31, 1937).
[2] *Y. Yoshio, O. Heizo, Y. Takaaki*, DAS 1592013 (Feb. 11, 1971).
[3] BASF AG, DOS 2442418 (March 18, 1976); US Pat. 4017593 (April 12, 1977).
[4] Philips ABD 10 automatic diffractometer (CuK_α radiation). We are grateful to Dr. *L. Marosi* for recording and evaluating the powder diagrams.
[5] *G. Ertl, E. Hädicke*, unpublished.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0314 $ 02.50/0*

α,β-Unsaturated Isocyanates by Thermolysis of *N*-(1-Alkenyl)-*N*-alkylcarbamoyl Chlorides

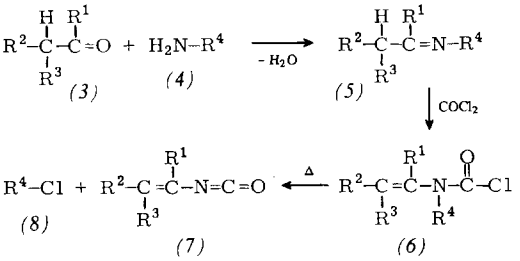
By *Karl-Heinz König, Christian Reitel, Dietrich Mangold, Karl-Heinz Feuerherd*, and *Heinz-Günter Oeser*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

α,β-Unsaturated isocyanates should behave similarly to enamines[1] and are of interest for the synthesis of active substances and polymers. A method for the thermal dehydrochlorination of chlorinated alkyl isocyanates but giving only chlorinated α,β-unsaturated isocyanates[2] can be exploited in a new industrially useful method affording entry to this class of compounds.—Isocyanates *(2)* are formed on pyrolysis of the disubstituted carbamoyl chlorides *(1)*. The tendency for an alkyl group (R^1) to be cleaved increases with increasing branching at C_α in R^1[3].

$$\underset{(1)}{RR^1N{-}COCl} \xrightarrow{\Delta} \underset{(2)}{R{-}N{=}C{=}O}$$

Phosgenation of Schiff bases *(5)* provides access to polysubstituted α,β-unsaturated carbamoyl chlorides of type *(6)*[4]. The *N*-(1-alkenyl)-*N*-*tert*-alkylcarbamoyl chlorides *(6)* formed on catalyzed thermolysis[3] open up a novel and safe route for the production of α,β-unsaturated isocyanates *(7)*[5] (see Table 1). The reaction (R^4 = *tert*-alkyl) can be directed in such a



way that almost exclusively alkyl chlorides *(8)* are formed as cleavage products, but no alkenes and hydrogen chloride. This ensures high yields of the α,β-unsaturated isocyanates *(7)*, which are very sensitive towards halogen hydrides.—Vinyl isocyanate *(7a)* has already been prepared on a pilot-plant scale.

Table 1. α,β-Unsaturated isocyanates *(7)* prepared by thermal fragmentation of *N*-(1-alkenyl)-*N*-*tert*-butylcarbamoyl chlorides *(6)* R^1 = H, R^4 = $C(CH_3)_3$.

Cpd. [a]	R^2	R^3	Yield [b] [%]	B.p. [°C/mbar]
a	H	H	96	38.5 [c]
b	H	CH_3	70	81 [d]
c	H	C_2H_5	80	109
d	H	$CH(CH_3)_2$	54	121
e	H	C_4H_9	53	66/40
f	H	C_6H_{13}	48	46/4
g	CH_3	CH_3	66	106 [e]
h	CH_3	C_2H_5	43	40/33
i	C_2H_5	C_2H_5	42	62/33
j	C_2H_5	C_4H_9	66	88/32
k	$-(CH_2)_5-$		74	76/20
l	H	$CH{=}CH_2$	58	34/14
m	H	$CH_2{-}C_6H_5$	78	52/0.14
n	CH_3	C_6H_5	59	125/29

[a] All the compounds gave correct elemental analyses and characteristic IR and NMR spectra. [b] Moderate yields attributable to losses during rectification of the mixture of *(7)* and *(8)*. [c] B.p. 39°C [7]. [d] B.p. 81°C [7]. [e] B.p. 40—41°C/140 mbar [8].

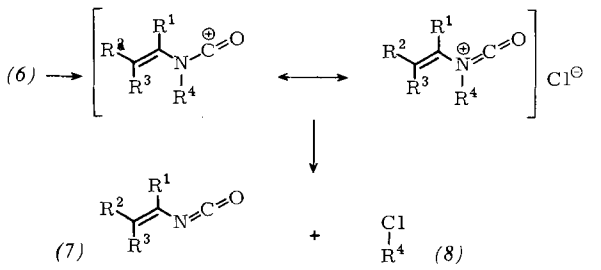
[*] Dr. K.-H. König [+], Dr. Ch. Reitel, Dr. D. Mangold, Dr. K.-H. Feuerherd, Dr. H.-G. Oeser
BASF AG, Hauptlaboratorium, WHW
D-6700 Ludwigshafen (Germany)

[+] Author to whom correspondence should be addressed.

In contrast to previous views[3], groups R^4 other than *tert*-alkyl are also readily cleaved. Thus, in the case of *(6)*, $R^1 = R^2 = R^3 = H$, R^4 = *sec*-butyl or cyclohexyl, and given sufficient activation of *(6)*, R^1 = H or CH_3, $R^2 = R^3 = H$, R^4 = benzyl, thermolysis leads to moderate or satisfactory yields of *(7)*.

The metal-salt-catalyzed thermolysis of the carbamoyl chlorides *(6)* can be carried out in the gas-phase on an industrial scale.

The observation (i) that isocyanates *(7)* are also accessible from *(6)*, R^4 = benzyl, and (ii) that our usual method of preparation from *(6)*, R^4 = *tert*-alkyl, gives almost exclusively the *tert*-alkyl chloride *(8)* besides *(7)*, would indicate the presence of a stabilized carbenium ion[6].



Procedure[5a, c]

Synthesis of *(5a)*: *tert*-Butylamine (12.8 kg, 175 mol) is added with stirring within 1.5 h at 10 to 15°C to a solution of acetaldehyde (9.8 kg, 223 mol) in *n*-pentane (technical) (70 l). After one hours' stirring and subsequent cooling to 0°C the aqueous phase is separated off and the pentane removed from the organic phase by distillation at a maximum internal temperature of 40°C. Yield of *(5a)* 16.5 kg (95 %).

Synthesis of *(6a)*: A solution of phosgene (25 kg, 252.5 mol) in CH_2Cl_2 (125 l) is treated at −5°C within 2 h with 16.5 kg (167 mol) of *(5a)* and 20.8 kg of *N*,*N*-dimethylcyclohexylamine. After 15 minutes' stirring at −5°C the excess of phosgene and CH_2Cl_2 is removed at +15°C. The phosgene is removed in a NaOH washing tower. The residue from the distillation is stirred with 165 l of *n*-pentane, the hydrochloride separated on a suction filter, and the combined filtrates distilled at 40°C (internal temperature) to remove the *n*-pentane. The crude *(6a)* is distilled at 2—4 mbar; yield 23.6 kg (88 %).

Synthesis of *(7a)*: *(6a)* (6 kg, 37.2 mol) is pumped within 4 h at 150°C/1—2 mbar through an evaporator into a reactor filled with a zinc salt fixed bed catalyst[5a,c] and decomposed at 120°C. The cleavage products are trapped by liquid nitrogen and separated by distillation; yield of *(7a)* 2.45 kg (96 %).

Received: January 29, 1978 [Z 182 IE]
German version: Angew. Chem. *91*, 334 (1979)

CAS Registry numbers:
(3a), 75-07-0; *(3b)*, 123-38-6; *(3c)*, 123-72-8; *(3d)*, 590-86-3; *(3e)*, 66-25-1; *(3f)*, 124-13-0; *(3g)*, 78-84-2; *(3h)*, 96-17-3; *(3i)*, 97-96-1; *(3j)*, 123-05-7; *(3k)*, 2043-61-0; *(3l)*, 7319-38-2; *(3m)*, 104-53-0; *(3n)*, 93-53-8; *(4)*, 75-64-9; *(5a)*, 7020-80-6; *(5b)*, 7020-81-7; *(5c)*, 6852-59-1; *(5d)*, 56175-48-5; *(5e)*, 56951-64-5; *(5f)*, 69668-20-8; *(5g)*, 6852-60-4; *(5h)*, 69668-21-9; *(5i)*, 69668-22-0; *(5j)*, 7003-27-2; *(5k)*, 53188-66-2; *(5l)*, 69668-23-1; *(5m)*, 69668-24-2; *(5n)*, 33215-91-7; *(6a)*, 28705-47-7; *(6b)*, 69668-25-3; *(6c)*, 69668-26-4; *(6d)*, 69668-27-5; *(6e)*, 69668-28-6; *(6f)*, 69668-29-7; *(6g)*, 28794-88-9; *(6h)*, 69668-30-0; *(6i)*, 69668-31-1; *(6j)*, 69668-32-2; *(6k)*, 69668-33-3; *(6l)*, 34887-43-9; *(6m)*, 69668-34-4; *(6n)*, 69668-35-5; *(7a)*, 3555-94-0; *(7b)*, 4737-18-2; *(7c)*, 40352-23-6; *(7d)*, 69668-36-6; *(7e)*, 69668-37-7;

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0319 $ 02.50/0*

(7f), 69668-38-8; *(7g)*, 28705-49-9; *(7h)*, 69668-39-9; *(7i)*, 69668-40-2; *(7j)*, 69668-41-3; *(7k)*, 69668-42-4; *(7l)*, 44610-34-6; *(7m)*, 69668-43-5; *(7n)*, 69668-44-6; *(8)*, 507-20-0

[1] *H. Böhme, H. G. Viehe* in *E. C. Taylor:* Advances in Organic Chemistry. Vol. 9, Part 1. Wiley-Interscience, New York 1976, p. 399.
[2] *K.-H. König, H. Pommer*, DAS 1232951 (1960).
[3] *J. N. Tilley, A. A. R. Sayigh*, J. Org. Chem. *28*, 2076 (1963).
[4] *H. Kiefer*, Synthesis *1972*, 39.
[5] a) *K.-H. König, H. Kiefer*, DAS 1922412 (1969); b) *H. Naarmann, H. R. Merkle*, DOS 2247724 (1972); c) *D. Mangold, H. Merkle, Ch. Reitel*, DOS 2461963 (1974).
[6] *Ch. Reitel, H. Kiefer, K.-H. König*, IUPAC Congress, Tokyo, Sept. 1977.
[7] *M. Sato*, J. Org. Chem. *26*, 770 (1961).
[8] *Y. Iwakura, J. Suzuki*, Nippon Kagaku Zasshi *77*, 64 (1956).

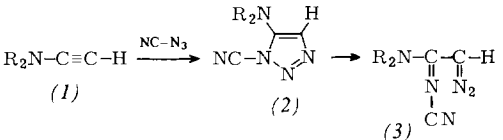
Iminocarbene/Ketenimine Rearrangement[**]

By *Bernhard Arnold* and *Manfred Regitz*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

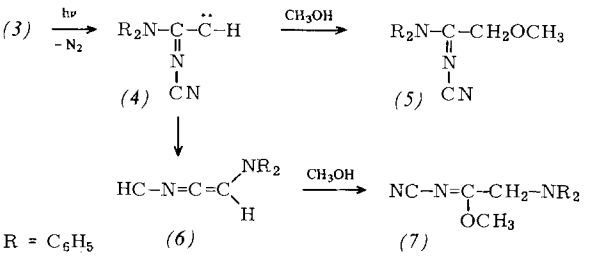
In contrast to α-oxocarbenes[1] little is known about α-iminocarbenes. They have so far only been generated by pyrolysis or photolysis of 1*H*-1,2,3-triazoles[2]. The synthesis of α-diazoamidines *(3)* by diazo group transfer to ynamines with electron-poor azides[3] opens an entry to carbenes of type *(4)*.

Reaction of the ynamine *(1)*[4] with cyanogen azide[5] in anhydrous acetonitrile afforded [most likely *via* the cycloadduct *(2)*] the α-diazoamidine *(3)* in 90% yield [m.p. 81°C; IR (KBr): 2180 (C≡N), 2100 (C=N_2), 1520 cm^{-1} (C=N); ^{1}H-NMR ($CDCl_3$): δ=5.0 (1H, CH)].



R = C_6H_5

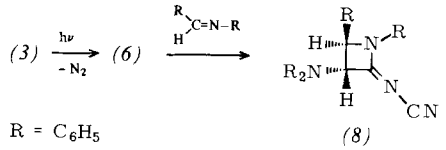
Irradiation of *(3)* in methanol (Duran-50 filter, Philips HPK-125W) and subsequent column chromatography furnished the amidine *(5)* [oil, IR (film): 2180 (C≡N), 1570 cm^{-1} (C=N); ^{1}H-NMR ($CDCl_3$): δ=3.32 (3H, OCH_3), 4.23 (2H, CH_2)][6] and the imidate *(7)* [m.p. 72°C; IR (KBr): 2210, 2180, (C≡N), 1600 cm^{-1} (C=N); ^{1}H-NMR ($CDCl_3$): δ=3.85 (3H, OCH_3), 4.82 (2H, CH_2)] in the ratio 1:3.



R = C_6H_5

The reaction branches at the carbene stage *(4)*, with the novel iminocarbene/ketenimine rearrangement *(4)*→*(6)* [which after addition of methanol to the heterocumulene leads to *(7)*] dominating over the insertion reaction *(4)*→*(5)*. Such extensive migration of a diphenylamino group has not yet been found in the related Wolff rearrangement[1].

Since neither aminoketenimines such as *(6)* nor cycloadducts of these heterocumulenes with azomethines were previously known, we have also trapped the photochemically generated *(6)* (in benzene) with benzylideneaniline; after chromatography on silica gel with chloroform the β-lactam imide *(8)* was obtained in 46% yield [m.p. 211°C; IR (KBr): 2180 (C≡N), 1650 cm^{-1} (C=N); ^{1}H-NMR ($CDCl_3$): δ=5.24, 5.45 (each d, $^3J_{H,H}$=2.0 Hz)].



R = C_6H_5 *(8)*

The magnitude of the H,H coupling constant is consistent with a *trans*-configuration of the hydrogen atoms; for *cis*-configuration a coupling constant of J=5—6 Hz would be expected[7]. The mass spectrometric fragmentation of *(8)* proceeds mainly in accord with the two conceivable [2+2]cycloreversions, reversion of the formation reaction predominating.

Received: January 8, 1979 [Z 183 IE]
German version: Angew. Chem. *91*, 337 (1979)

CAS Registry numbers:
(1), 4231-39-4; *(2)*, 69686-99-3; *(3)*, 69687-00-9; *(4)*, 69687-01-0; *(5)*, 69687-02-1; *(6)*, 69687-03-2; *(7)*, 69687-04-3; *(8)*, 69687-05-4; cyanogen azide, 764-05-6; benzylideneaniline, 538-51-2

[1] Review: *H. Meier, K.-P. Zeller*, Angew. Chem. *87*, 52 (1975); Angew. Chem. Int. Ed. Engl. *14*, 32 (1975).
[2] Review: *C. Wentrup*, Top. Curr. Chem. *62*, 173 (1976).
[3] *M. Regitz:* Diazoalkane. Thieme, Stuttgart 1977, pp. 216ff.
[4] *J. Ficini, C. Barbara*, Bull. Soc. Chim. Fr. *1965*, 2787.
[5] *F. D. Marsh*, J. Org. Chem. *37*, 2966 (1972).
[6] In the acid decomposition of *(3)* (perchloric acid/methanol), *(5)* is the sole product formed; rearrangements are usually suppressed under such conditions.
[7] See also the situation at the β-lactam ring: *K. D. Barrow, T. M. Spotswood*, Tetrahedron Lett. *1965*, 3325.
[8] Fragmentation of β-lactams: *M. J. Jackson, T. M. Spotswood, J. H. Bowie*, Org. Mass Spectrom, *1968*, 857.

[*] Prof. Dr. M. Regitz, Dipl.-Chem. B. Arnold
Fachbereich Chemie der Universität
Paul-Ehrlich-Strasse, D-6750 Kaiserslautern (Germany)

[**] Part 20 of the series, "Carbenes". This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 19: *H. Heydt, M. Regitz*, J. Chem. Res. (S) *1978*, 326; *ibid.* (M) *1978*, 4248.

Selective Deuteration of Enamines with Deuterated Formic Acids

By *Walter Himmele, Wolfgang Bremser*, and *Hardo Siegel*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

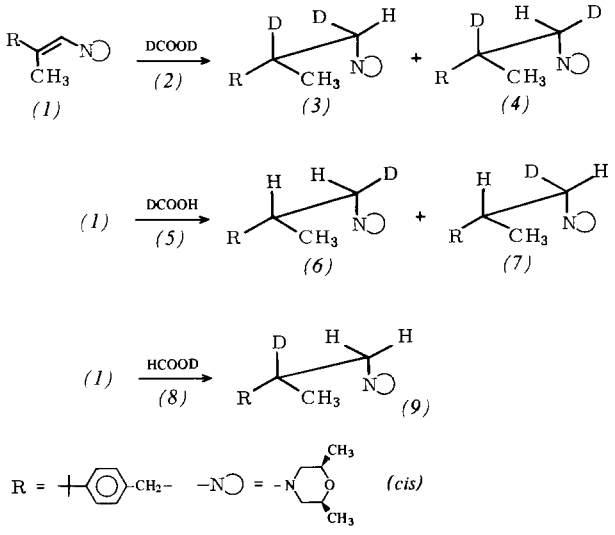
In some cases deuteration as well as ^{14}C-labeling can be used for monitoring and identifying the metabolites of active substances, provided it proceeds selectively and without H/D exchange. Such a deuteration can be achieved by the known reduction of enamines with formic acid[1] using deuterated formic acids [*(2)*, *(5)*, *(8)*].

Reaction of the enamine *(1)*[2] with stoichiometric amounts of variously deuterated formic acids at *ca.* 120°C in an inert solvent such as toluene leads to selective deuteration to *(3)* + *(4)*, *(6)* + *(7)*, and *(9)*, respectively, depending upon the formic acid employed.

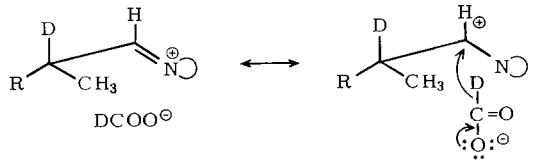
[*] Dr. W. Himmele, Dr. W. Bremser, Dr. H. Siegel
Hauptlaboratorium der BASF AG
D-6700 Ludwigshafen (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979*

0570-0833/79/0404-0320 $ 02.50/0



The deuteration pattern of the amines obtained indicates that the reaction proceeds, as previously suggested, *via* an immonium formate, which is then reduced by deuteride transfer to the amine.



Procedure

A solution of 3-(*p-tert*-butylphenyl)-2-methylpropanol (10.2 g, 0.05 mol) in toluene (70 ml) is treated with *cis*-2,6-dimethylmorpholine (6 g). After azeotropic removal of the water with toluene (which distills over until an internal flask temperature of *ca.* 120 °C is reached), 2.5 g of *(2)* in 5 ml toluene is slowly added and the mixture of amines *(3)* and *(4)* finally distilled at 142–145 °C/0.3 torr. In the case of *(6)* and *(7)* the $\{^1H\}$-noise-decoupled ^{13}C-NMR spectra show a triplet at $\delta = 64.77$, and in the case of *(9)* a triplet at $\delta = 31.82$; in all cases by coupling with the deuterium nucleus. *(3)* and *(4)* each show two triplets at $\delta = 64.53$ and 31.71. The ^1H-NMR spectra of *(6)* and *(7)* with signals at 7.3 (2, d), 7.1 (2, d), 3.7 (2, t), 2.8 (1, m), 2.7 (1, m), 2.35 (1, m), 2.2 (1, m), 2.15 (1, m), 2.0 (1, m), 1.7 (2, m), 1.3 (9, s), 1.15 (6, d) and 0.85 (3, d) confirm this assignment by the changing signal splitting; *(3)* and *(4)* as well as *(6)* and *(7)* are present as 40:60 mixtures.

Received: January 31, 1979 [Z 184 IE]
German version: Angew. Chem. *91*, 341 (1979)

CAS Registry numbers:
(1), 69668-13-9; *(2)*, 920-42-3; *(3)*, 69668-14-0; *(4)*, 69743-83-5; *(5)*, 917-71-5; *(6)*, 69668-15-1; *(7)*, 69743-84-6; *(8)*, 925-94-0; *(9)*, 69668-16-2; 3-(*p-tert*-butylphenyl)-2-methylpropanal, 80-54-6; *cis*-2,6-dimethylmorpholine, 6485-55-8

[1] *P. de Benneville, J. Macartney*, J. Am. Chem. Soc. *72*, 3073 (1950).
[2] ^{13}C-NMR (Bruker WH-270, $CDCl_3$, TMS int.): $\delta = 148.19$ (1, s), 137.77 (1, s), 128.90 (2, d), 124.80 (2, d), 71.53 (2, d), 64.99 (1, t), 60.09 (1, t), 59.98 (1, t), 40.75 (1, t), 34.20 (1, s), 32.04 (1, d), 31.47 (3, q), 19.12 (2, q), 18.04 (1, q).
[3] *N. J. Leonard, R. R. Sauers*, J. Am. Chem. Soc. *79*, 6210 (1957); *J. J. Panouse et al.*, Bull. Soc. Chim. Fr. *1963*, 1753.

Effects of Long-Chain Branches on the Degradation Kinetics of Polymers

By *Klaus H. Ebert, Hanns J. Ederer*, and *Arno Max Basedow*[*]

Dedicated to Professor Horst Pommer on the occasion of his 50th birthday

Experimental investigations on the kinetics of the hydrolytic degradation of dextran in solution[1] showed that small molecules are formed more frequently than should be the case in a random reaction. On assuming, firstly that the dextran molecules are unbranched, and secondly that the "individual" degradation constants ($K_{s,l}$) along the polymer chain vary according to a parabolic function, we could establish the curvature of this parabola as $b = 0.4$ from experimentally determined molecular-weight distributions *via* the combined polydispersity ratio $CPR = \bar{M}_w^2/(\bar{M}_n \cdot M_z)$ by mathematical simulation. This means that the polymer bonds at the ends of the molecule are about three times more reactive than in the center of the molecule. *Freudenberg, Kuhn, et al.*[2] likewise deduced a non-random degradation from the acid hydrolysis of cellulose and starch.

The assumption that the dextrans are unbranched is especially critical, since the experimentally determined molecular-weight distributions of the degradation products can in principle also be explained by long-chain branching and random degradation (see [1]).

Relatively little is known about branching in dextran[3,4]. Dextran obtained enzymatically from *Leuconostoc Mesenteroides* B 512 F has, at most, branching on 5% of its repeating units[5]. Of these at most 15% are longer than two glucose units[6], so that the proportion of branching points with side-chains longer than ten monomer units can be assumed to be about 0.1%, *i.e.* for every 1000 structural moieties there is one long-chain branch. Short-chain branches (side-chain lengths < five monomer units) do not influence the molecular weight distribution of the degradation products.

We have investigated the influence of long-chain branching on the product distribution in a random degradation reaction by mathematical simulations of various branched model molecules, which were generated by a Monte Carlo method. The results are expressed in terms of the dependence of $K_{s,l}$ on l. Here $K_{s,l}$ is the rate constant for the cleavage of a molecule having a degree of polymerization s into two fragments with degrees of polymerization l and s-l. For unbranched molecules, $K_{s,l}$ is a measure of the probability of cleavage at site l. These diagrams are identical with the molecular weight distributions obtained, assuming every molecule has undergone a simple chain rupture.

Our model calculations are based on molecules having a degree of polymerization of 1000 (Table 1). Model 1 is for singly branched molecules in which the length and position of the side-chain are randomly distributed. In models 2 and 3 the number of long-chain branches is increased respectively to three and seven, while the lengths and positions of the side chains are again randomly distributed; however, only one side chain can branch at each position of the main chain. Figure 1a shows that the curvature of the curves increases with increasing number of branches. The effect is very pronounced even with one side chain; the curve is almost parabolic with $b = 0.8$. The unbranched molecule gives a straight line parallel to the abscissa at 1.

[*] Prof. Dr. K. H. Ebert, Dr. H. J. Ederer, Dr. A. M. Basedow
Institut für Angewandte Physikalische Chemie und SFB 123 der Universität
Im Neuenheimer Feld 253, D-6900 Heidelberg 1 (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0321 $ 02.50/0*

Table 1. Parameters of model molecules. s = degree of polymerization = 1000, h = length of the main chain, v_i = length of the side chain ($i = 1 \ldots z$), z = number of side chains, p_i = position of the branch i on the main chain, rnd. $(x \ldots y)$ = random choice within interval $(x \ldots y)$, RE = residue of s not used in the selection process.

Model	1	2	3	4	5	6	7
h	rnd. $\{1 \ldots s-1\}$	rnd. $\{3 \ldots s-3\}$	rnd. $\{8 \ldots s-8\}$	$s/2 = 500$	10	10	10
v_i	$v_1 = s-h$	v_1 = rnd. $\{1 \ldots s-1\}$	v_1 = rnd. $\{1 \ldots s-h\}$	v_i = rnd. $\{30 \ldots 80\}$ RE rnd. distributed over v_i	v_i = rnd. $\{20 \ldots 220\}$ RE corr. like 4	v_1 = rnd. $\{1 \ldots {}^2/_3(s-h)\}$	v_1 = rnd. $\{1 \ldots s-h\}$
		v_2 = rnd. $\{1 \ldots \mathrm{RE}-1\}$	v_i = rnd. $\{1 \ldots \mathrm{RE}-(z-i)\}$ for $1 < i < 7$			v_{2-8} = rnd. $\{1 \ldots \mathrm{RE}_i\}$	v_{2-8} = rnd. $\{1 \ldots {}^2/_3 \mathrm{RE}_i\}$
		$v_3 = \mathrm{RE}$	$v_7 = \mathrm{RE}$			$v_9 = \mathrm{RE}$	$v_9 = \mathrm{RE}$
z	1	3	7	9	9	9	9
p_i	rnd. $\{1 \ldots h-1\}$	rnd. $\{1 \ldots h-1\}$ each p_i selectable only once	rnd. like 2	rnd. like 2	i	i	i
Fig.	1a	1a	1a	1b	1b	1c	1c

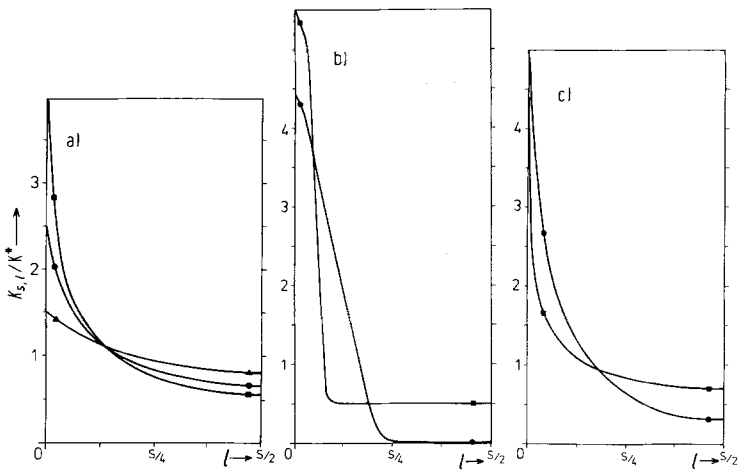


Fig. 1. Dependence of the rate constants $K_{s,l}$ on the degree of polymerization l of the fragment (K^* = experimental degradation constant). The curves are symmetric about $s/2$. a) ▲ model 1, ● model 2, ■ model 3; b) ■ model 4, ● model 5; c) ● model 6, ■ model 7.

Model 4 contains nine long-chain branches and the main chain is as long as the sum of the side chains; these were varied randomly between 30 and 80 monomer units. The branching points on the main chain were likewise randomly chosen. In model 5 the main chain was shortened to ten monomer units and the lengths of the side chains distributed randomly between 20 and 220. Model 4 can be regarded as a "comb", model 5 as a "star". Figure 1b shows that shorter side chains lead to higher $K_{s,l}$-values at small l-values; in the case of larger l-values (up to $s/2$) longer side chains and the main chain are decisive. The models 6 and 7 are "stars" with a greater distribution in the length of the side chains. Model 6 permits a random choice of $^2/_3$ of the residual monomer units available in the generating process, in the case of model 7 the lengths of the side chains are chosen randomly (Fig. 1c) from the total number of the residual monomer units (Table 1). Model 6 contains more side chains with average degrees of polymerization; hence the curve falls more slowly at low l-values. In the random model 7 the number of large fragments is greater; hence the larger values near to the center of the molecule $s/2$.

Our models cover all polymer molecules without compound branches as well as all molecules in which double branching is peripheral. More strongly branched or crosslinked molecules require more complicated models.

Our simultaneous show that long-chain branches have considerable influence on the distribution of the molecular weights of the products in degradation reactions. From the shape of the distributions, quantitative information can be gained about the number of branches and lengths of the side chains, and sometimes also about the main chain. Thus, *e.g.*, from our experiments on dextran it can be concluded, assuming random probability of cleavage, that the number of long-chain branches lies below 0.2%.—For a more accurate analysis of the long chain branching, the shape of the $K_{s,l}$ curve should be determined from the experimental molecular weight distributions, and not only from molecular weight averages and the CPR.

Received: February 5, 1979 [Z 185 IE]
German version: Angew. Chem. *91*, 341 (1979)

[1] *A. M. Basedow, K. H. Ebert, H. J. Ederer*, Macromolecules *11*, 774 (1978).
[2] *K. Freudenberg, W. Kuhn, W. Dürr, F. Bolz, G. Steinbrunn*, Ber. Dtsch. Chem. Ges. *63*, 1510 (1930).
[3] *K. H. Ebert, M. Brosche*, Biopolymers *5*, 423 (1967).
[4] *K. H. Ebert, G. Schenk*, Adv. Enzymol. *30*, 179 (1968).
[5] *K. Frömbling, F. Patat*, Makromol. Chem. *25*, 41 (1957).
[6] *O. Larm, B. Lindberg, S. Svensson*, Carbohydr. Res. *20*, 39 (1971).

trans-Bis(1-alkynyl)-4B-metal Phthalocyanines[**]

By *Michael Hanack, Konrad Mitulla, Georg Pawlowski*, and *L. R. Subramanian*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Monomeric phthalocyanine derivatives of type *(3)* of elements of the 4th main group having two axial metal-carbon bonds are model substances for new polymer structures, which according to EHMO calculations ought to show pronounced electrical conductivity[1].

Octahedral silicon phthalocyanines having one axial Si—C bond have already been reported[2]; and the tin phthalocyanine *(3)*, R = C_6H_5, has been synthesized, but only in 1% yield[3]. Analogous *meso*-tetraphenylporphyrins were recently described[4].

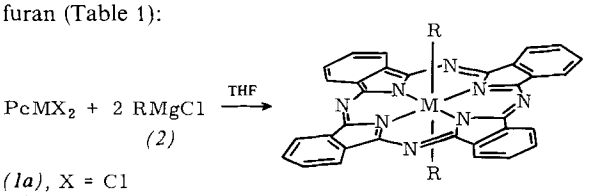
We obtained *trans*-bis(1-alkynyl)-4B-metal phthalocyanines *(3)* in yields of about 90% by reaction of the corresponding

[*] Prof. Dr. M. Hanack, Dipl.-Chem. K. Mitulla, Dipl.-Chem. G. Pawlowski, Dr. L. R. Subramanian
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

[**] Part 3 of The Synthesis and Properties of Novel One-Dimensional Conductors.—Parts 1 and 2: [1].

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0322 $ 02.50/0

dichlorides *(1a)*[5] with Grignard reagents *(2)* in tetrahydrofuran (Table 1):



(3)

Table 1. Selection of new phthalocyanines *(3)* from *(1a)* and *(2)*; reaction conditions and physical properties.

M	*(3)* R	T [°C]	t [h]	Yield [%]	IR [cm^{-1}] $\nu C{\equiv}C$ ($\nu{\equiv}C{-}H$)	^{1}H-NMR δ	*m/e* [a]
Si	C≡CPh	[b]	15	83	2148		742
	C≡CMe	[b]	15	90	2164		618
	C≡CH	[b]	15	90	2017 (3262)		590
	C≡C*t*Bu	[b]	15	90	2132, 2140	9.6 (m, arom.) 8.3 (m, arom.) −0.82 (s, CH_3)	702
Ge	C≡CPh	[b]	15	89	2145		788
	C≡CH	[b]	15	90	2013 (3273)		636
	C≡C*t*Bu	[b]	15	92	2128, 2137	9.62 (m, arom.) 8.36 (m, arom.) −0.77, −0.67 (d, CH_3)	748
Sn	C≡CPh	20	72	90 [c]	2120		834
	C≡CMe	20	72	90 [c]	2125		710

[a] M^+ with ^{28}Si, ^{74}Ge, ^{120}Sn. [b] THF, reflux. [c] Not analytically pure.

The products *(3)* were purified by extraction with acetone or methanol; their solubility in organic solvents is dependent upon the substituents R; *e.g.* the bis(3,3-dimethyl-1-butynyl) compounds *(3)*, M = Si, Ge, are readily soluble in tetrahydrofuran, acetone, or trichloromethane.

In contrast to the silicon- and germanium phthalocyanines *(3)*, the homologous tin compounds are difficult to isolate in pure form since they readily undergo reduction with formation of PcSn. Attempts to recrystallize the 4B-phthalocyanines from high-boiling solvents led to cleavage of the metal-carbon bonds[3]. Hydrolysis with THF/HCl/H_2O and with NaOH/H_2O respectively gave the chlorides *(1a)* and the corresponding dihydroxides *(1b)*[5], thus confirming the structure *(3)*.

Reaction of *(1a)* with organolithium compounds in diethyl ether likewise affords *(3)*, but the products are highly contaminated owing to uncontrollable side reactions.

General Procedure

(1a) (1 mmol) is added with stirring under nitrogen to a solution of *(2)* (6 mmol) in 50 ml of THF. On completion of reaction (cf. Table 1) the mixture is hydrolyzed with 10 ml of 5% hydrochloric acid, filtered, and the residue washed with water and dried. Insoluble products *(3)* were purified by extraction with methanol and then dried at 100 °C. Soluble products were isolated by fractional extraction with THF and concentration of the deep-blue solution with exclusion of light.

Received: February 1, 1979 [Z 186 IE]
German version: Angew. Chem. *91*, 343 (1979)

[1] a) *M. Hanack, F. F. Seelig, J. Strähle*, Z. Naturforsch. *B*, in press; b) *F. F. Seelig, ibid.*, in press.

[2] *J. N. Esposito, J. E. Lloyd, M. E. Kenney*, Inorg. Chem. *5*, 1979 (1966); *J. N. Esposito*, Ph. D. Thesis, Case Inst. Tech., Cleveland, Ohio 1966.

[3] *D. Bonderman, E. D. Cater, W. E. Bennett*, J. Chem. Eng. Data *15*, 396 (1970); cf. also *S. L. Douglas*, Ph. D. Thesis, Case Inst. Tech., Cleveland, Ohio 1975.

[4] *C. Cloutour, D. Lafargue, J. A. Richards, J. C. Pommier*, J. Organomet. Chem. *137*, 157 (1977); *C. Cloutour, D. Lafargue, J. C. Pommier, ibid. 161*, 327 (1978).

[5] *M. K. Lowery, A. J. Starshak, J. N. Esposito, P. C. Krueger, M. E. Kenney*, Inorg. Chem. *4*, 128 (1965); *W. J. Kroenke, M. E. Kenney, ibid. 3*, 251 (1964); *R. D. Joyner, M. E. Kenney*, J. Am. Chem. Soc. *82*, 5790 (1960); *M. Hartmann, G. Meyer, D. Wöhrle*, Makromol. Chem. *176*, 831 (1975).

Characterization of Short-Lived Photoproducts by Pulse Raman Spectroscopy[**]

By *Walter Hub, Siegfried Schneider*, and *Friedrich Dörr*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

On the basis of a series of selected chemical reactions and from the similarity of the transient spectra observed in the visible spectral region on irradiating 2,3,4,4-tetrachloro-1-oxo-1,4-dihydronaphthalene ("β-TKN") *(1)* in the crystalline state or in solid solution, *Scheibe* and *Feichtmayr* concluded[1] that the phototropy first observed on this compound by *Marckwald* as long ago as 1899 cannot be explained in terms of physical interaction (crystal structure) but is due instead to photodissociation of *(1)*. The naphthoxyl radical *(2)* formed in this photodissociation disappears by recombination with a chlorine radical, by dimerization, or even by addition of an H atom abstracted from the solvent.

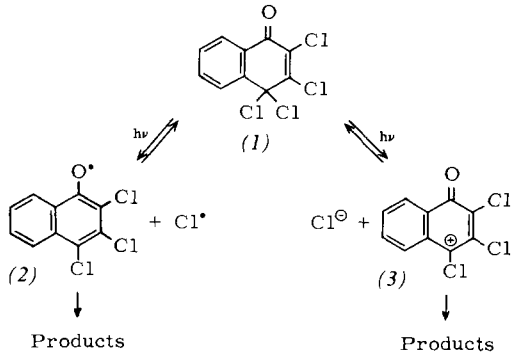
In contrast, *Zweegers*[2] reports to have been able to demonstrate that the cation *(3)* is formed as principal photoproduct by heterolytic cleavage of *(1)* on irradiation with light of wavelength $\lambda = 353$ nm in CCl_4 as solvent.

One of the difficulties in clarifying this problem is that according to quantum mechanical model calculations both products *(2)* and *(3)* show two bands of similar oscillator strength in the same spectral region. As in many cases this

[*] Prof. Dr. F. Dörr, Dipl.-Chem. W. Hub, Univ.-Doz. Dr. S. Schneider
Institut für Physikalische und Theoretische Chemie der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. We thank *M. Sell, A. Geiger*, and Dr. *J. R. Taylor* for their assistance in developing the electrical components.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0323 $ 02.50/0*



means that the transient electronic spectrum obtained in a flash-photolysis experiment provides no decisive information. More characteristic differences are to be expected in the vibrational spectra, even in the case of similar compounds.

The aim of our present studies was to record the first highly time-resolved Raman spectra of transient photoproducts in order to determine their structure. For this purpose the light pulse of a N_2-laser (Lambda Physik M2000) is focused into the reaction cell. A dye laser (Zeiss 807103, 19000—21000 cm^{-1}) is triggered after a delay time of Δt ($\geq 0.2\,\mu s$); its beam follows the trace of the N_2 photolysis laser. The Raman light generated by the photoproduct is spectrally analyzed in a double grating spectrograph (Coderg UF 76). After amplification by an image converter (EMI 9912), which is externally gated during the "photoflash"[3], the spectrum is recorded with an optical multichannel analyzer (PAR 1205). The spectra can be immediately displayed or fed to a computer for further processing (*e.g.* for difference spectra).

The Raman spectrum of the transient from *(1)* in CCl_4 (300 K) was detected in the time interval 0.2 μs (apparatus limit) to 100 ms. Figure 1a shows the spectrum one obtains if the dye laser is triggered 4.5 μs after the N_2 photolysis laser; it contains contributions from the photoproduct, from unchanged starting material, and from the solvent. Figure 1b shows the spectrum recorded after spectrum 1a without photolysis laser; it corresponds with that of *(1)*, except for the broad CCl_4 solvent band at 1539 cm^{-1}. Finally, Figure 1c shows the difference spectrum, *i.e.* the Raman spectrum of the photochemically generated transient in the form in which it exists 4.5 μs after the photoflash.

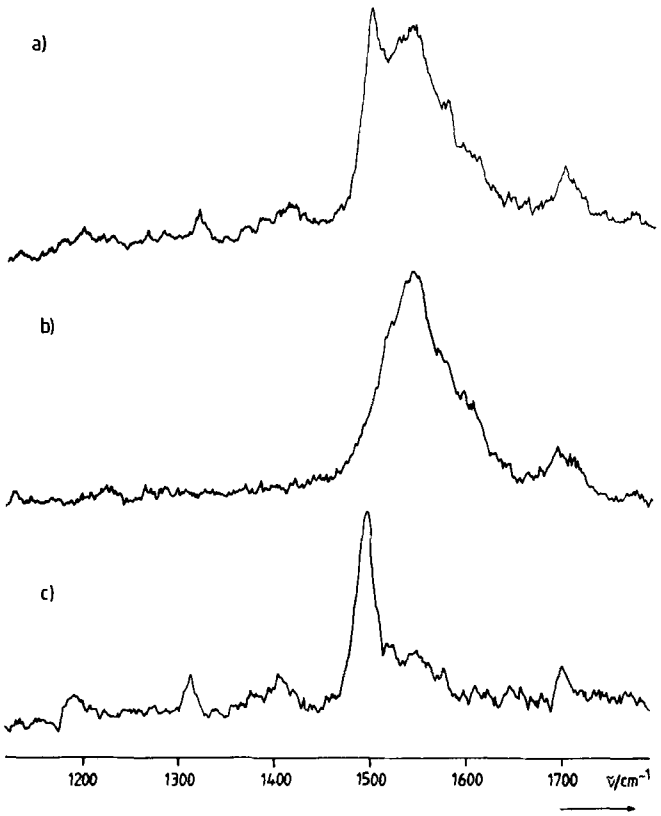


Fig. 1. Raman spectra of a 10^{-2} M solution of *(1)* in CCl_4: a) probe laser delay 4.5 μs ($\tilde{\nu}_L = 20576\ cm^{-1}$); b) without photolysis laser; c) difference spectrum.

In the spectrum of *(1)* in CCl_4, we assign the band at 1680 cm^{-1} to the C=O stretching vibration, and that at 1570 cm^{-1} to the non-aromatic C=C stretching vibration; the bands at 1600, 1296, 1260, and 1170 cm^{-1} are characteristic for the benzoyl moiety. The difference IR spectrum of *(1)* in an irradiated and an unirradiated KBr disc[4] reveals new bands at 1638 cm^{-1} [ν(C=O)] and at 1610, 1520, 1490, 1380, and 1284 cm^{-1} (decay time ≈2 h at 300 K). We assign these bands to the radical *(2)*, since according to model calculations its bond orders are similar to those of an unsubstituted naphthalene. In particular, the decrease in the frequency of the (C=O) stretching vibration is consistent with the smaller π-bond order of this bond in the radical. In contrast, the Raman spectrum of the photoproduct in CCl_4 (Fig. 1c) shows no substantial bands at frequencies appearing in KBr and assigned to the radical. The strongest line appears at 1495 cm^{-1}, others at 1190, 1320, 1400, 1575, and 1700 cm^{-1}. We thus conclude that two different photoproducts predominate in KBr and CCl_4, respectively. An increased C=O frequency (1700 cm^{-1}) compared to that observed for *(1)* would be in agreement with *Zweegers*'[2] assignment as cation *(3)*, since the model calculation yields a higher π-bond order. As yet, we cannot explain the high intensity of the line at 1495 cm^{-1}; whether a resonance effect is responsible is presently under investigation.

Received: February 9, 1979 [Z 187 IE]
German version: Angew. Chem. *91*, 348 (1979)

CAS Registry numbers:
(1), 17735-13-6; *(2)*, 23390-09-2; *(3)*, 69707-05-7

[1] *F. Feichtmayr, G. Scheibe*, Z. Naturforsch. *B13*, 51 (1958); *G. Scheibe*, Chem. Ing. Tech. *31*, 321 (1959); *G. Scheibe, F. Feichtmayr*, J. Phys. Chem. *66*, 2449 (1962).
[2] *F. P. A. Zweegers*, Dissertation, Universität Leiden 1978.
[3] *F. Dörr, W. Hub, S. Schneider, J. R. Taylor*, EMI Appl. Note: Application of a negative H. V.-square wave generator for gating image intensifier tubes.
[4] *W. Hub*, Dissertation, Technische Universität München 1979.

Homogeneously Catalyzed Dimerization of Isoprene to 2,7-Dimethyl-2,*trans*-4,6-octatriene at Chromium[**]

By *Heindirk tom Dieck* and *Alois Kinzel*[*]

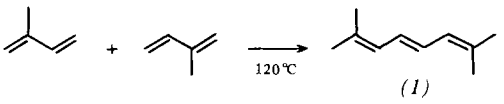
Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

In our studies on homogeneously catalyzed oligomerizations of dienes on dad-modified metal catalysts (dad = 1,4-*diaza*-1,3-*diene*) we found that a chromium-dad system is able to transform isoprene in a highly specific manner into 2,7-dimethyl-2,*trans*-4,6-octatriene *(1)*. The reaction involves *tail-to-tail linkage with a double hydrogen shift.*

[*] Prof. Dr. H. tom Dieck, Dipl.-Chem. A. Kinzel
Institut für Anorganische und Angewandte Chemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

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

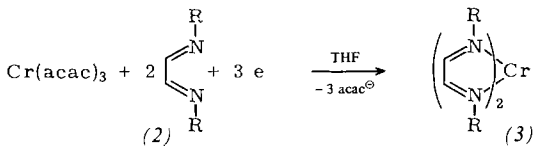
© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0324* $ 02.50/0



(1)

Open-chain dimers of isoprene are formed by numerous catalyst systems. The head-to-tail dimer 2,6-dimethyl-1,3,6-octatriene (5) is then formed—often only in poor yield. Only palladium[1] is found to give not only polymers but also 2,7-dimethyl-1,3,7-octatriene, which undergoes base-catalyzed rearrangement to (1) in modest yield.

The catalytic direct synthesis of (1) preferably starts with generation of the chromium(0) complex (3) from chromium(III) compounds and the dad-ligand *N,N'*-ethanediylidenebis(2,4-dimethyl-3-pentanamine) (2).



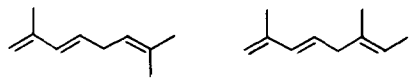
(2) (3)

R = $(CH_3)_2CH-\underset{|}{C}H-CH(CH_3)_2$

Activation of (3) with Et_2AlOEt in the presence of isoprene (molar ratio *ca.* 1:2:500) leads to the best result obtained so far: a small amount of trimeric (10%) and higher products is accompanied by 80% of (1).

In the simplified version of the reaction, compound (3) is not isolated. Reduction in THF is followed by evaporation to dryness, (3) is extracted from the residue with isoprene and then activated with Et_2AlOEt. A chromium(III) compound, the ligand (2), and AlR_3 as reducing agent also gives (1) as the sole dimer on reaction in a steel autoclave, admittedly together with much polymeric material; the yield of (1) is improved if ligand (2) is added in excess.

Chromium complexes of type (3) bearing other substituents R give less specific reactions; the products contain no (1). When R = cyclohexyl reaction gives *inter alia* 2,7-dimethyl-1,3,6-octatriene (4), the intermediate probably present before the final hydrogen shift, alongside the head-to-tail dimer 2,6-dimethyl-1,3,6-octatriene (5).



(4) (5)

The exclusive formation of the tail-to-tail dimer (1) on a catalyst system (3) suggests a strong steric interaction during the primary C—C linkage.

Similar steric control leading to tail-to-tail linkage in metal-diazadiene catalysis has also been observed in the $V(dad)_3/AlR_3$ system[2].

Compound (1), m.p. 35—37°C, b.p. 110—115°C/55 torr, forms the expected Diels-Alder adduct 3,3-dimethyl-6-(2-methyl-1-propenyl)-4-cyclohexene-1,1,2,2-tetracarbonitrile with tetracyanoethylene, while only a yellow-orange charge-transfer complex is formed with maleic anhydride. The nonuniform bromination gives *inter alia* 2,3,6,7-tetrabromo-2,7-dimethyl-*trans*-4-octene in *ca.* 10% yield[2].

Experimental

Synthesis of (3): Synthesis was successful only in flame-treated Schlenk tubes under re-purified argon in anhydrous solvents. Tris(2,4-pentanedionato)chromium(III) (3.49 g, 10 mmol), (2)[3] (5.04 g, 20 mmol), and sodium (0.69 g, 30 mmol) are stirred together in THF (150 ml) at room temperature for 20 h. The brown solution is evaporated to dryness, the residue taken up in *n*-hexane (150 ml), the solution filtered through a fine frit and evaporated down. Compound (3) precipitates in a freezer as a dark-brown solid which is washed with acetonitrile. It deliquesces, turning reddish brown, on exposure to air: MS: $m/e = 556$ (M^+), 304 ($dadCr^+$), 278 [$(dad)_2Cr^{2+}$], *etc.*; VIS spectrum (*n*-hexane): 13250, 15750, 17290 (sh), 21100 (sh), 24690, 28170 cm^{-1}.

Dimerization of isoprene to give (1): Dimerization was performed in a flame-treated glass ampoule in a steel autoclave under *n*-pentane back-pressure at 120°C. Compound (3) (265.1 mg) is transferred under argon into an ampoule. After freshly distilled isoprene (25 ml) and Et_2AlOEt have been pipetted into the ampoule, it is frozen, evacuated at oil-pump vacuum, and sealed. After 20 h at 120°C (volume contraction *ca.* 10%) the reaction solution no longer contains isoprene. Distillation affords 13 g (80%) of (1) and 1.8 g (11%) of trimer; the rest is undistillable. UV (cyclohexane): 34250, 35710, 37170 cm^{-1}; 270-MHz ^1H-NMR spectrum ($CDCl_3$, int. TMS): $\delta = 1.76$ (s, 6H), 1.78 (s, 6H), 5.78—6.35 (m, 4H, AA'BB' system); ^{13}C-NMR ($CDCl_3$, int. TMS): $\delta = 18.3$, 26.1 (CH_3), 125.7, 126.7 (=CH—), 134.3 (=C<).

Received: December 27, 1978 [Z 190 IE]
German version: Angew. Chem. *91*, 344 (1979)

CAS Registry numbers:
(1), 42588-68-1; (2), 59725-31-4; (3), 69795-69-3; $Cr(acac)_3$, 21679-31-2

[1] *A. D. Josey*, J. Org. Chem. *39*, 139 (1974).
[2] *A. Kinzel*, Projected Dissertation, Universität Hamburg, 1979.
[3] *H. tom Dieck, M. Svoboda*, Chem. Ber. *109*, 1657 (1976).

Novel Titanium Halides Containing Metal-Metal Bonds: Ti_7Cl_{16} and Ti_7Br_{16}

By *Harald Schäfer, Reinhard Laumanns, Bernt Krebs*, and *Gerald Henkel*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Among the halides of titanium, no stoichiometric compound having a composition between TiX_2 and TiX_3 has so far been reported. The thermal disproportionation of $TiCl_3$ is usually formulated as involving formation of $TiCl_{4,g}$ and $TiCl_{2,s}$. However, it initially leads to low-order products of varying composition[1] before ending up as $TiCl_2$. The latter compound is also of low order and can spontaneously ignite in moist air. To explain this behavior it was assumed—as in the case of the $TiBr_3$ analogue[2]—that there is a large range of homogeneous solid solutions.

The observation that the trihalides already disproportionate at 400—500°C, *i.e.* at temperatures at which atoms could not be very mobile in the solid state, posed the question whether the equilibration can be improved with the aid of transport reagents such that well crystallized solid phases are formed. Aluminum halides are suitable as transporting agents for lower titanium halides; the gaseous complexes $TiAlCl_6$ and $TiCl_2 \cdot nAlCl_3$ are already well known[3]. Our experiments led to the discovery of the crystalline compounds Ti_7Cl_{16} and Ti_7Br_{16}.

[*] Prof. Dr. H. Schäfer, Dipl.-Chem. R. Laumanns, Prof. Dr. B. Krebs, Dr. G. Henkel
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

Ti_7Cl_{16} can be synthesized in several different ways, one of the most convenient being, *e.g.*, as follows: 400 mg of Ti foil and 50 mg of NH_4Cl are transferred to a cylindrical ampoule. After purging with nitrogen, sufficient Al_2Cl_6 (prepared from Al and Cl_2) is sublimed into the tube such that the Al_2Cl_6-pressure at 375 °C is *ca.* 5 atm; after further purging with nitrogen 100 mg of $TiCl_2$ (prepared according to the method of *Ehrlich et al.*[4]) is added and the ampoule sealed under a high vacuum. After three days' heating black crystals of Ti_7Cl_{16} (37.2 % Ti, 62.6 % Cl) are formed in the 350 °C-zone of the 400—350 °C temperature gradient. The X-ray diagram of this product differs from those of $TiCl_2$ and $TiCl_3$. The new compound Ti_7Cl_{16} is sensitive to hydrolysis and oxidation, but can be stored indefinitely in an inert atmosphere; treatment with dilute acids leads to evolution of H_2 and formation of brown solutions.

Ti_7Br_{16} can be prepared by reaction of Br_2 with an excess of Ti in the presence of Al_2Br_6 (conversion to $TiBr_3$ at 350 → 250 °C and then to Ti_7Br_{16} at 300 → 250 °C). This compound is also analytically pure.

Ti_7Cl_{16}, which according to Guinier photographs is isotypic with Ti_7Br_{16}, forms orthorhombic crystals ($a = 14.421$, $b = 9.987$, $c = 6.890$ Å), space group Pnnm, $Z = 2$. The molecule contains two sorts of Ti atoms, which we provisionally regard as Ti^{II} and Ti^{IV}. Trigonal Ti_3Cl_{13} units consisting of $Ti^{II}Cl_6$ octahedra coupled edge-to-edge and containing Ti—Ti bonds (2.954(2) Å) are present [equilateral Ti_3 triangles centered at *ca.* 1/6 1/3 1/2; 2/3, 1/6 0; 5/6 2/3 1/2 and 1/3 5/6 0]. The $Ti_3^{II}Cl_{13}$ groups are coupled three-dimensionally *via* octahedral edges without Ti—Ti bonds (Ti...Ti > 3.80 Å) with one another and with $Ti^{IV}Cl_6$ octahedra [in 0 0 0 and 1/2 1/2 1/2]. This is consistent with the formula $Ti^{IV}Cl_{6/3}[Ti_3^{II}Cl_{12/3}Cl_{6/2}]_2$ (= "$TiCl_4 \cdot 6TiCl_2$"). The Cl atoms form a distorted cubic close packing with layers parallel to (210).

A relationship is recognizable between the occurrence of Ti_3-units and the structures of Nb_3Cl_8, Nb_3Br_8, Nb_3I_8, and $Zn_2Mo_3O_8$[5]. Starting with an equal distribution of the Ti valence electrons the additional electrons necessary for the formation of the Ti_3-groups are provided by the "isolated" Ti.

Received: January 18, 1979 [Z 188 IE]
German version: Angew. Chem. *91*, 343 (1979)

[1] *B. S. Sanderson, G. E. MacWood*, J. Phys. Chem. *60*, 316 (1956).
[2] *E. H. Hall, J. M. Blocher*, J. Phys. Chem. *63*, 1525 (1959).
[3] *M. Sørlie, H. A. Øye*, Inorg. Chem. *17*, 2473 (1978).
[4] *P. Ehrlich, H. J. Hein, H. Kühnl*, Z. Anorg. Allg. Chem. *292*, 139 (1957).
[5] Cf. *H. Schäfer, H. G. v. Schnering*, Angew. Chem. *76*, 833 (1964); *A. Simon, H. G. v. Schnering*, J. Less-Common Met. *11*, 31 (1966).

Bis(dichloroboryl)silylamines and Tris(dichloroboryl)-amine

By *Theo Gasparis, Heinrich Nöth*, and *Wolfgang Storch*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

According to MO calculations, the D_{3h} molecule $N(BF_2)_3$ should be stable[1]; it was not examined, however, whether the expected decomposition products BF_3 and BN are thermodynamically more stable. Nevertheless, $N[B(CH_3)_2]_3$[2] exhibits considerable thermal stability—in contrast to the diborylamines $RN[B(CH_3)_2]_2$[3]—suggesting that tris(dihaloboryl)-amines would also show little tendency to decompose. And yet attempts to prepare $N(BF_2)_3$ and $N(BCl_2)_3$ have hitherto remained unsuccessful[4].

Although reaction of $N[Si(CH_3)_3]_3$ with CH_3BBr_2 leads to the *B*-halogenated diborylamine $Br(CH_3)_2SiN[BCH_3Br]_2$[5], only methylation of the boron halides is observed with BCl_3 or BBr_3[6]. In contrast, we have now found that Sn—N cleavage according to (a) predominates in the reaction of BCl_3 with $N[Sn(CH_3)_3]_3$ at low temperatures, while methylation of the reactant BCl_3 or the product $N(BCl_2)_3$ *(1)* only occurs at higher temperatures; an excess of BCl_3 prevents methylation of *(1)*. The bis(dichloroboryl)amines *(2)*—*(5)* are obtained analogously, increasingly high reaction temperatures being required along this series.

$$N[Sn(CH_3)_3]_3 + 3\,BCl_3 \rightarrow \underset{(1)}{N(BCl_2)_3} + 3(CH_3)_3SnCl \qquad (a)$$

$$RN[Sn(CH_3)_3]_2^{[7]} + 2\,BCl_3 \rightarrow \underset{(2)-(5)}{RN(BCl_2)_2} + 2(CH_3)_3SnCl \qquad (b)$$

Table 1. NMR data of the new dichloroborylamines *(1)*—*(5)*; standards $BF_3 \cdot OR_2$, $NaNO_3$, TMS.

$RN(BCl_2)_2$	R	$\delta^{11}B$	$\delta^{14}N$	$\delta^{1}H$
(1)	BCl_2	39.8	−218	—
(2)	$SiCl_3$	40.4	−238	—
(3)	$SiCl_2CH_3$	40.0	−240	1.2
(4)	$SiCl(CH_3)_2$	39.3	−242	0.78
(5)	$Si(CH_3)_3$	39.2	−242	0.43

All the new compounds are water-clear liquids that are extremely sensitive to hydrolysis. *(1)* exhibits remarkable thermal stability; it survives heating to 200 °C for 2 h. Nor do *(2)*—*(5)* decompose up to 100 °C. We regard this observation as further evidence that decomposition of the *B*-methylated diborylamines is initiated by intermolecular BN coordination. This step fails to occur with dichloroborylamines because the basicity of the nitrogen is greatly reduced by the Cl_2B groups. The very low field ^{14}N-NMR signals of a trigonal-planar nitrogen confirm the low electron density at this atom. Accordingly, the boron atoms in *(1)*—*(5)* experience only slightly greater shielding by BN-π interaction. The $\delta^{11}B$ values in the series $(Cl_3Si)_2NBCl_2$[8] (43.6) > *(2)* > *(1)* indicate that the Cl_2B group of *(1)* is least twisted relative to the $NB_{3-n}Si_n$ plane.

Synthesis of tri(dichloroboryl)amine (1)

Trichloroborane (21.5 g, 183 mmol) is condensed at −196 °C onto tris(trimethylstannyl)amine (15.2 g, 30 mmol) in *n*-pentane (30 ml). The mixture is thawed with stirring to −78 °C, warmed to −15 °C after 1 h, and then cooled again to −78 °C after 1.5 h. Insoluble material [$(CH_3)_3SnCl$ and $(CH_3)_2SnCl_2$] is filtered off, the filtrate is washed with cold pentane (−78 °C), and the solution evaporated down to 2/3 of its volume *in vacuo*. After removal of the precipitate formed at −78 °C, all volatiles are stripped off at −10 °C/10 torr and the product *(1)* isolated at 27 °C/1.5 torr (yield 3.4 g, 44 %).

Compounds *(2)*—*(5)* are prepared analogously. The reactions go to completion at 0—20 °C with *(2)*—*(4)*, and at 35 °C in the case of *(5)*. All compounds gave correct elemental

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

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0326 $ 02.50/0

analyses and showed the isotope pattern characteristic of the molecular ion in the mass spectrum.

Received: March 6, 1979 [Z 192 IE]
German version: Angew. Chem. *91*, 357 (1979)

[1] *A. D. Buckingham*, Proc. Chem. Soc. London *1962*, 351.
[2] *W. Storch, H. Nöth*, Angew. Chem. *88*, 231 (1976); Angew. Chem. Int. Ed. Engl. *15*, 235 (1976); Chem. Ber. *110*, 1636 (1977).
[3] *H. Nöth, H. Vahrenkamp*, J. Organomet. Chem. *16*, 357 (1969).
[4] *R. A. Geanangel*, J. Inorg. Nucl. Chem. *32*, 3697 (1970); *R. Storr, A. N. Wright, C. A. Winkler*, Can. J. Chem. *40*, 1296 (1962).
[5] *K. Barlos, H. Christl, H. Nöth*, Justus Liebigs Ann. Chem. *1976*, 2272.
[6] *K. Barlos, H. Nöth*, Chem. Ber. *110*, 2783, 3460 (1977); *W. Haubold, U. Kraatz*, Z. Anorg. Allg. Chem. *421*, 105 (1976).
[7] *H. W. Roesky, H. Wiezel*, Chem. Ber. *107*, 3186 (1974).
[8] *U. Wannagat, P. Schmidt*, Inorg. Nucl. Chem. Lett. *4*, 355 (1968).

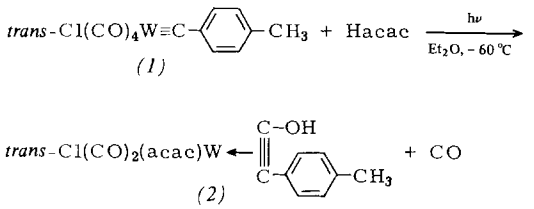
Complex-Stabilized Hydroxy(*p*-tolyl)acetylene by Reaction of *trans*-Chlorotetracarbonyl(tolylcarbyne)tungsten with Acetylacetone[1]

By *Ernst Otto Fischer* and *Peter Friedrich*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

The reaction of *trans*-halotetracarbonyl- or cyclopentadienyldicarbonyl-carbyne complexes with nucleophiles was observed to involve not only substitution of halogen and carbonyl but primarily specific transformations of the carbyne ligand ≡CR[2].

We have now discovered a new combined variant of the reaction by photochemical interaction of *trans*-chlorotetracarbonyl(*p*-tolylcarbyne)tungsten *(1)*[3] with acetylacetone. Fractional crystallization of the crude product yielded a dark blue complex (1:1 adduct with diethyl ether) which is air and temperature sensitive and readily soluble in polar solvents, but only sparingly soluble in pentane. On the basis of the analytical and spectroscopic data of the diamagnetic compound *(2)*, and the results of an X-ray structural analysis (Fig. 1), its formation can be envisaged as follows:



Two *cis* carbonyl ligands have been substituted by the acetylacetonate ion coordinated in *(2)* *via* the oxygen atoms. One of the two CO groups is evolved as carbon monoxide, whereas the second one combines with the tolylcarbyne ligand and a H atom to give a new ligand, *viz.* η^2-hydroxy(*p*-tolyl)acetylene, located *trans* to the halogen atom. 1-Hydroxy-1-alkynes were formerly regarded as incapable of existence, at least in the free state[4].

As shown by the crystal structure analysis of *(2)*, the two acetylenic carbon atoms are coordinated entirely symmetrically to the central atom; the W—C distances are 204(2) pm and thus, like the other bond lengths and angles in the Tol—C≡C—O fragment [$d_{C\equiv C}$ = 130(2) pm, ∢ C≡C—C = 141(1)°, ∢ C≡C—O = 138(1)°], closely resemble those in other η^2-acetylenetungsten complexes[5].

[*] Prof. Dr. E. O. Fischer, Dipl.-Chem. P. Friedrich
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

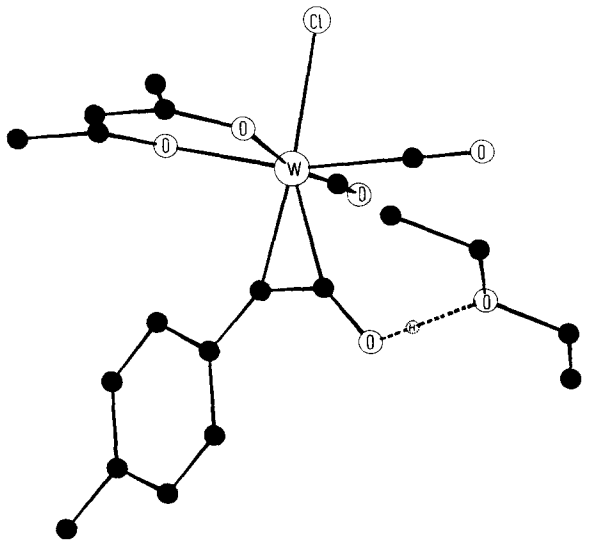


Fig. 1. Structure of the adduct *(2)*·$O(C_2H_5)_2$ in the crystalline state. Crystal data: monoclinic $P2_1/c$, Z = 4; a = 1069, b = 1716, c = 1547 pm, β = 126.8°, $V = 2272 \times 10^6$ pm^3, $\rho_{calc.} = 1.697$, $\rho_{exp} = 1.64$ g cm^{-3}. 2423 independent reflections. Syntex $P2_1$ four-circle diffractometer. Solution: Syntex XTL, conventional $R_1 = 0.042$.

A very short contact distance between the oxygen atom of the OH group in *(2)* and that in the solvate ether [257(1) ppm, ∢ C—O···O(Et_2) = 125(1)°] indicates strong hydrogen bonding, which is characteristic of NH or OH acidic systems such as carboxylic acids and phenols[6].

A ^{1}H-NMR signal of *(2)* at δ = 14.4 ([D_6]acetone, rel. to int. TMS, −80 °C), whose chemical shift and half-width are highly temperature dependent, is to be assigned to the hydroxyl H atom; the chemical shift reveals the acidic character of the proton[7]. The other signals (−20 °C) at δ = 7.63 (M, 4; C_6H_4), 5.78 (S, 1; C*H*(acac)[8]), 3.42 (Q, 4; $CH_2(Et_2O)$), 2.49 (S, 3; C_6H_4—CH_3), 2.16 (S, 6; CH_3(acac)), and 1.17 (T, 6; $CH_3(Et_2O)$) lie in the expected range.

The IR spectrum (KBr disc, room temperature) shows the ν_{CO} bands of the two *cis* carbonyl groups at 2060 (s) and 1960 cm^{-1} (vs). Absorptions at 1590 (s) and 1517 cm^{-1} (s) are assigned to the stretching vibrations of the acetylacetonate ligand[8]. A medium strength band at 1675 cm^{-1} is attributable in accord with other acetylenetungsten complexes[9] to the C≡C bond of the hydroxy(tolyl)acetylene ligand which is greatly weakened by coordination to the metal.

Procedure

All preparative work is carried out under N_2 and with oxygen- and moisture-free solvents.—Compound *(1)* (304 mg, 0.7 mmol) and acetylacetone (900 mg, 9 mmol) are dissolved in ether (250 ml) at −60 °C in a photochemical reactor fitted with a cold finger (UV mercury high-pressure lamp, 150 W, Hanau) and irradiated at that temperature with stirring until the evolution of CO has ceased. After stripping off the solvent at −20 °C and the excess of acetylacetone at −15 °C (cold finger), the violet residue is recrystallized several times from ether at low temperature. Analytically pure *(2)*·OEt_2 is isolated, yield 77 mg (19 %).

Received: January 17, 1979 [Z 179 IE]
German version: Angew. Chem. *91*, 345 (1979)

CAS Registry numbers:
(1), 68480-95-5; *(2)*, 69631-49-8; acetylacetone, 123-54-6

[1] Transition-Metal Carbyne Complexes, Part 48. This work was supported by the Deutsche Forschungsgemeinschaft. We are grateful to Ms *B. Zimmer-Gasser* for measuring the low temperature ^{1}H-NMR spectra.—

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0327 $ 02.50/0*

Part 47: *N. Q. Dao, E. O. Fischer, W. R. Wagner, D. Neugebauer*, Chem. Ber., in press.
[2] *E. O. Fischer, A. Ruhs, F. R. Kreissl*, Chem. Ber. *110*, 805 (1977); *E. O. Fischer, U. Schubert*, J. Organomet. Chem. *100*, 59 (1975); *F. R. Kreissl, P. Friedrich, G. Huttner*, Angew. Chem. *89*, 110 (1977); Angew. Chem. Int. Ed. Engl. *16*, 102 (1977); *E. O. Fischer, A. Ruhs, P. Friedrich, G. Huttner, ibid. 89*, 481 (1977) and *16*, 465 (1977).
[3] *F. R. Kreissl, W. Uedelhoven, G. Kreis*, Chem. Ber. *111*, 3283 (1978).
[4] Cf. Houben/Weyl: Methoden der organischen Chemie, Vol. V/2a. Thieme, Stuttgart 1977, p. 301.
[5] *N. G. Bokiy, Yu. V. Gatilov, Yu. T. Struchkov, N. A. Ustynyuk*, J. Organomet. Chem. *54*, 213 (1973); *R. M. Laine, R. E. Moriarty, R. Bau*, J. Am. Chem. Soc. *94*, 1402 (1972).
[6] *A. R. Ubbelohde, K. J. Gallagher*, Acta Crystallogr. *8*, 71 (1955); *H. Gillier-Pandraud*, Bull. Soc. Chim. Fr. *1967*, 1988.
[7] *Y. Murakami, J. Sunamoto*, J. Chem. Soc. Perkin Trans. II *1973*, 1231; *H. P. Fritz, F. H. Köhler, B. Lippert*, Chem. Ber. *106*, 2918 (1973); *K. Yates, P. G. Mezey, I. G. Csizmadia*, J. Chem. Phys. *67*, 517 (1977).
[8] *B. Bock, K. Flatau, H. Junge, M. Kuhr, H. Musso*, Angew. Chem. *83*, 239 (1971); Angew. Chem. Int. Ed. Engl. *10*, 225 (1971); and references cited therein.
[9] *D. P. Tate, J. M. Augl, W. M. Ritchey, B. L. Ross, J. G. Grasselli*, J. Am. Chem. Soc. *86*, 3261 (1964).

Photochemical Behavior of N_2-Complexes: Photoluminescence of *trans*-$(N_2)_2W(diphos)_2$ and *trans*-$(CO)_2W(diphos)_2$

By *Albert Caruana* and *Horst Kisch*[*]

Dedicated to Prof. O. E. Polansky on the occasion of his 60th birthday

In connection with our studies on the photochemical reactivity of complexed diazenes[1], we have now investigated dinitrogen-transition metal complexes. According to simple MO considerations the photochemical excitation of the ligand-field states (LF) should preferably lead to elimination of dinitrogen, while excitation of the charge-transfer state (CT), on the other hand, should increase the reactivity of the M—N_2 fragment[2]. Photochemical reduction[3] of complexed N_2 in the presence of suitable reagents should therefore preferably take place from CT states. A knowledge of the energies of the lowest excited states is therefore necessary in order to permit selective excitation.

On these grounds we report here on the electronic absorption and emission spectra of *trans*-$(N_2)_2W(diphos)_2$ *(1)*[4] and *trans*-$(CO)_2W(diphos)_2$ *(2)*[5] [diphos = ethylenebis(diphenylphosphane)] in 2-methyltetrahydrofuran. *(1)* is the first example of a photoluminescing N_2-complex.

On optical excitation of *(1)* ($\bar{\nu}_{excit} = 26000\,cm^{-1}$) at 77 K, a structured emission spectrum is observed with $\bar{\nu}_{max} = 17700\,cm^{-1}$ and a halfwidth $\Delta\bar{\nu}_{1/2} = 1500\,cm^{-1}$. The quantum yield of the emission is $\Phi = 0.08 \pm 0.02$[6] and the lifetime $\tau = 19\,\mu s$. The few other photoluminescing W^0-complexes all show unstructured emission bands: $W(CO)_5L$ (L = pyridines[7a], diazenes[1]), $W(CO)_4L_2$ (L_2 = α,α'-bipyridyl, phenanthroline[7b]) and $M(CNR)_6$ (M = Cr, W[7c]). Structured emission bands were previously observed only in the case of M^{II}- and M^{III}-complexes; *e.g.* $Ru(\alpha,\alpha'\text{-bipyridyl})_3^{2+}$[8]. In analogy to these complexes the emitting state of *(1)* probably has CT character (dπ*). The question of whether the observed vibrational fine structure arises from a δ(W—N_2) mode is currently being investigated by studies on the $^{15}N_2$ derivative.

The analogous *trans*-$(CO)_2W$ complex exhibits almost the same behavior. Under the same experimental conditions as in the case of *(1)*, an emission spectrum with $\bar{\nu}_{max} = 17600\,cm^{-1}$, $\Delta\bar{\nu}_{1/2} = 2400\,cm^{-1}$, $\Phi = 0.14$[6] and $\tau = 23\,\mu s$ is obtained. In contrast to the case of *(1)*, the low-energy side of the emission band of *(2)* is only weakly structured.

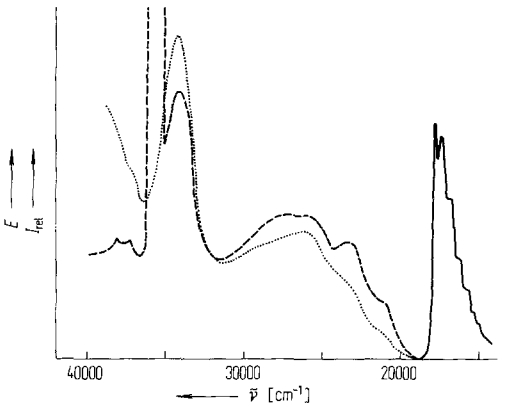


Fig. 1. Electronic spectrum of *trans*-$(N_2)_2W(diphos)_2$ *(1)* in 2-methyltetrahydrofuran: (.....) absorption at 143 K, (------) corrected excitation ($\bar{\nu}_{emiss} = 17700\,cm^{-1}$) at 77 K, (——) emission ($\bar{\nu}_{excit} = 26000\,cm^{-1}$) at 77 K.

The essentially equal energy of the emitting states of *(1)* and *(2)*, and the low-temperature (143 K) absorption spectra suggest that the two complexes have essentially identical electronic structures. The two lowest absorption bands (shoulders) of *(1)* and *(2)* at 20800 ($\varepsilon = 4000\,l \cdot mol^{-1} \cdot cm^{-1}$) and 23100 (6000), and at 20400 (2100) and 23200 (3600) respectively, are tentatively assigned to LF transitions; in *trans*-$Mo(N_2)_2(Et_2PCH_2CH_2PEt_2)_2$ these appear as isolated absorption bands at 20600 (589) and 21800 cm^{-1} (569)[9]. The broad, energetically higher band of *(1)* at 25800—27000 cm^{-1} (11000) is tentatively assigned to two superimposed CT transitions (dπ*); consistent with this assignment, *(2)* shows two separate maxima at 25600 (5400) and 27800 cm^{-1} (8400). The somewhat greater energy ($\approx 800\,cm^{-1}$) of the latter CT transition compared to that in *(1)* can be interpreted in terms of the higher energy of the lowest π* orbital or CO as compared to that of N_2, in analogy to the observed difference[2d] between *cis*-$[Os(NH_3)_4(N_2)_2]^{2+}$ and *cis*-$[Os(NH_3)_4(CO)(N_2)]^{2+}$.

Received: November 15, 1978 [Z 169 IE]
German version: Angew. Chem. *91*, 335 (1979)

CAS Registry numbers:
(1), 28915-54-0; *(2)*, 51202-31-4

[*] Priv.-Doz. Dr. H. Kisch, A. Caruana
Institut für Strahlenchemie im Max-Planck-Institut für Kohlenforschung
Stiftstrasse 34—36, D-4330 Mülheim/Ruhr (Germany)

[1] *C. C. Frazier, H. Kisch*, Inorg. Chem. *17*, 2736 (1978).
[2] a) *I. Fischler, E. Koerner von Gustorf*, Naturwissenschaften *62*, 63 (1975); b) *D. L. DuBois, R. Hoffmann*, Nouv. J. Chim. *1*, 479 (1977), and references cited therein; c) *A. B. P. Lever, G. A. Ozin*, Inorg. Chem. *16*, 2012 (1977); d) *A. D.* Allen, J. R. Stevens, Can. J. Chem. *50*, 3093 (1972).
[3] The previously known reductions are:

cis-$(N_2)_2W(PMe_2Ph)_4$ + MeOH $\xrightarrow{h\nu}$ NH_3 [*J. Chatt, A. J. Pearman, R. L. Richards*, J. Chem. Soc. Dalton Trans. *1977*, 1852] and

trans-$(N_2)_2W(diphos)_2$[*(1)*] + RX $\xrightarrow[-N_2]{h\nu}$ *trans*-(X)(R—N=N—)W(diphos)$_2$, R = alkyl, acyl, aroyl, X = Cl, Br [*V. W. Day, T. A. George, S. D. A. Iske*, J. Am. Chem. Soc. *97*, 4127 (1975); *A. A. Diamantis, J. Chatt, G. J. Leigh, G. A. Heath*, J. Organomet. Chem. *84*, C11 (1975); *J. Chatt, A. A. Diamantis, G. A. Heath, N. E. Hooper, G. J. Leigh*, J. Chem. Soc. Dalton Trans. *1977*, 688; *J. Chatt, R. A. Head, G. J. Leigh, Ch. J. Pickett*, J. Chem. Soc. Chem. Commun. *1977*, 299.
[4] We thank Prof. *J. Chatt* for supplying a detailed experimental procedure.
[5] *S. Datta, T. J. McNeese, S. S. Wreford*, Inorg. Chem. *16*, 2661 (1977).
[6] Determined relative to 9,10-diphenylanthracene [Φ(77 K) = 1]; see *G. Heinrich, S. Schoof, H. Güsten*, J. Photochem. *3*, 315 (1974/75).
[7] a) *M. S. Wrighton, H. B. Abrahamson, D. L. Morse*, J. Am. Chem. Soc. *88*, 4105 (1976); b) *M. S. Wrighton, D. L. Morse*, J. Organomet. Chem. *97*, 405 (1975); c) *K. R. Mann, H. B. Gray, G. S. Hammond*, J. Am. Chem. Soc. *99*, 306 (1977).
[8] Summary: *G. A. Crosby*, Acc. Chem. Res. *8*, 231 (1975).

[9] The absorption spectra of *trans*-$(N_2)_2$Mo(diphos)$_2$ and *(1)* are almost identical; all values for THF as solvent. We thank Prof. *T. A. George* for supplying the absorption spectrum of the molybdenum complex.

[2.2.2.2](1,2,3,4)Cyclophane[**]

By *Jürgen Kleinschroth* and *Henning Hopf*[*]

Dedicated to Professor Donald J. Cram on the occasion of his 60th birthday

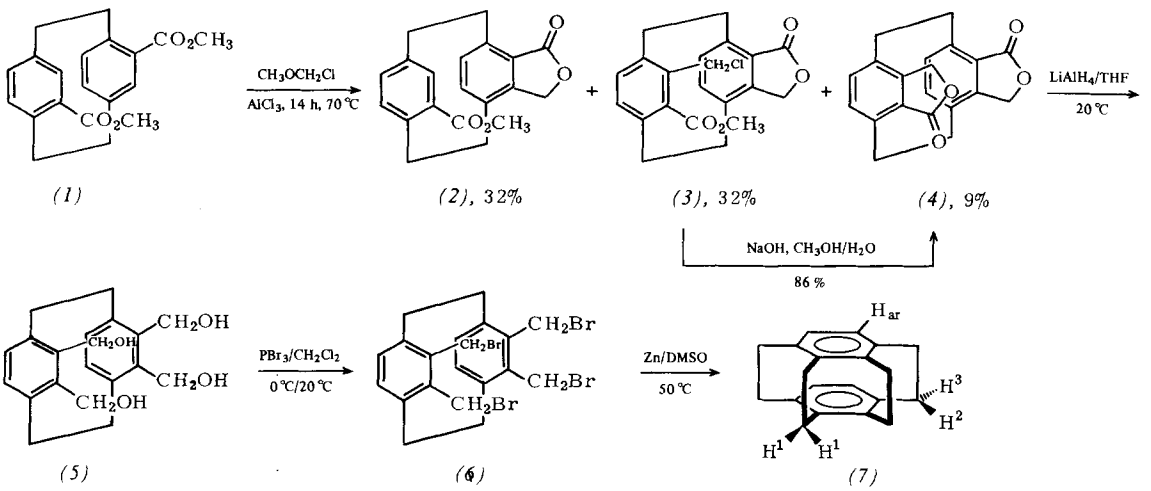
Of the three possible [2.2.2.2]cyclophanes, the (1,2,4,5)-[1a] and the (1,2,3,5)-isomers[1b] are already known. In the present communication we describe the synthesis of the hitherto missing (1,2,3,4)-isomer *(7)*, the first phane system having four adjacent ethano bridges[2]. Multibridged phanes are of interest, *inter alia*, because the unusual properties of the parent compound [2.2]paracyclophane—*i.e.* extremely short distance between the (non-planar) benzene rings, and hence pronounced transannular interactions—ought to be more pronounced in such systems[3].

Reaction of the *pseudo-ortho* diester *(1)*[4] with chloromethyl methyl ether/aluminum trichloride at 70 °C[1] affords a mixture of the phthalides *(2)*—*(4)* in the yields shown in the reaction scheme (separation by column chromatography on Merck 60 silica gel with dichloromethane/ethyl acetate = 96:4)[5].

tion with activated zinc dust[7] in dimethyl sulfoxide (5 h, 50 °C) affords the desired hydrocarbon *(7)* (35 %).

The vibrational spectrum [(KBr): 3040 (w), 2940 (s), 2915 (s), 2890 (m), 1475 (s), 805 (m), 745 (m), 700 cm^{-1} (w)] and electronic spectrum [(ethanol): $\lambda_{max} = 200$ ($\varepsilon = 91150$), 225 (sh, 14100), 240 (sh, 3950), 283 (370), 297 nm (sh, 280)] of [2.2.2.2](1,2,3,4)cyclophane (prisms from pentane, m. p., 265 °C, dec. [5]) differ very little from those of its isomers[1]. However, the NMR-signal of the aromatic protons H_{ar} [$\delta = 6.32$ (4H)] appears at significantly lower field than the corresponding signals of the isomeric cyclophanes (H_{ar} at $\delta = 5.96$ in both cases[1]). Presumably this deshielding is brought about by non-parallel arrangement of the benzene rings in *(7)*. As molecular models show, the substituted ring carbon atoms in *(7)* are pressed still more closely than in [2.2]paracyclophane. At the same time the distance between the benzene rings on the unbridged side is larger: hence the arene protons no longer project so deeply into the anisotropy region of the oppositely placed rings and thus absorb at lower field. This interpretation is supported by the NMR spectrum of [2.2.2](1,2,4)cyclophane[3, 8]. The remaining protons of *(7)* absorb at $\delta = 3.22$ (m, 4H, H^3), 2.90 (s, 8H, H^1) and 2.58 (m, H, H^2).

Received: February 14, 1979 [Z 177 IE]
German version: Angew. Chem. *91*, 336 (1979)



Of particular importance for the subsequent synthetic steps is the observation that reaction of *(3)* with a boiling solution of sodium hydroxide in methanol/water (1:2) leads to formation of the bisphthalide *(4)*[5]. Reduction of *(4)* with $LiAlH_4$ in tetrahydrofuran at room temperature yields a mixture of several paracyclophane ethers and -alcohols, from which the *syn*-tetrakis(hydroxymethyl)-[2.2]paracyclophane *(5)*[5] can be isolated in 54 % yield. This alcohol differs markedly from the previously prepared *anti*-isomer in its spectroscopic and physical data[6]. Reaction of *(5)* with phosphorus tribromide in dichloromethane (initially at 0 °C, then at room temperature) leads to the tetrabromide *(6)* (65 %)[5], which on dehalogena-

CAS Registry numbers:
(1), 53957-02-1; *(2)*, 69631-52-3; *(3)*, 69631-53-4; *(4)*, 69631-54-5; *(5)*, 69684-86-2; *(6)*, 69684-87-3; *(7)*, 69631-55-4

[*] Prof. Dr. H. Hopf, Dipl.-Chem. J. Kleinschroth
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Part 10 of Cyclophanes. This work was supported by the Deutsche Forschungsgemeinschaft (Project Ho 534/16), the Fonds der Chemischen Industrie and Van't-Hoff Fonds.—Part 9: *A. F. Mourad, H. Hopf*, Tetrahedron Lett., in press.

[1] a) *R. Gray, V. Boekelheide*, Angew. Chem. *87*, 138 (1975); Angew. Chem. Int. Ed. Engl. *14*, 107 (1975); for derivatives of this system see *H. A. Staab, V. Schwendemann, ibid. 90*, 805 (1978) and *17*, 756 (1978); b) *W. Gilb, K. Menke, H. Hopf, ibid. 89*, 177 (1977) and *16*, 191 (1977).
[2] *V. Boekelheide et al.* (University of Oregon) have independently synthesized a dimethyl derivative of *(7)*: private communication, December 13, 1978.
[3] *F. Vögtle, G. Hohner*, Top. Curr. Chem. *74*, 1 (1978).
[4] *H. Hopf, F. Th. Lenich*, Chem. Ber. *107*, 1891 (1974); cf. *I. Böhm, H. Herrmann, H. Hopf, K. Menke, ibid. 111*, 523 (1978).
[5] The IR, UV, NMR, and mass spectra as well as the elemental analysis are consistent with the given structures.
[6] *H. Hopf*, Angew. Chem. *84*, 471 (1972); Angew. Chem. Int. Ed. Engl. *11*, 419 (1972); *J. Kleinschroth*, unpublished.
[7] *K. Alder, M. Fremery*, Tetrahedron *14*, 190 (1961).
[8] *E. A. Truesdale, D. J. Cram*, J. Am. Chem. Soc. *95*, 5825 (1973); *S. Trampe, K. Menke, H. Hopf*, Chem. Ber. *110*, 371 (1977).

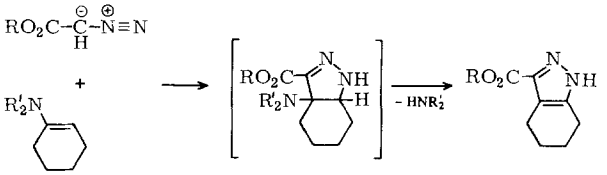
© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0329 $ 02.50/0*

Cycloadditions of α-Diazo Carbonyl Compounds to Enamines

By *Rolf Huisgen* and *Hans-Ulrich Reissig*[*]

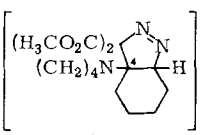
Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Although diazomethane is inert towards enamines, α-diazo carbonyl compounds can undergo 1,3-dipolar cycloadditions with these compounds. *Piozzi et al.*[1] refluxed ethyl diazoacetate with *N*-(1-cyclohexenyl)pyrrolidine, -piperidine, or -morpholine for 2 h in $CHCl_3$, evaporated the mixture, and treated it for 15 min with 2 N HCl: they isolated the esters *(2)*, R = C_2H_5, in 55, 35, and 2% yield, respectively. Does cyclization of an open-chain precursor occur only after acid treatment?

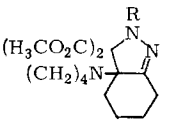


(1) *(2)*

Such doubts proved groundless: we obtained compound *(2)*, R = CH_3 (82%), on reaction of methyl diazoacetate with *N*-(1-cyclohexenyl)pyrrolidine (3 weeks, 20 °C) without acidification. The analogous reaction with *p*-nitrodiazoacetophenone (1 h, 20 °C) gave 85% of *(2)*, *p*-$NO_2C_6H_4CO$ in place of RO_2C; pale yellow needles, m.p. 209—210 °C.



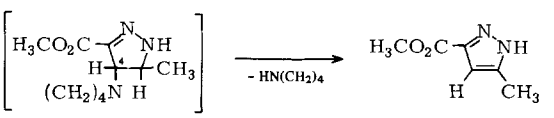
(3)



(4), R = H

(5), R = CO–NHC$_6$H$_5$

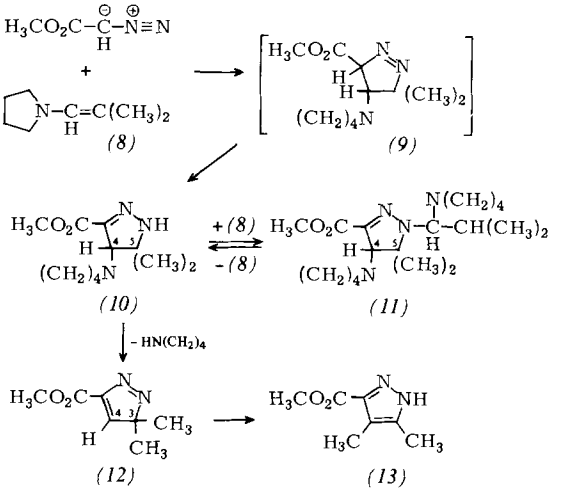
While aromatization induces elimination of HNR'_2 from *(1)*, this does not occur on reaction (4 d, 20 °C, ether) of dimethyl diazomalonate with *N*-(1-cyclohexenyl)pyrrolidine. The adduct (73% yield) was not *(3)* but its stable tautomer *(4)* (Table 1). The NH function of *(4)* is confirmed by reaction with phenyl isocyanate to give the phenylurea *(5)*. Compound *(4)* was transformed with HCl in boiling methanol into *(2)*, R = CH_3. The appearance of the NH function also establishes that the reactants are oriented according to *(3)* on cyclization; the primary product would not be able to tautomerize to the 2-pyrazoline *(4)* if the opposite orientation were to apply.



(6) *(7)*

Addition of methyl diazoacetate to freshly prepared *N*-(1-propenyl)pyrrolidine (*trans*:*cis* = 4:1, 3 d, 20 °C) was also followed by pyrrolidine elimination to give the pyrazole *(7)* (85% yield), whose synthesis from diazoethane and methyl propiolate served as structural proof. 3,5-Disubstitution left no doubt as to the intermediacy of *(6)*.

[*] Prof. Dr. R. Huisgen, Dr. H.-U. Reissig
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)



(8) *(9)* *(10)* *(11)* *(12)* *(13)*

Use of a β,β-disubstituted enamine suppresses release of the secondary amine. Methyl diazoacetate combines with *N*-isobutenylpyrrolidine *(8)* (1:1, 8 h, boiling $CHCl_3$, 73%) to give the pyrazoline *(10)*[2]. Reaction in the ratio 1:2 (4 weeks, −5 °C, neat) gave the 1:2 adduct *(11)* (66% yield) which was also formed from *(10)* with further *(8)*. Just a little silica gel was sufficient to bring about the transformation *(11)* → *(10)*, whereas chromatography of *(10)* in ether over a large amount of SiO_2 afforded 92% of the 3*H*-pyrazole *(12)* with liberation of pyrrolidine [*(10)*—*(12)*, see Table 1]. Synthesis of *(12)* from methyl propiolate and 2-diazopropane[3] is known.

Table 1. Selected physical data of compounds *(4)*, *(10)*, *(11)*, and *(12)*.

Cpd.	M.p. [°C]	νNH [cm^{-1}]	^{1}H-NMR ($CDCl_3$), δ values
(4)	86—88	3360	6.15 (NH, disappears with D_2O), 3.74, 3.75 (2 s, 2 OCH_3)
(10)	64—66	3390	6.36 (s, br., NH), 3.83 (s, OCH_3), 3.88 (s, 4-H), 1.15, 1.28 (2 s, 2 CH_3)
(11)	62—68		3.82 (s, 4-H), 3.50 (s, OCH_3), 1.14, 0.70 (2 s, 2 5-CH_3), 1.03, 0.73 (2 d, 6 H, isopropyl-CH_3, J = 6.0 Hz) [a]
(12)	93.5—95		7.79 (s, 4-H), 3.98 (s, OCH_3), 1.52 (s, 2 CH_3)

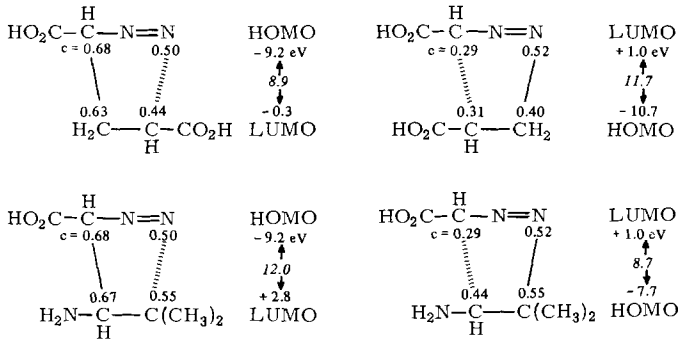
[a] In C_6H_6.

On distillation of *(12)* (180–205 °C/12 torr) or on reaction with cold conc. sulfuric acid, van Alphen-Hüttel rearrangement[4] gave 63 and 57%, respectively, of the pyrazole *(13)*. It is also formed from diazoethane and methyl 2-butynoate.

The invariant orientation of the diazocarbonyl compound and enamines in the 1,3-dipolar cycloaddition is remarkable: 4-Aminopyrazolines [*(1)*, *(3)*, *(6)*, *(9)*] are the primary adducts. Addition to acrylic ester occurs in the opposite orientation, *i.e.* the ester group is located in position 3 of the adduct[5]. If cycloaddition were to proceed *via* a diradical intermediate[6], then the mentioned substituents on the dipolarophile should effect the *same* orientation in the adduct because the ester group, like alkyl or amino groups, can stabilize carbon radicals.

In concerted reactions, MO perturbation theory accounts for the observed *bidirectional behavior*. The second-order perturbation term gives the greatest bonding interaction for an orientation in which the atomic orbital coefficients are combined according to large-times-large and small-times-small. Only frontier-orbital interactions are considered in Scheme 1[8].

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* 0570-0833/79/0404-0330 $ 02.50/0



Scheme 1.

For diazoacetic acid + acrylic acid the two HOMO-LUMO interactions determine the opposite directions of addition; owing to the small energy difference HOMO(diazoacetic acid)-LUMO(acrylic acid) prevails, *i.e.* the 3,5-pyrazolinedicarboxylic ester is formed. With diazoacetic acid + *N*-isobutenylamine two HOMO-LUMO interactions cooperate in formation of the 4-amino compound.

Received: February 6, 1979 [Z 174a IE]
German version: Angew. Chem. *91*, 346 (1979)

CAS Registry numbers:
(2), R = CH_3, 32286-98-9; *(2)*, RO_2C = *p*-$NO_2C_6H_4CO$, 69668-68-4; *(4)*, 69668-69-5; *(5)*, 69668-70-8; *(7)*, 25016-17-5; *(8)*, 2403-57-8; *(10)*, 69668-71-9; *(11)*, 69668-72-0; *(12)*, 21603-19-0; *(13)*, 60858-33-5; methyl diazoacetate, 6832-16-2; *N*-(1-cyclohexenyl)pyrrolidine, 1125-99-1; *p*-nitrodiazoacetophenone, 4203-31-0; dimethyl diazomalonate, 6773-29-1; *trans*-*N*-(1-propenyl)pyrrolidine, 13044-42-3; *cis*-*N*-(1-propenyl)pyrrolidine, 13098-67-4

[1] *F. Piozzi, A. Umani-Ronchi, L. Merlini*, Gazz. Chim. Ital. *95*, 814 (1965).
[2] *E. Wenkert, C. A. McPherson*, J. Am. Chem. Soc. *94*, 8084 (1972), described the oily impure ethyl ester of type *(10)*.
[3] *A. C. Day, R. N. Inwood*, J. Chem. Soc. *C 1969*, 1066.
[4] *J. van Alphen*, Rec. Trav. Chim. Pays-Bas *62*, 485, 491 (1943); *R. Hüttel, J. Riedl, H. Martin, K. Franke*, Chem. Ber. *93*, 1425, 1433 (1960).
[5] *E. Buchner*, Ber. Dtsch. Chem. Ges. *21*, 2637 (1888); *23*, 701 (1890).
[6] *R. A. Firestone*, J. Org. Chem. *37*, 2181 (1972).
[7] We are grateful to Prof. *R. Sustmann*, Essen, for the CNDO/2 calculations.
[8] The orbital energies were estimated from experimental data; *H.-U. Reissig*, Dissertation, Universität München 1978, Section 8.6.

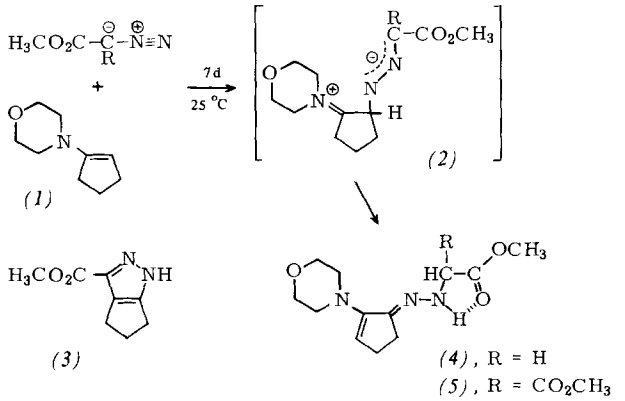
Azo Coupling of α-Diazo Carbonyl Compounds with *N*-(1-Cyclopentenyl)amines

By *Rolf Huisgen, Werner Bihlmaier*, and *Hans-Ulrich Reissig*[*]

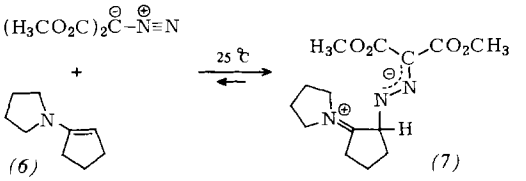
Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

Combination of methyl diazoacetate with *N*-(1-cyclopentenyl)morpholine *(1)* (1 week, 20°C) gave a yellow crystalline 1:1 adduct, *viz.* enamine hydrazone *(4)*, in 51% yield [^{1}H-NMR ($CDCl_3$): δ = 4.2 (s, br. NH, vanishes with D_2O), 5.4 (t, J = 2.2 Hz, vinylic H, disappears with $D_3O^{\oplus}$), 3.95 (s, CH_2 of side chain) 3.70 (s, OCH_3)]. Compound *(4)* was accompanied by only 1—2% of the cycloadduct *(3)*; *(4)* could not be converted into *(3)*. The 1,3-dipolar cycloaddition[1] which dominates reaction of *N*-(1-*cyclohexenyl*)dialkylamines is suppressed by an azo coupling—presumably *via* the zwitterion *(2)*.

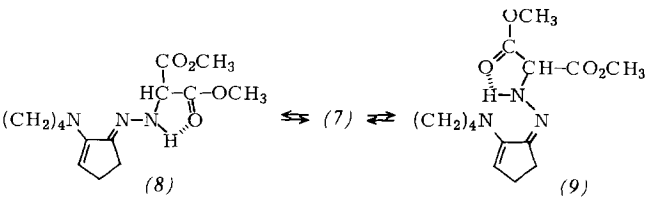
The enamine system of *(4)* added 4-nitrophenyl azide to give a triazoline (92% yield), which still contains the NH group ($\tilde{\nu}$ = 3290 cm^{-1}). Mild hydrolysis on silica gel transformed *(4)* into an oxo hydrazone with intramolecular NH bridge.



Dimethyl diazomalonate reacted with *(1)* even at −30°C in ether; an orange-yellow 65:35 mixture of crystalline enamine hydrazones *syn-(5)* and *anti-(5)*, respectively, (66% yield) could be precipitated with hexane. According to the ^{1}H- and ^{13}C-NMR spectra, the ester groups are equivalent [^{1}H-NMR (nitrobenzene): *syn-(5)* and *anti-(5)*, respectively, δ = 5.70 and 5.55 (NH), 5.12 and 4.98 (malonic ester H), 5.33 (vinylic H); all these protons exchange with $D_3O^{\oplus}$]. The UV maximum at 355 nm (log ε = 2.6, dioxane) reflects the conjugation of the enamine and the hydrazone system.



Are zwitterions of type *(2)* likely candidates as primary products? The zwitterion *(7)* obtained from the more nucleophilic species *N*-(1-cyclopentenyl)pyrrolidine *(6)* and diazomalonic ester is isolable. *(7)* was formed in ether or cyclohexane at 25°C in 93% yield; brick-red needles m. p. 89°C (dec.), which can be stored at −30°C; IR (KBr): $\tilde{\nu}$C=N$^+$ 1694, $\tilde{\nu}$C=O 1650 cm^{-1}. The color is due to intramolecular charge transfer interaction; λ_{max} ($CHCl_3$) 477 nm (log ε = 4.3). The weak diazomalonate absorption at 2135 cm^{-1} (in $CHCl_3$) indicated a dissociation equilibrium of *(7)* with the reactants. Distillation of *(7)* at 80—90°C/0.001 torr proceeded *via* retrocleavage and recombination; *(6)* was trapped by triazoline formation with 4-nitrophenyl azide placed in the receiver.



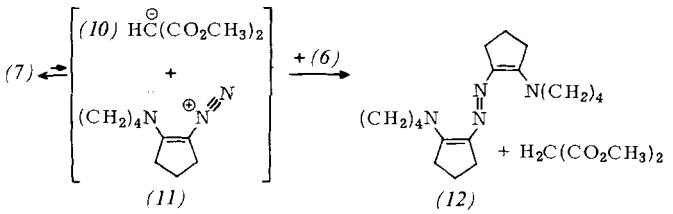
The IR solution spectra and the ^{1}H- and ^{13}C-NMR spectra of *(7)* also indicate equilibration with the *syn,anti* isomeric enamine hydrazones *(8)* and *(9)*. Their structural resemblance to the stereoisomers of *(5)* permitted assignment of the NMR signals to the zwitterion *(7)*. In pyridine at 32°C, 43% of *(7)* was present with 57% of *(8)* + *(9)* (in the ratio 1.4:1); the equilibrium is temperature dependent [in $CDCl_3$: 40% of *(7)* at −49°C, and 15% of *(7)* at +28°C]. The occurrence

[*] Prof. R. Huisgen, Dipl.-Chem. W. Bihlmaier, Dr. H.-U. Reissig
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0331 $ 02.50/0

of two ester methyl signals ($\delta = 3.70$ and 3.75 in pyridine, 3.85 and 3.88 in $CDCl_3$) demonstrates the limited rate of equilibration[2].

Yet another equilibrium was indicated by the transformation of *(7)* in acetonitrile into orange crystals of $C_{18}H_{28}N_4$ (24 % yield), probably the azo-bis(enamine) *(12)*. We suspect a dissociation of *(7)*, with prototropic shift, into the anion *(10)* and the cation *(11)*, which combines with *(6)*, formed in the other dissociative equilibrium, to give *(12)*. Dimethyl



malonate could be detected. Such azo-bis(enamines) have been observed on reaction of dimesyl- and bis(phenylsulfonyl)diazomethane with substituted α-morpholinostyrenes[3].

Azo coupling of α-diazo carbonyl compounds with *N*-(1-cyclopentenyl)amines can be described in terms of MO perturbation theory by combination of the HOMO and LUMO centers with the greatest atomic orbital coefficients (cf. [1]). According to the ^{13}C-NMR spectra, C-4 has a somewhat greater charge density in cyclopentenylamines than in cyclohexenylamines. It could not be predicted, however, that this would lead to such drastic differences in reactions with α-diazo carbonyl compounds: azo coupling in the case of *N*-(1-cyclopentenyl)- and 1,3-dipolar cycloaddition with *N*-(1-cyclohexenyl)dialkylamines.

Received: February 6, 1979 [Z 174b IE]
German version: Angew. Chem. *91*, 347 (1979)

CAS Registry numbers:
(1), 936-52-7; *(3)*, 69631-56-7; *(4)*, 69631-57-8; *syn-(5)*, 69631-58-9; *anti-(5)*, 69631-59-0; *(6)*, 7148-07-4; *(7)*, 69631-60-3; *(8)*, 69631-61-4; *(9)*, 69631-62-5; *(12)*, 69631-63-6; methyl diazoacetate, 6832-16-2; dimethyl diazomalonate, 6773-29-1

[1] *R. Huisgen, H.-U. Reissig*, Angew. Chem. *91*, 346 (1979); Angew. Chem. Int. Ed. Engl. *18*, 330 (1979).
[2] The rate phenomena in the H, D exchange are informative; *H.-U. Reissig*, Dissertation, Universität München 1978, pp. 35–49.
[3] *U. Schöllkopf, E. Wiskott, K. Riedel*, Justus Liebigs Ann. Chem. *1975*, 387.

Oxidative Addition to a Quadruple Bond. The Complete X-ray Structure of $[Mo_2Cl_8H]^{3-}$ [**]

By *Avi Bino* and *F. Albert Cotton*[*]

The preparation of the $[Mo_2Cl_8H]^{3-}$ anion was first described about ten years ago[1] although the presence of the hydrogen atom was not then recognized. A few years later the bromo analog, $[Mo_2Br_8H]^{3-}$ was reported[2]. In 1976 the coordinated hydrogen atom was demonstrated by a combination of chemical observations, isotopic labeling experiments and infrared spectra[3]. The chemical process by which these ions are obtained was thus shown to be represented by eq. (1):

[*] Dr. A. Bino, Prof. Dr. F. A. Cotton
Department of Chemistry
Texas A & M University
College Station, Texas 77843 (USA)

[**] This work was supported by the Robert A. Welch Foundation under Grant No. A-494.

$$Mo_2^{II}(O_2CCH_3)_4 + 8\,HX \rightarrow [Mo_2^{III}X_8H]^{3-} + 3\,H^+ + 4\,CH_3CO_2H \quad (1)$$

This reaction appears to be quantitative when carried out (a) at temperatures of 60 °C and above, and (b) with exclusion of O_2. It had earlier[4] been shown that at 0 °C a simple metathesis takes place according to:

$$Mo_2^{II}(O_2CCH_3)_4 + 8\,HX \rightarrow [Mo_2^{II}X_8]^{4-} + 4\,H^+ + 4\,CH_3CO_2H \quad (2)$$

Reaction (1) constitutes the first unambiguous recognition of oxidative addition to a well-defined metal-metal multiple bond.

The $[Mo_2Cl_8H]^{3-}$ anions have since been shown to have interesting chemical properties[5]; however, their characterization remained incomplete in two respects: Direct structural evidence for the bridging hydrogen atom was lacking, and the conformation of the anion, when not constrained to occupy, in a disordered fashion, a position of D_{3h} symmetry, was unknown.

We report here experimental results that supply the above information. We have found that by modifying the reaction conditions and using cations other than those of the alkali metals, a great variety of well-crystallized salts of the $[Mo_2X_8H]^{3-}$ anions can be easily prepared. One of these new salts, the pyridinium salt $[C_5NH_6]_3[Mo_2Cl_8H]$, has been studied by X-ray crystallography and a complete structural characterization of the anion (including the location of the hydrogen atom) was achieved for the first time.

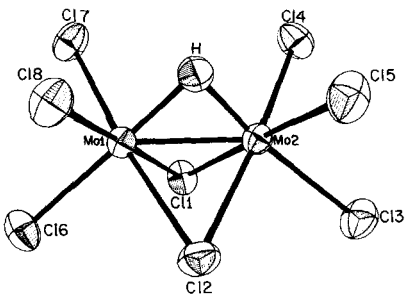


Fig. 1. The structure of the $[Cl_3Mo(\mu\text{-}Cl)_2(\mu\text{-}H)MoCl_3]^{3-}$ ion as it occurs in $[C_5NH_6]_3[Mo_2Cl_8H]$. Atoms are represented by their ellipsoids (sphere for H) of thermal vibration at the 50 % probability level.

The pyridinium salt crystallizes in the space group $P\bar{1}$ with $Z = 2$; the anion has no crystallographically imposed symmetry (Fig. 1). After a structural model omitting hydrogen atoms had been refined to convergence a difference electron density map revealed peaks corresponding to hydrogen atoms, one of which was in a bridging position in the anion. Hydrogen atoms for the three independent $[C_5NH_6]^+$ cations were placed at calculated positions and not refined, while the H atom in the anion was refined isotropically and the other atoms were all refined anisotropically. Using 2786 reflections with $I > 3\,\sigma(I)$ and 257 variables final discrepancy indices of $R_1 = 0.026$, $R_2 = 0.040$ and a goodness-of-fit parameter equal to 1.008 were obtained.

It is clear that in the previous structures the fact that the $[Mo_2X_8H]^{3-}$ anions were constrained to disordered occupation of sites of $\bar{6}m2$ (D_{3h}) symmetry obscured important details of their structure. The virtual symmetry of the $[Mo_2Cl_8H]^{3-}$ anion is mm (C_{2v}), where the mirror planes intersect at the μ-H atom; one contains the Mo atoms and the other the μ-Cl atoms. The terminal atoms *trans* to μ-H have a mean Mo—Cl bond distance (Table 1) significantly longer (0.10 Å)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979
0570-0833/79/0404-0331 $ 02.50/0
© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0404-0332 $ 02.50/0

Table 1. Dimensions of the $[Mo_2X_8H]^{3-}$ anion in the Rb^+ and pyridinium salts.

	$Rb_3[Mo_2Cl_8H]$	$[C_5NH_6]_3[Mo_2Cl_8H]$
Mo—Mo [Å]	2.38(1)	2.371(1)
Mo—Cl_t [Å]	2.38(1)	2.39(1) [a]
		2.49(2) [b]
Mo—Cl_b [Å]	2.50(2)	2.497(2)
∢ Mo—Cl_b—Mo' [°]	56.8(9)	56.82(2)
∢ Cl_t—Mo—Cl_t [°]	93.1(14)	92.7(16)
Mo—H [Å]	—	1.74(1)
Mo'—H [Å]	—	1.62(1)
∢ Mo—H—Mo' [°]	—	89.6(3)

[a] Bonds *trans* to μ-Cl. [b] Bonds *trans* to μ-H.

than those *trans* to μ-Cl. The Mo—Mo and Mo—Cl_b distances and the mean Mo—Cl_b—Mo' are the same as those found before.

The μ-H atom refined as well as can be expected using X-ray data[6,7]. The mean Mo—H distance, the Mo—H—Mo' angle (Table 1) and an isotropic temperature parameter of 3.0 Å^2 for this atom are reasonable values and are consistent with the view that a symmetrically bridging hydrogen atom with appreciable hydride character is present.

Received: January 16, 1979 [Z 191 IE]
German version: Angew. Chem. *91*, 356 (1979)

CAS Registry numbers:
$Rb_3[Mo_2Cl_8H]$, 57719-39-8; $[C_5NH_6]_3[Mo_2Cl_8H]$, 69706-30-5

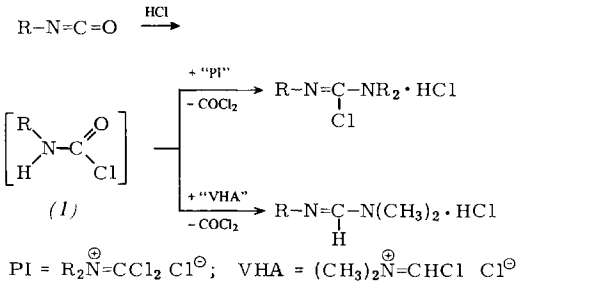
[1] *M. J. Bennett, J. V. Brencic, F. A. Cotton*, Inorg. Chem. *8*, 1060 (1969).
[2] *F. A. Cotton, B. A. Frenz, Z. C. Mester*, Acta Crystallogr. *B29*, 1515 (1973).
[3] *F. A. Cotton, B. J. Kalbacher*, Inorg. Chem. *15*, 522 (1976).
[4] *J. V. Brencic, F. A. Cotton*, Inorg. Chem. *8*, 7 (1969).
[5] *A. Bino, M. Ardon*, J. Am. Chem. Soc. *99*, 6446 (1977); *J. San Filippo, Jr., M. A. Schaeffer King*, Inorg. Chem. *15*, 1228 (1976).
[6] *M. R. Churchill*, Adv. Chem. Ser. *167*, 36 (1978); *M. R. Churchill, R. A. Laskewycz*, Inorg. Chem. *17*, 1950 (1978).
[7] A more precise study using neutron diffraction will be undertaken if suitable crystals can be grown.

N^2-(Trichlorovinyl)amidines—New 1,3-Biselectrophilic Reagents[**]

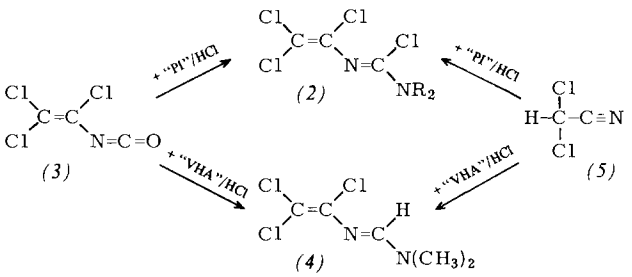
By *Didier Van Broeck, Zdenek Janousek, Robert Merényi*, and *Heinz Günter Viehe*[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday.

Isocyanates and vinyl isocyanates behave as masked primary amines and vinylamines towards strongly electrophilic iminium salts in the presence of hydrogen chloride. The unstable carbamoyl chlorides *(1)* formed as intermediates suffer electrophilic attack by either phosgeniminium chloride [dialkyl(dichloromethylene)ammonium chloride] (PI)[1] or by the Vilsmeier-Haack-Arnold reagent (VHA)[2] with simultaneous loss of phosgene.

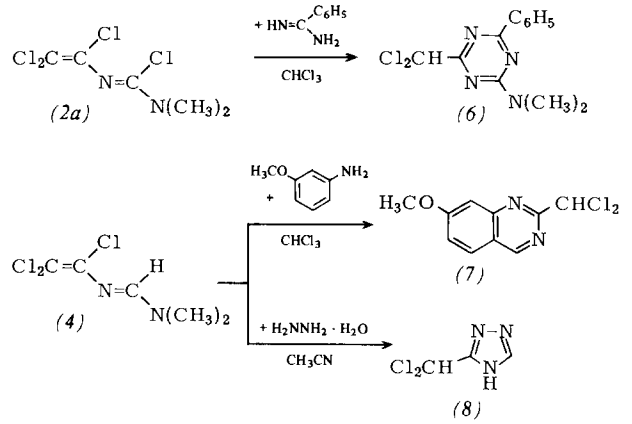


Thus, trichlorovinyl isocyanate *(3)* reacts smoothly both with PI and VHA/HCl to give the new N^2-(trichlorovinyl)-chloroformamidines *(2)* and N^1,N^1-dimethyl-N^2-(trichlorovinyl)formamidine *(4)*, respectively. An equally useful alternative route to *(2)* and *(4)* consists in using dichloroacetonitrile *(5)* as starting material[3].



Like trichlorovinyl isocyanate[4] both *(2)* and *(4)* are valuable 1,3-biselectrophilic reagents, especially for heterocyclizations.

Thus *(2a)* (R=CH_3) reacts with benzamidine to give the trisubstituted triazine *(6)* in 80% yield, while reaction of *(4)* with *m*-methoxyaniline affords the quinazoline *(7)* (50%), and with hydrazine hydrate the triazole *(8)* (55%).



Some physical data are listed in Table 1.

Table 1. Physical data of the compounds *(2a)*, *(4)*, *(4)*·HCl, *(6)*·HCl, *(7)* and *(8)*.

(2a), ^{1}H-NMR ($CDCl_3$): δ=3.2 (s); ^{13}C-NMR ($CDCl_3$): 39.5 (q, ^1J=139.9 Hz), 107.1 (s, =CCl_2), 132.7 (s, =CCl), 144.6 (s, N=CClN; IR (CH_2Cl_2): $\tilde{\nu}$=1630, 1600 cm^{-1}; MS: *m/e*=234, 236, 238 (M^+, four Cl atoms), 199, 201 (M^+ – Cl)

(4), ^{1}H-NMR ($CDCl_3$): δ=3.05 (s, 6H), 7.65 (s, 1H); IR (CH_2Cl_2): $\tilde{\nu}$=2925, 1635, 1595, 1365, 1100, 945, 880 cm^{-1}; MS: *m/e*=200, 202 (M^+, three Cl atoms), 165, 167 (M^+ – Cl)

(4)·HCl, m.p. 121 °C; ^{1}H-NMR (CF_3COOD): δ=3.4, 3.6 (s, 6H), 8.2 (s, 1H), 11.2 (s, 1H)

(6)·HCl, m.p. 142—143 °C; ^{1}H-NMR ($CDCl_3$): δ=3.45 (s, 6H), 7.4 (m, 3 arom. H), 7.85 (s, 1H), 8.5 (m, 2 arom. H), 12.1 (s, 1H)

(7), m.p. 170—171 °C; ^{1}H-NMR ($CDCl_3$): δ=3.95 (s, 3H), 6.75 (s, 1H), 7.2 (m, 2 arom. H), 7.67 (d, 1 arom. H, *J*=9 Hz), 9.15 (s, 1 arom. H)

(8), m.p. 166—167 °C; ^{1}H-NMR ([D_6]-acetone): δ=7.25 (s, 1H), 8.6 (s, 1H), 12 (s, br., 1H)

[*] Prof. Dr. H. G. Viehe, Lic. Chim. D. Van Broeck, Dr. Z. Janousek, Dipl.-Ing. R. Merényi
Laboratoire de Chimie Organique, Université de Louvain
Place Louis Pasteur 1, B-1348 Louvain-La-Neuve (Belgium)

[**] Phosgeniminium Chemistry Part 25. – Part 24: *B. Stelander, J. P. Declerq, M. Van Meerssche, G. Germain, H. G. Viehe*, Bull. Soc. Chim. Belg. *86*, 291 (1977).

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979*

0570-0833/79/0404-0333 $ 02.50/0

Experimental

(2a) from *(3)*: Dry HCl is slowly introduced into a refluxed suspension of 0.012 mol PI (R = Me) and 0.01 mol *(3)* in 60 ml dry $CHCl_3$ until all the PI has dissolved. The residue obtained after evaporation of the solvent is distilled in a Kugelrohr at 85—90 °C/0.01 torr; 2.03 g (86 %) of *(2a)* is obtained as a colorless oil.—Similarly, with PI, R = C_2H_5 and NR_2 = pyrrolidino, 93 % of *(2b)* and 90 % of *(2c)*, respectively, were obtained.—*(2a)* from *(5)*: A suspension of 0.045 mol PI (R = CH_3) and 0.04 mol dichloroacetonitrile in 100 ml anhydrous $CHCl_3$ is refluxed in the presence of gaseous HCl until all the PI has dissolved. Yield after workup (see above): 88 %.

(4) from *(3)*: A solution of 0.01 mol of *(3)* in 20 ml anhydrous CH_2Cl_2 is added to a stirred solution of 0.01 mol VHA in 40 ml of the same solvent at 0 °C, while anhydrous HCl is introduced slowly into the reaction mixture (about one hour at 0 °C). The solution is then refluxed for 30 min, the solvent is removed and the residue washed twice with ether. The yellow powder so obtained is treated with a concentrated solution of K_2CO_3 and extracted with CH_2Cl_2. After drying and removal of the solvent, *(4)* is obtained as a white powder. Yield: 65—75 %.—Hydrochloride of *(4)* from *(5)*: A solution of 0.03 mol *(5)* in 50 ml anhydrous CH_2Cl_2 is added dropwise to a solution of 0.03 mol VHA in 80 ml anhydrous CH_2Cl_2 saturated with dry HCl and cooled to −20 °C. After about two hours the mixture is allowed to slowly warm to room temperature. The solvent is partially removed in a rotary evaporator, whereupon yellowish needles crystallize out; yield 60—65 %.

Received: January 30, 1979 [Z 181 IE]
German version: Angew. Chem. *91*, 355 (1979)

CAS Registry numbers:
(2a), 69668-53-7; *(2b)*, 69687-68-9; *(2c)*, 69668-54-8; *(3)*, 53472-29-0; *(4)*, 69668-55-9; *(4)*·HCl, 69668-56-0; *(5)*, 3018-12-0; *(6)*·HCl, 69668-57-1; *(7)*, 69668-58-2; *(8)*, 69668-59-3; PI·HCl (R = CH_3), 69668-60-6; PI·HCl (R = C_2H_5), 69668-61-7; PI·HCl (NR_2 = pyrrolidine), 69668-62-8; VHA·HCl, 3724-43-4; benzamidine, 618-39-3; hydrazine hydrate, 7803-57-8; *m*-methoxyaniline, 536-90-3

[1] For a review see *Z. Janousek, H. G. Viehe* in *H. Böhme, H. G. Viehe*: Iminium Salts in Organic Chemistry. Wiley-Interscience, New York 1976.
[2] For a review see *C. Jutz* in [1], p. 225.
[3] Such reactions of nitriles are well-known: *B. Stelander, H. G. Viehe*, Angew. Chem. *89*, 182 (1977); Angew. Chem. Int. Ed. Engl. *16*, 189 (1977); *J. Liebscher, H. Hartmann*, Collect. Czech. Chem. Commun. *41*, 1565 (1976).
[4] *J. Perronet, A. Teché*, J. Chem. Res. (S) *1978*, 43.

BOOK REVIEWS

Einführung in die Pharmazeutische Chemie (Introduction to Pharmaceutical Chemistry). By *O. E. Schultz*. Verlag Chemie, Weinheim 1978. xvi, 460 pp., 15 figs., 83 tables, bound, DM 56.00.

New textbooks on pharmaceutical chemistry are welcome, since there are not many of them in German. As is appropriate for an introduction, the author has made a representative selection of the most important pharmaceuticals. The book is divided into six sections: Central Nervous System, Peripheral Nervous System, Disinfectants, Substances for the Chemotherapy of Infections and Cytostatics, Organs, and Vitamins. Each chapter in these sections is introduced by a brief pharmacodynamic or biological characterization of the group of pharmaceuticals, at times with notes on the action mechanism or on structure-activity relationships. This is followed by a tabular summary of the substances with tradename, chemical name, formula, and international abbreviation; next come synthesis or source (natural products), qualitative tests (identity and purity), and quantitative determination, together with data on activity and application.

Even though it is assumed that the reader has some basic chemical knowledge, reference to the classical reactions of organic chemistry (*e.g.* named reactions) is often missing, as to a certain extent is the clear application of the concepts of tautomerism and resonance. There is a note in the foreword stating that in the analytical sections the procedures and requirements of DAB 7, EuPharm, and some other national pharmacopeias have been taken into account; nevertheless, detailed information should still have been given in the text. In the same way, notes on the areas of agreement and disagreement between the pharmacopeias mentioned would have been desirable. Further important aspects of pharmaceutical chemistry are the stability of pharmaceuticals and pharmacokinetic parameters; the latter could stimulate the synthesis of derivatives.

The development of pharmaceutical chemistry from a collection of random observations to a system of systematic research is not taken into account, though from the didactic viewpoint this is just as important as the listing of research workers who have made fundamental contributions to this multidisciplinary field of research. This type of information could have been included as footnotes or in a table.

There are also some inorganic pharmaceuticals (*e.g.* lithium carbonate) that have not been mentioned. In addition (and this is possibly due to the structure of the book), some important groups of pharmaceuticals get too short a mention (*e.g.* anticoagulants) or no mention at all (*e.g.* analeptics, pentetrazole).

The style of the book is good; the few errors in structural formulae could easily be corrected in a later edition. The over-all impression is that this "Introduction" has successfully extended the range of textbooks in the field of chemistry.

K. E. Schulte [NB 462 IE]

Transient Techniques in Electrochemistry. By *D. D. MacDonald*. Plenum Press, New York—London 1977. 1st edit., xii, 329 pp., numerous illustrations, bound, $ 45.00.

This book deals with the relaxation phenomena that may be observed at the electrodes of galvanic cells as the voltage or current changes with time. Since one can specify either the current or the voltage as external parameters in a large number of ways, a variety of experimental techniques has sprung up, so that it is difficult even for the expert to remember them all. In this book the author gives an ordered presentation of such techniques, and in particular chronoamperometry, chrono-potentiometry, cyclic voltammetry, and alternating-current methods. He places special emphasis on an explanation of the mathematical principles for the analysis of the reaction couplings that lead to relaxation phenomena. A good summary of the expected time lapses is provided, and this will prove

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0404-0334 $ 02.50/0*

very helpful to readers wishing to familiarize themselves with theoretical deviations.

The final aim of such studies is to obtain information on the mechanism of the electrode reactions concerned from the analysis of the relaxation process. However, the book is not very helpful in explaining which method is most suitable for a specific purpose. The techniques are arranged one after the other without any evaluation. One of the most effective techniques, the current-pulse method (coulostatic method) is not even mentioned. Practical examples are rare. The book is suitable for readers who enjoy clear mathematical derivations and who already have practical experience, or who are prepared to turn to other sources for advice.

Heinz Gerischer [NB 452 IE]

Biochemistry—The Chemical Reactions of the Living Cell. By *D. E. Metzler*. Academic Press, New York 1977, xxxii, 1129 pp., bound, $ 24.95.

The simple anatomical classification of physiological chemistry—chemistry here, metabolic chains there, and one or two appended chapters on hormones, body fluids, and organs—was a historical consequence of its predominantly medical alignment. General biochemistry appeared as biology became more and more aware of its chemical basis and the dynamic nature of the body's building blocks. It culminated in the clever idea of *Fruton* and *Simmonds* that proteins (as biocatalysts) should be the central teaching point, with physicochemical considerations and the structure and metabolism of other biological molecules grouped around them. The more successful of their followers hardly changed this principle of a predominantly biological functional point of view, but chose different aspects to emphasize. Thus, *Lehninger* made energetics and *Styrer* made molecular information the main theme, while *Mahler* and *Cordes* took as their starting point the physical chemistry of cellular processes. In principle, it is possible to break down the network of cellular organization from many aspects. Each of these books, however, set a standard, and any new attempt must be measured against its predecessors, although as far as the chemist is concerned they all lack the chemical perspective. A comprehensive textbook, which is intended to lead biochemistry systematically back to chemical concepts, will therefore unavoidably be regarded with critical curiosity.

Such an attempt has now been undertaken by *Metzler* with his monumental work, and the goal is impressively well achieved, for the author not only has available a wide range of material but is also given authority by his own work in the field of the transfer from chemical reaction models to biological catalysis. Since the book is intended for readers without much basic biological expertise, although it also makes provision for the biologist, it starts with an introduction to cellular structure, together with the fundamentals of molecular energetics and subject-related thermodynamics (all data are given in SI units). The interactions between biomolecules and the internal organization of the cell are treated in detail, and the characteristics of enzyme catalysis are discussed in relation to the chemical reaction types, which are admittedly rather limited[*]. This knowledge is applied to a detailed description of the metabolic process. Optical analytical techniques are accommodated in the chapter on photobiology. Nitrogen metabolism has a chapter to itself; so do biochemical genetics and metabolic homeostasis. At the end of each chapter there are study questions, some of them never likely to be answered. The text is very attractively printed and easy ro read, vividly supplemented by structural and reaction formulas, flowsheets, and tables; anecdotal information in green-colored boxes (shown in the same way in the table of contents) is added as a spice to the basic blend.

It is unavoidable that even a system as well thought out and consistently applied as this one should have its weaknesses. For example, it has recently become easier to give a clear chemical description of the role of selenium in metabolism, and the reason why the respiration chain phosphorylation cannot be chemically coupled in the given stoichiometry can now be given more intelligibly; the principal criticism that can be raised, however, is that today chemistry is capable of more than bending electron arrows or perfecting nucleophilic and electrophilic attacks. Chemistry has become a highly sophisticated extrapolating science, and I can see little sign of it here. Why, for example, is cobalt suitable as the central metal of vitamin B_{12}; what is the reason for the structure of the respiration chain (which has now been largely clarified); what is the salient point of the chemical osmosis hypothesis as against the "protonated membrane" hypothesis; what requirements must be met by a cofactor that takes up electrons and protons simultaneously but separately; how can we link molecular motion with the charge distribution? And so it goes on. But perhaps we are asking too much of a textbook that is already very extensive; we really need a new medium, allied to cinematography; words, even symbols, make everything static, two-dimensional, consecutive. However, what is such nitpicking when applied to an attempt designed on a grand scale, and in the final analysis so successful, which also, because of the many and carefully collated literature references, amounts to far more than a textbook? It would be wonderful if the book not only met with acclaim among chemists but were also used by biologists and introduced them to the chemical foundations of biochemistry. Our comparison of textbooks can be summarized as follows: *Stryer* for appearance—*Lehninger* for feeling—*Metzler* for understanding—but there is still no book on biochemistry that meets all the requirements.

L. Jaenicke [NB 460 IE]

Singlet Oxygen, Reactions with Organic Compounds and Polymers. Edited by *B. Rånby* and *J. F. Rabek*. John Wiley & Sons, New York, 1978. 1st edit., 331 pp., bound, £ 15.00.

"Singlet oxygen" ($^1O_2$) is the term used to describe two short-lived and reactive electronic excitation states of oxygen ($^3O_2$). The present book contains 34 papers presented at the EUCHEM conference on "Singlet Oxygen Reactions with Polymers", held in Södergarn, Sweden, in September 1976.

A historical survey is followed by papers on the properties of $^1O_2$ and on the spectroscopic determination and the deactivation of $^1O_2$ species in the gas phase. The greater part of the book (16 papers, 187 pages) is devoted to the reactions of $^1O_2$ in solution. The kinetics of the formation of $^1O_2$ by energy transfer from electronically excited sensitizers to $^3O_2$ is the main point of two contributions.—*Belluš* gives an excellent survey on the mechanism and the rate constants of the deactivation of $^1O_2$ by organic substrates (50 pages). This topic is further discussed in two other short papers. Attention should also be drawn to the review by *Gollnick* (24 pages) on the reactions of $^1O_2$ with organic compounds. This is followed by ten short papers (76 pages) on the photooxidation of selected compounds.

The last third of the book (14 papers, 114 pages) deals with the reactions of polymers with $^1O_2$ and is introduced

[*] In connection with this I recall *H. Meerwein*'s disapproving comment: How can you limit your interest to biochemistry if you want to be a proper chemist? There is an air of monotony about the few reactions that are found there: water in and water out; hydrogen out and back in again ... Keep well away from it. In contrast, how wide-ranging are the possibilities of synthetic catalysis!

by a review by *Rånby* and *Rabek* (13 pages). The main interest of the papers lies in the mechanism of photo-oxidation and photochemical degradation of polymers (polyenes, polydienes, polystyrene, lignin), and in the resultant changes of physical properties. Two final papers deal with the action of photostabilizers.

The book offers the specialist a survey of the whole range of work with $^1O_2$ as it was in about the middle of 1976. Anyone wanting a detailed introduction to a specific topic would, however, do better to consult other monographs and review articles.

Andreas Henne [NB 448 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Chemie und Hochschule. Beiträge zum Komplementaritätsdenken in Lehre und Forschung. By *H. Zollinger*. Birkhäuser Verlag, Basel 1978. 163 pp., paper, DM 24.00.—ISBN 3-7643-1044-8

A Perspective of Physics, Vol. 2. By *R. Peierls*. Gordon and Breach Science, London 1978. xxxiv, 259 pp., bound, £ 16.70.—ISBN 0-677-12400-7

Silicones under the Monogram. A Story of Industrial Research. By *H. A. Liebhafsky*. John Wiley & Sons, New York 1978. xiv, 381 pp., bound, $ 31.00.—ISBN 0-471-04610-8

Beiträge zur Forschungstechnologie. Sonderband 1. Forschung und Nutzen. Wilhelm Ostwald zur wissenschaftlichen Arbeit. Akademie-Verlag, Berlin 1978. xlviii, 278 pp., bound, *ca.* DM 38.00

Polymer Blends. Edited by *D. R. Paul* and *S. Newman*. Academic Press, New York 1978. Vol. 1: xv, 501 pp., bound, $ 47.50.—ISBN 0-12-546801-6; Vol. 2: xv, 435 pp., bound, $ 42.00.—ISBN 0-12-546802-4

Photoelectron Spectroscopy and Molecular Orbital Theory. By *R. E. Ballard*. Adam Hilfer, Bristol 1978. ix, 192 pp., bound, £ 18.00.—ISBN 0-85274-341-6

Organisch-chemische Arzneimittel und ihre Synonyma. By *M. Negwer*. Akademie-Verlag, Berlin 1978. 5th improved and revised edition. Vol. I: xv, 624 pp.; Vol. II: pp. 625—1273; Vol. III: pp. 1275—1863, bound, *ca.* DM 225.00 (for Vol. I—III)

Moderne Biowissenschaften. Band 11. Molekulare Matrizen. I. Evolution. Von *S. Hoffmann*. Akademie-Verlag, Berlin 1978. 115 pp., bound, *ca.* DM 22.00

Amino Acid Determination: Methods and Techniques. Edited by *S. Blackburn*. Marcel Dekker, New York 1978. 2nd improved and revised edition. x, 367 pp., bound, SFrs. 82.00.—ISBN 0-8247-6349-1

Transform Techniques in Chemistry. Edited by *P. R. Griffiths*. Heyden, London 1978. xviii, 385 pp., bound, £ 25.25.—ISBN 85501-0-173-4

Gmelin Handbuch der Anorganischen Chemie. Springer-Verlag, Berlin 1978. 8th Edit. Supplementary Vol. 9. Cm—Fr. xv, 292 pp., bound, DM 681.00.—ISBN 3-540-93374-3

Gmelin Handbuch der Anorganischen Chemie. Springer-Verlag, Berlin 1978. 8th Edit. Fe—Eisen. Part A. Section I. Gmelin-Durrer: Metallurgie des Eisens. 4th Edit. Also supplementary to Gmelin Handbuch System No. 59, "Eisen" Part A, Instal. 3 to 5. Vol. 6: Theorie der Stahlerzeugung (Vol. 6a: Text, Vol. 6b: Figures). 6a: xxvi, 232 pp., 6b: x, 158 pp. (2 volumes, which may not be purchased separately). Bound, DM 793.00.—ISBN 3-540-93366-2

Gmelin Handbuch der Anorganischen Chemie. Springer-Verlag, Berlin 1978. 8th Edit. Sc, Y. La—Lu—Seltenerdelemente. Part B: Die Elemente. Instalment 5: S, Y, La und Lanthanide: Darstellung, Anreicherung und Abtrennung der Isotope (Sc, Y, La bis Sm). xx, 152 pp., bound, DM 403.00.—ISBN 3-540-93371-9

Sc, Y, La—Lu—Seltenerdelemente. Part C: Die Verbindungen. Instalment 6: Sc, Y, La und Lanthanide: Bromide. Jodide. Entsprechende basische Halogenide. Salze der Halogensauerstoffsäure und Alkalidoppelsalze. xxx, 274 pp., bound, DM 653.00.—ISBN 3-540-93370-0

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstraße 12, D-6940 Weinheim, Germany, Telephone (06201) 14036. Telex 465516 vchwh d.

Editor: *O. Smrekar* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*). Pappelallee 3. P.O. Box 1260/1280, D-6940 Weinheim, Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 5
May 1979
Pages 337–420

Permeability of the Outer Membrane of Bacteria

By Hiroshi Nikaido[*]

The outer membrane of Gram-negative bacteria is an attractive system for the study of the structure-function relationships in biological membranes. This membrane has, *inter alia*, the task of regulating the inflow of nutrients and outflow of waste products. Investigations with the aid of mutants showed that there are at least two general pathways for the diffusion of small molecules across the outer membrane: one for hydrophobic and one for hydrophilic compounds. In the case of the "hydrophobic pathway" the hydrophobic compound dissolves in the interior of the membrane and then crosses the membrane in accordance with the partition coefficient. In wild-type forms of enteric bacteria this pathway cannot be used—presumably owing to the absence of regions with phospholipid bilayers. Small hydrophilic molecules, on the other hand, penetrate the membrane through water-filled pores.

1. Introduction

Bacterial cells are usually covered by cell wall, which is located outside the cytoplasmic membrane. Under the electron microscope, thin sections of Gram-positive bacteria usually reveal the cell wall as a thick, diffuse, structureless layer. It consists mainly of murein (peptidoglycan). In contrast, thin sections of Gram-negative bacteria, *e.g. Escherichia coli* and *Salmonella typhimurium*, show that their cell wall is composed of at least two layers, an outer layer ("outer membrane") that gives a trilaminar image resembling any other biological membrane, and an inner, structureless layer that corresponds to the main component of Gram-positive cell wall, the murein[1] which is mainly responsible for the mechanical strength of the wall (Fig. 1).

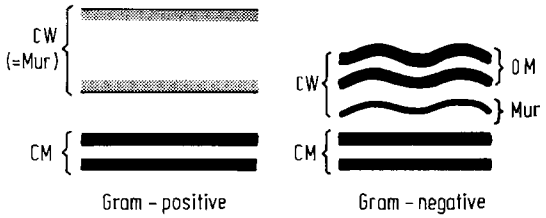


Fig. 1. Appearance of the surface layers of bacteria in thin sections. CW, cell wall; CM, cytoplasmic membrane; OM, outer membrane; Mur, murein (= peptidoglycan). Both Gram-positive and Gram-negative cells may contain extra layers of cell wall in addition to those shown here.

The outer membrane can be isolated from *E. coli* or *S. typhimurium*[2, 3], and was found to contain only a few major species of proteins (Fig. 2)[3–6]. These include (a) one to three proteins with molecular weights of 34000—36000, which are referred to as "porins", because they produce transmembrane diffusion channels (see Section 4), (b) usually one "heat-modifiable" protein (HMP, molecular weight of about 33000),

[*] Prof. Dr. H. Nikaido
Department of Bacteriology and Immunology
University of California, Berkeley, Calif. 94720 (USA)

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0337 $ 02.50/0

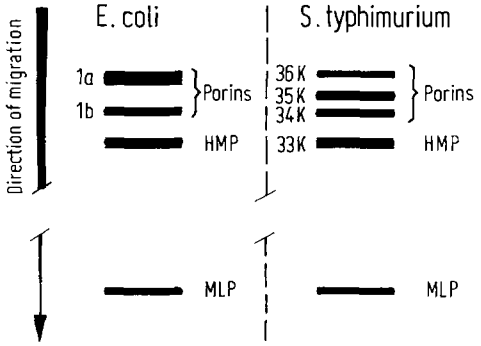


Fig. 2. Patterns of major proteins of the outer membrane as revealed by SDS-polyacrylamide gel electrophoresis. HMP, "heat-modifiable protein"; MLP, murein lipoprotein. Porins in *E. coli* have been called protein(s) 1, protein(s) I, "matrix protein", proteins b and c, and 0—9 and 0—8, in various laboratories. HMP in *E. coli* has been called protein 3a, II*, d, and 0—10. Porins in *Salmonella* have been called 36K, 35K, and 34K on the basis of their apparent molecular weights, and HMP, 33K (SDS = sodium dodecyl sulfate).

so called because its mobility in acrylamide gel electrophoresis changes in an unexpected manner upon heating, and (c) murein lipoprotein (MLP), a small protein containing 58 amino acid residues and covalently bound lipids[7]. About 30% of the lipoprotein is covalently linked to the underlying murein layer. It also contains two kinds of amphipathic molecules: phospholipids and lipopolysaccharides (LPS) (cf. also Fig. 15).

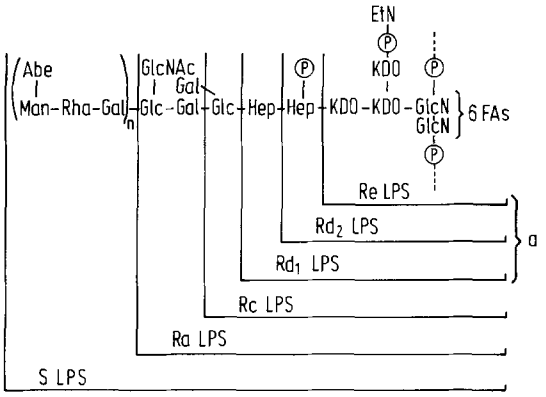


Fig. 3. Structure of lipopolysaccharides (LPS) from *S. typhimurium*. Biosynthesis proceeds generally toward the left in this figure. Thus wild-type cells complete the synthesis of the entire structure ("S-LPS"), whereas R mutants blocked at various steps of biosynthesis produce incomplete structures ("Ra through Re LPS"; a: deep rough mutants). Abbreviations: Abe, abequose; Man, D-mannose; Rha, L-rhamnose; Gal, D-galactose; GlcNAc, N-acetyl-D-glucosamine; Glc, D-glucose; Hep, L-*glycero*-D-*manno*heptose; P, phosphate; KDO, 3-deoxy-D-*manno*octulosonic acid (2-keto-3-deoxy-octonic acid); EtN, ethanolamine; and FA, fatty acid.

A series of genetic mutants producing LPS with variously defective polysaccharide chains are known; the structure of LPS produced by these mutants (Ra through Re) of *S. typhimurium* is shown in Figure 3[8, 9]. Mutants lacking one or more outer membrane proteins have recently been reported[10–14]. The availability of these mutants makes it possible to intentionally alter the composition of the membrane, and this possibility of "genetic engineering", together with the simple protein composition, makes the outer membrane an attractive system for the study of the structure-function relationships in biological membranes.

The lipid bilayer structure, in which the hydrocarbon chains are arranged approximately at right angles to the plane of the membrane and form its hydrophobic interior, seems to correspond to the basic continuum of the outer membrane as in other biological membranes. The data supporting this conclusion include the following:

(i) At least some of the lipid hydrocarbons of the outer membrane are arranged in one orientation, and the hexagonal quasi-crystalline packing of these chains disappears at high temperature through the process of cooperative "melting", as can be shown by X-ray diffraction[15, 16], as well as electron spin resonance performed after the insertion of spin-labeled probe molecules[17, 18].

(ii) With lipid bilayer membranes, freeze-fracturing produces cleavage in the center of the membrane[19]. Similar cleavage of the outer membrane has been observed repeatedly[20–23].

The major function of the outer membrane apparently is to serve as a penetration barrier and to protect the underlying murein layer from attack by hydrolytic enzymes (such as lysozyme) that are prevalent in Nature. This is suggested by the observation that during evolution the structure of the murein has undergone a tremendous diversification in Gram-positive bacteria, presumably owing to the selective pressure for novel, hydrolase-resistant structures, whereas in Gram-negative bacteria there is no sign of such an evolutionary diversification of the murein structure[23, 24]. The outer membrane should, however, also allow the passage of nutrients and waste products, *i.e.* it should possess a selective permeability, and in this respect should be similar to many other biological membranes. In the latter membranes, however, the transmembrane diffusion is often accomplished by the process of active transport, a process unlikely to operate in the outer membrane because of its location outside the cytoplasmic membrane.

Up to 1975 only a few scattered observations had been published on the selective permeability of the outer membrane. Thus, careful kinetic studies of the exit of β-galactosides from *E. coli* cells revealed the presence of a partial diffusion barrier "outside the cytoplasmic membrane"[25]. *Payne* and *Gilvarg*[26] found that *E. coli* could not utilize peptides exceeding a certain size limit, presumably because they were excluded by "a barrier located outside the cytoplasmic membrane". Since these results told us little about what molecules are excluded by, and what kind of molecules diffuse through, the outer membrane, or about the mechanisms involved in their exclusion or penetration, we decided to define systematically the selective permeability properties of the outer membrane, using mostly *S. typhimurium* and *E. coli*. But before such an attempt was undertaken, it was essential to know whether there are one or more pathways of transmembrane diffusion operating in the outer membrane. Studies on LPS mutants[27, 28] provided an important clue to this question.

2. Multiplicity of Diffusion Pathways

The availability of mutants with defined biochemical defects in LPS synthesis[8, 9] (Fig. 3) made it possible to experimentally alter the structure of a component of the outer membrane, and to study the effect of such alterations on the permeability of the membrane. These studies, initiated by *Roantree* and *Stocker*[27] as well as *Schlecht*, *Schmidt*, and *Westphal*[28], revealed the following: (a) Wild type strains of *Salmonella*,

E. coli, and other related bacteria are naturally sensitive to a number of antibiotics including neomycin, cycloserine, ampicillin, and cephalothin. The sensitivity to these antibiotics was not affected much by alterations in LPS structure. (b) On the other hand, these strains are much more resistant than most Gram-positive bacteria to some other antibiotics including actinomycin D, erythromycin, novobiocin, and rifamycin SV, to such dyes as crystal violet, and to such detergents as bile salts and sodium dodecyl sulfate. The sensitivity to these agents, however, increases drastically in "deep-rough" mutants of *Salmonella*[27,28] and *E. coli*[29] that produce extremely defective LPS of Rd_1, Rd_2, and Re-type (Fig. 3), and approaches the level seen in Gram-positive bacteria.

In addition to the approach described above, the structure of the outer membrane can be altered by removing up to 50% of LPS molecules by treating *Salmonella* or *E. coli* cells briefly with ethylenediaminotetracetic acid (EDTA)[30]. *Leive*[31] discovered that the partial removal of LPS increases the sensitivity of the organism toward actinomycin D. Subsequent studies[32] showed that the treated cells became sensitive also to polymyxin, novobiocin, rifampicin, long-chain fatty acids, and detergents.

Since the outer membrane is the only subcellular structure that contains LPS in substantial amounts[2,3], and since the targets of action of antibiotics and dyes examined are usually located in the cytoplasmic membrane or in the cytoplasm, the results described above suggest that the outer membrane normally acts as penetration barrier for certain kinds of molecules and that this barrier function can be diminished by the mutational alteration of LPS or by the removal of LPS with EDTA. Furthermore, the presence of another group of agents whose efficacy is not influenced by mutations in LPS synthesis suggests the multiplicity of the mechanism of diffusion across the outer membrane: thus there would be at least one diffusion pathway that is influenced by the structure or the amount of LPS in the outer membrane, and at least another that is not.

How, then, is any compound assigned to one of these pathways? A review of the structure of various compounds tested suggested to us that the compounds whose efficacy is increased in deep rough mutants and in EDTA-treated cells are usually hydrophobic. When the hydrophobicity of these compounds was determined quantitatively by measuring their partition coefficients in 1-octanol/phosphate buffer (pH 7.0), it was indeed found that the greater number of them had partition coefficients higher than 0.07[33] (Table 1). In contrast, the majority of the compounds whose efficacy was unaffected by LPS structure were quite hydrophilic, with partition coefficients lower than 0.02[33] (Table 1). The simplest explanation of these results is as follows: (a) There are at least two *general* pathways for the diffusion of small molecules across the outer membrane, one for hydrophilic compounds, and one for hydrophobic compounds. (b) The "hydrophilic pathway" is not affected much by the structure of LPS present. (c) The "hydrophobic pathway" is almost inactive in wild type strains producing complete LPS; it becomes fully active only in deep rough mutants or in EDTA-treated cells. The nature of this hydrophobic pathway is described in the next section.

Table 1. Hydrophobicity, molecular weight and relative efficacy (based on wild type = 1) of inhibitors against deep rough mutants [a].

Inhibitor Agent	Rel. efficacy	Hydrophobicity [b]	Mol. wt.
Actinomycin D	≥10	>20	1255
Novobiocin		>20	613
Phenol		>20	94
Crystal Violet		14.4	408
Rifamycin SV		8.8	698
Malachite Green		4.2	365
Nafcillin		0.31	414
Oxacillin		0.07	418
Vancomycin		> 0.01 [c]	≈3300
Penicillin G	0.5—1.0	0.02	334
Ampicillin		> 0.01	349
Cephalothin		> 0.01	395
Carbenicillin		> 0.01	378
Neomycin		> 0.01	615
Cycloserine		> 0.01	102
Chloramphenicol		12.4 [c]	323
Tetracycline		0.07 [c]	444

[a] Modified after ref. [33]. [b] Determined in a system containing equal volumes of 1-octanol and 0.05 M sodium phosphate buffer (pH 7.0) at 24°C. [c] For unknown reasons, these compounds do not follow the general tendency.

3. Barrier Properties against Hydrophobic Molecules

3.1. Measurement of Transmembrane Diffusion Rates

Most biological membranes are known to allow the transmembrane diffusion of small, hydrophobic compounds[34]; the outer membrane of deep rough mutants apparently behaves in a similar manner. In contrast, the results described in the preceding section suggest that the outer membranes of wild type *Salmonella* and *E. coli* constitute an exception in that they are not penetrated by many hydrophobic compounds.

These conclusions, however, were based on the inhibitory effects measured by using whole cells, and we could only infer that the difference in sensitivity reflected differences in penetration rates. A more direct approach was taken by *Gustafsson et al.*[35], who showed that the rates of uptake of crystal violet by intact cells were dependent on the nature of LPS present. These results, however, were complicated by the massive adsorption of the dye to unidentified cellular constituents. We have overcome this difficulty by using a high concentration of a semi-synthetic penicillin, nafcillin, as the permeant[33]. When nafcillin was added to thick suspensions of the cells of deep rough mutants, its extracellular concentrations at time $t=0$ and $t=\infty$ (actually 5 to 10 min at 22°C), determined on supernatants after centrifugation, were equal to those predicted on the assumption that nafcillin existed only in the extracellular space at $t=0$ and was distributed uniformly in extracellular and intracellular spaces at $t=\infty$. Adsorption, degradation, or active transport was therefore negligible under these conditions. Furthermore, the kinetics of diffusion followed a theoretical equation, and first-order rate constants for permeation could thus be calculated. These quantitative diffusion assays led us to the following conclusions[33]: (a) Permeation through the cytoplasmic membrane (measured with sphaeroplasts[*]) was at least ten times more rapid than the penetration rates into intact deep rough mutant cells. Thus in whole cells the permeation through the outer

[*] Sphaeroplasts are formed in the case of Gram-negative bacteria, *e.g.* by the action of lysozyme plus EDTA.

membrane is the rate-limiting step. (b) The permeation rate constants were low in the wild type (S) as well as in Ra and Rc mutants (see Fig. 3), but were much higher in deep rough (*i.e.* Rd_1, Rd_2, and Re) mutants (Fig. 4).

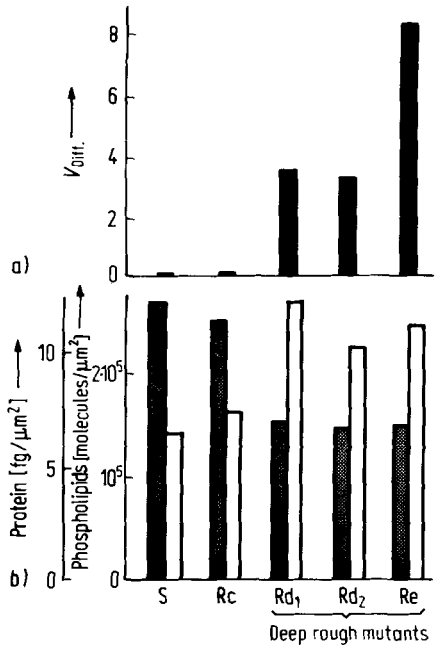


Fig. 4. a) Rate of diffusion of a hydrophobic solute, nafcillin, across the outer membranes of *S. typhimurium* strains (arbitrary units); b) composition of the outer membrane in these strains (after [22]). Rates of diffusion into intact cells were actually determined, but they reflect the diffusion rates across the outer membrane [33]. The diffusion rate does not increase significantly even when about 90% of the saccharide residues are lost as in the Rc mutant, but increase suddenly in correspondence with the increase in phospholipid content (and decrease in protein content) occurring in the deep rough mutants. In b), open and stippled bars represent phospholipids and proteins, respectively.

3.2. Mechanism of Diffusion of Hydrophobic Compounds

The mechanism of transmembrane diffusion of hydrophobic molecules has been studied extensively since the pioneering work of *Collander* and *Bärlund*[36], and it is known that the diffusion rates are faster with molecules of smaller size, with those of higher hydrophobicity, and at higher temperature[34,37–39]. The critical analysis of these results suggested that the permeant molecules first dissolve in the hydrophobic interior of the membrane, diffuse through the thickness of the hydrocarbon layer, and then cross the membrane by partitioning into the aqueous phase on the other side of the membrane[37]. In order to test whether hydrophobic substances penetrate through the outer membrane of deep rough mutants by a similar mechanism, we measured the influence of various conditions on diffusion rates, and obtained the following results: (a) Among compounds of similar size, the diffusion rate was faster with the more hydrophobic compounds. (b) The diffusion rates were extremely dependent on temperature, with a Q_{10} value (ratio of the rates at T°C and $(T-10)$°C) close to 10. (c) Compounds with fairly large size apparently penetrated the outer membrane by this mechanism, and there was no indication of a clear-cut size limit. These results strongly suggest that the hydrophobic compounds cross the deep rough outer membrane through dissolution into the membrane interior.

3.3. Structural Basis for the Lack of Permeability toward Hydrophobic Compounds

We have seen that the outer membrane of the wild type *Salmonella* is essentially impermeable to hydrophobic compounds. This is surprising, since small hydrophobic molecules diffuse rapidly across artificial phospholipid bilayers as well as most biological membranes[34,40]. Our first explanation was that the hydrophobic molecules could not diffuse through the hydrophilic surface layer that is composed of the saccharide chains of LPS. However, the outer membrane of Rc mutants, which are missing 80—90% of the saccharide residues found in the wild type (Fig. 3), is still impermeable to hydrophobic antibiotics, whereas Rd_1 mutants, which lack only one more sugar residue in LPS in comparison with Rc mutants (Fig. 3), produce an extremely permeable membrane. Thus there is a sudden and discontinuous increase in the hydrophobic permeability (Fig. 4a) when we compare strains producing LPS with saccharide chains of gradually diminishing chain length; these results are difficult to explain with the hypothesis presented above.

An important observation that later led us to an alternative hypothesis was made by *G. F.-L. Ames* in 1974[5]. She found that the protein content of the outer membrane remains more or less constant as the length of the saccharide chain of LPS becomes progressively shorter, down to the level of Rc LPS, but decreases suddenly and drastically in deep rough (*i.e.* Rd_1, Rd_2, and Re) mutants. A similar observation was made on an Re mutant of *E. coli* by *Koplow* and *Goldfine*[41]. Since some of the proteins presumably penetrate into the hydrophobic interior of the membrane, we expected that the reduction in proteins might be compensated for by an increase in either phospholipids or LPS. Quantitative analysis of outer membrane components in mutants producing Rc-, Rd_1-, Rd_2-, and Re-type LPS indeed revealed that in deep rough mutants there was a compensatory increase in phospholipids (Fig. 4b), while the number of LPS molecules per unit area of the outer membrane remained constant[22]. Furthermore, the absolute amount of phospholipids in the outer membrane of S and Rc strains was slightly less than that which was necessary to cover one side of the membrane as a monolayer. It was also known that practically all of the LPS molecules were located in the outer half of the outer membrane[42,43]. These results suggested a possible model in which the phospholipid molecules are distributed in an extremely asymmetrical manner in the outer membranes of S and Rc strains, being present *only* in the inner leaflet, the outer leaflet containing essentially only proteins and LPS molecules (Fig. 5a). Since this structure does not contain any phospholipid bilayer region, it can explain the lack of penetration by hydrophobic compounds if one assumes that these compounds cannot penetrate through the hydrophilic surface regions of the proteins and the hydrocarbon regions of LPS. The low permeability of the latter regions can be explained as follows: The hydrocarbon chains of LPS are likely to be tightly clustered together because at least six chains are connected to a single backbone structure and because unsaturated fatty acids are entirely absent. This idea is supported by spin labeling studies which showed that the motion of the segments of LPS hydrocarbon chains near the carboxyl end is severely restricted[18]. It is also consistent with the monolayer studies of *Romeo et al.*[44], who found

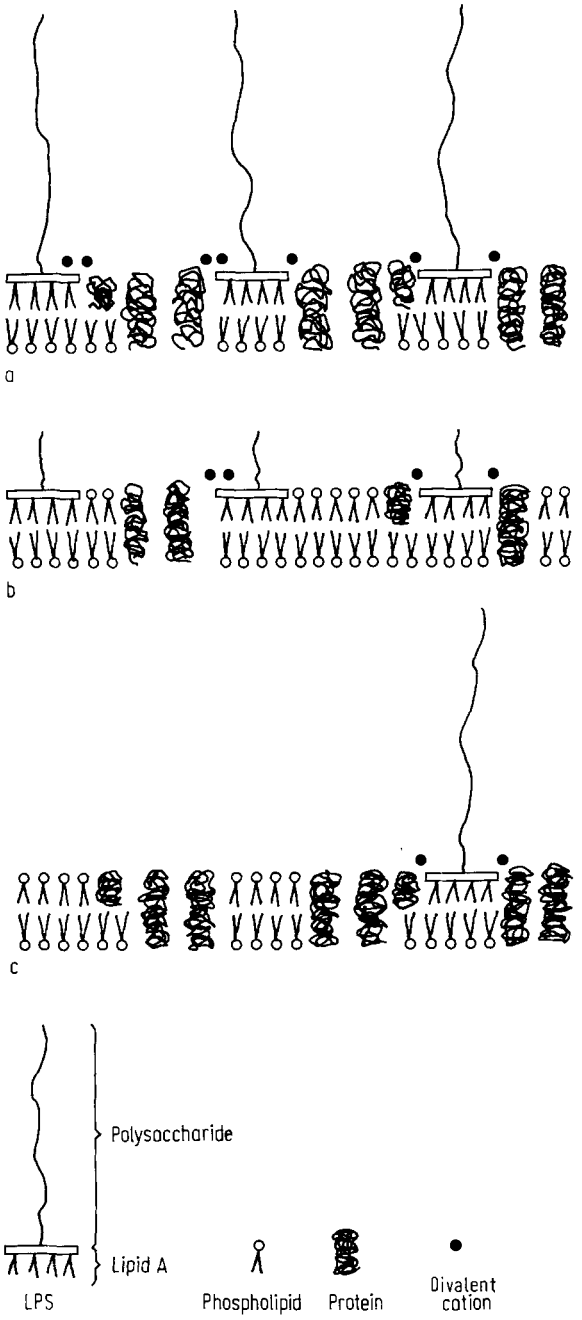


Fig. 5. Schematic structure of the outer membrane of *E. coli* and *S. typhimurium*. a) Wild type strains. b) "Deep rough" mutants producing LPS of Rd- or Re-type. c) Wild type strains after EDTA treatment (for details see text).

a smaller cross-sectional area for LPS hydrocarbons than for phospholipid hydrocarbon chains. Since a major portion of the resistance in the transmembrane diffusion of hydrophobic compounds arises because of the difficulty in making a hole between the associated hydrocarbon chains[39], it is easily seen that the presence of the tightly clustered hydrocarbon chains of LPS will drastically slow down the permeation process.

In deep rough mutants, the extremely abbreviated structure of LPS presumably hinders the proper interaction between LPS and proteins at the time of outer membrane assembly. This results in the decreased incorporation of outer membrane proteins, which in turn produces a compensatory increase in phospholipids, some of which are now found in the outer half of the membrane (Fig. 5b). Hydrophobic molecules can obviously diffuse through the "phospholipid bilayer" regions of this membrane.

The treatment of wild-type cells with EDTA releases LPS or LPS-protein complexes[30,45]. This selective removal of the components of the outer half of the membrane is presumably quickly followed by the flip-over of phospholipids from the inner half, or by the lateral diffusion of phospholipids from the inner membrane in a manner similar to that described by *Jones* and *Osborn*[46]. Thus "phospholipid bilayer" regions are generated also in this case (Fig. 5c), and the outer membrane will become permeable to hydrophobic molecules.

In order to examine whether phospholipid molecules are indeed distributed asymmetrically as predicted by our model, several experiments were performed[47]. In one approach, we attempted labeling the exposed head groups of phosphatidylethanolamine, the major phospholipid of *E. coli*, with a covalent labeling reagent. Since most of the previously developed "non-penetrating" reagents were expected to pass through the aqueous pores of the outer membrane (see Section 4) owing to their small size, we used BrCN-activated dextran as the covalent labeling reagent for amino groups (Fig. 6).

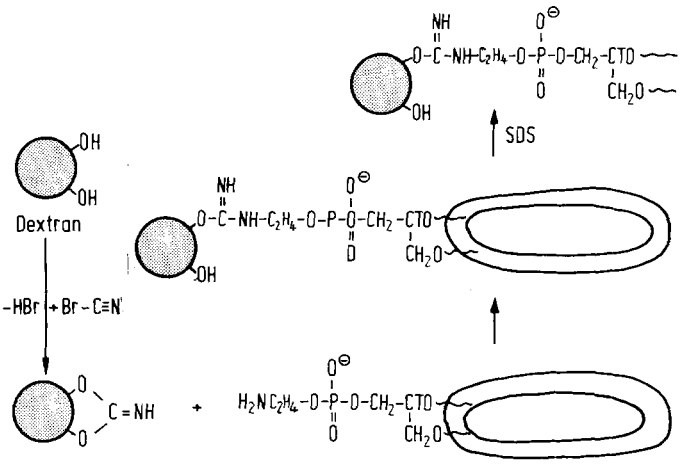


Fig. 6. Covalent labeling of phosphatidylethanolamine head groups on cell surface with a macromolecular reagent [47]: Soluble dextran was "activated" by treatment with CNBr, and the reagent was added to a suspension of intact bacterial cells. If phospholipids, the major portion of which is phosphatidylethanolamine in *Salmonella*, are located in the outer half of the outer membrane (cf. Fig. 5b), the reagent will become bound to the ethanolamine portion of the phospholipid through an amidine linkage. The dextran-phospholipid complex can be quantitated after dissolving the cells with SDS.

When intact cells were incubated with this reagent, with deep rough mutants a significant fraction of total cellular phospholipids became linked to the activated dextran in the medium, whereas with an S or Rc strain no such labeling took place. It must be emphasized that these results are difficult to explain in terms of the possible steric hindrance by the saccharide chains of LPS, as the transition occurred precipitously following the loss of a single sugar residue (compare Rc with Rd_1, Fig. 3).

The presence of this rather extreme form of asymmetry, LPS outside and phospholipids inside, is also supported by other observations: (1) Freeze-fracture of the outer membrane of *E. coli* and *S. typhimurium*[20,22] reveals a concave fracture face densely filled with particles, the major constituent of which was shown to be proteins (Fig. 7)[22]. In *Pseudomonas*

aeruginosa similar particles seen on the concave fracture face appear to be protein-LPS complexes, since EDTA treatment

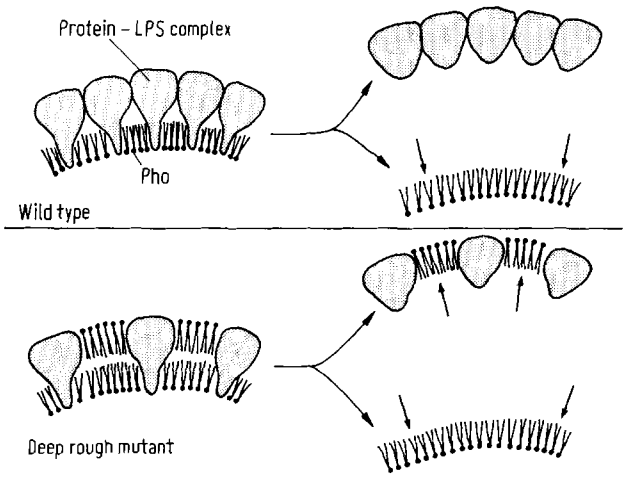


Fig. 7. Outer membrane after freeze-fracturing (schematic). When ice blocks containing cells are fractured, the fracturing occurs frequently through the middle of the membrane. This generates characteristic appearances on fracture faces. Thus the presence of smooth fracture faces (arrows), characteristic of the fractured halves of phospholipid bilayers, are seen on convex faces as well as on the concave face of deep rough mutants, but not on the concave face of the wild type cells.

which releases such complexes from the whole cell[45] results in the disappearance of a major fraction of these particles[21]. Thus it seems likely that the outer half of the outer membrane (corressponding to the concave fracture face) of *E. coli* and *Salmonella* is filled with protein-LPS complexes (or "particles"). It should be emphasized that smooth faces corresponding to the phospholipid monolayer were found abundantly on the convex face, but not on the concave face. However, such smooth faces were prominently seen on the concave fracture faces of deep rough mutants (Fig. 8)[23]. (2) Electron spin resonance studies with spin-labeled probes show that the hydrocarbon chains of LPS have rather low fluidity. Thus artificial mixed bilayers, with LPS molecules interdigitated among phospholipid molecules, exhibit significantly lower fluidity than the bilayers made of phospholipids alone[18]. Yet phospholipid hydrocarbon chains in the outer membrane have a level of fluidity very similar to that in the cytoplasmic membrane[16, 18], a result indicating that phospholipids in the outer membrane occupy a domain completely separated from LPS. This conclusion was also supported by the determination of the size of domains by exchange broadening of electron spin resonance line widths[18].

The low permeability of the outer membrane of wild type *E. coli* or *Salmonella* to hydrophobic molecules must confer an enormous selective advantage on these organisms, by making them resistant to bile salts and long-chain fatty acids that must be abundant in their usual habitat, the mammalian intestinal tract. There is no obvious reason, however, that all Gram-negative bacteria should produce hydrophobe-impermeable outer membranes. In fact, some non-enteric Gram-negative bacteria, for example *Neisseria gonorrhoeae*, are extremely sensitive to such hydrophobic agents as erythromycin, rifampin, acridine orange, and ethidium bromide[48], and it can be expected that these bacteria have an outer membrane of the phospholipid-bilayer-type.

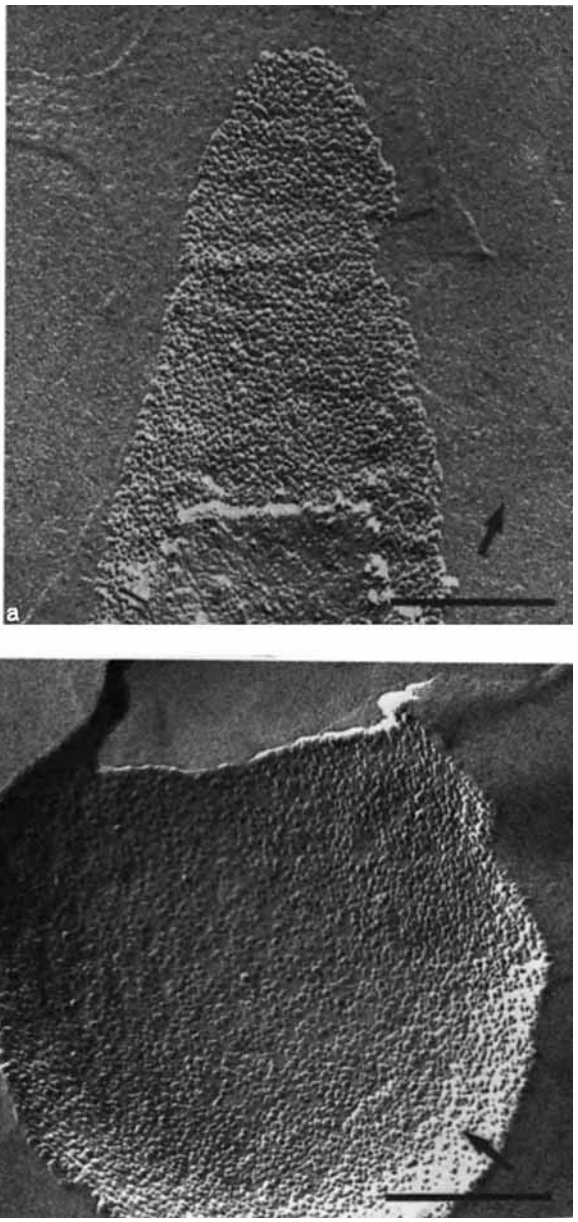


Fig. 8. Freeze-fracture electron micrographs of the concave faces of the outher membrane [22]. a) Wild-type *Salmonella typhimurium*. b) A deep rough mutant, TA2168. Note the "smooth" space between the "particles". The bar corresponds to 0.2 μm. The arrow shows the direction of metal shadowing. (Reproduced by permission of the American Society for Microbiology.)

4. Non-Specific Permeability toward Small, Hydrophilic Molecules

4.1. Equilibrium Studies with Intact Cells

Gram-negative bacteria are sensitive to a number of hydrophilic antibiotics (Table 1), which must penetrate through the outer membrane in order to reach their targets of action. Similar diffusion is required also for nutrients including sugars, amino acids, and inorganic salts, as well as for waste products of metabolism. These compounds penetrate through by a mechanism different from the "hydrophobic pathway" (Section 2), and we postulated the existence of a separate, hydrophilic pathway, a mechanism presumed to operate fully in wild type as well as in deep rough mutants. We studied the proper-

ties of this postulated pathway by using oligosaccharides as permeants[49].

In order to study the penetration through the outer membrane, it was necessary to use oligosaccharides that neither penetrated through nor were actively transported across the cytoplasmic membrane. Oligosaccharides of the saccharose-raffinose series fulfilled these conditions in *S. typhimurium*, and were used in most of our experiments. Since the space between the outer membrane and the cytoplasmic membrane (*i.e.* the "periplasmic space") is small, the diffusion into this space was difficult to measure[50]. We therefore expanded this space by "plasmolyzing" cells in 0.3 to 0.5 M NaCl or in 0.5 M saccharose solution[49]. Under these conditions, 40—50 % of the cell volume was occupied by the periplasmic space, and the extent of penetration of oligosaccharides into this space could easily be measured (see Fig. 9).

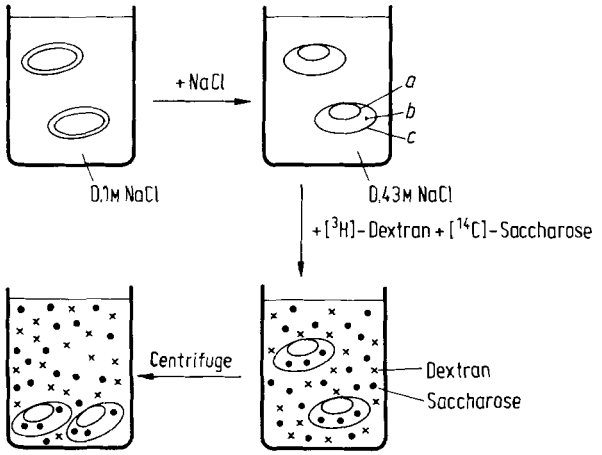


Fig. 9. Determination of permeability to oligosaccharides using plasmolyzed cells. Intact bacterial cells are suspended in a moderately concentrated solution of NaCl or saccharose. These solutes cross the outer membrane, but cannot penetrate through the cytoplasmic membrane (a). Water therefore flows out of the cytoplasm; the cytoplasm shrinks, but the mechanically rigid cell wall (c) does not, and in the "plasmolyzed" cell the space between the cell wall and cytoplasmic membrane ("periplasmic space" (b)) is greatly expanded. Addition of [^{3}H]-dextran and [^{14}C]-saccharose results in the penetration of saccharose, but not dextran, into the periplasmic space. This can be quantitated by centrifuging the cells down and by determining the ^{14}C- and ^{3}H-contents of the supernatant as well as the cell pellet.

These studies showed the existence of a clear size limit in the penetration process through this pathway[49]. Saccharose (342 daltons) and raffinose (504 daltons) penetrated fully into the periplasmic space after 5 min incubation at room temperature, but stachyose (666 daltons) and larger oligosaccharides showed only partial penetration. The partial penetration was apparently due to diffusion into damaged cells[49], and we conclude that the cell wall of *S. typhimurium* is permeable to a disaccharide (saccharose) and a trisaccharide (raffinose), but is essentially impermeable to tetrasaccharides and higher oligosaccharides. There thus seems to be a sharp exclusion limit around 550—650 daltons for the raffinose series of oligosaccharides.

It was gratifying to note that these results were consistent with the results of a pioneering study by *Payne* and *Gilvarg*[26], who found that peptides larger than about 600—650 daltons could not enter *E. coli* cells. However, neither the investigations by *Payne* and *Gilvarg* nor our results described above told us which of the two layers of the cell wall, the outer membrane and murein, acted as the limiting barrier for the penetration of hydrophilic molecules. Our later studies, however, clearly showed that the outer membrane, rather than the murein layer, acted as a limiting molecular sieve[52]. In one series of experiments, for example, the murein layer was degraded by lysozyme treatment or by growth in the presence of penicillin. The plasmolyzed cells or sphaeroplasts produced from these bacteria still showed the same molecular sieving properties seen before, despite absence of the intact murein layer.

How do the hydrophilic molecules pass through the outer membrane? As stated earlier, a mechanism involving dissolution in the membrane interior is impossible, as this would require breaking very many hydrogen bonds between the oligosaccharides and water molecules, thermodynamically a very unfavorable operation. The only possible mechanisms seem to be diffusion through water-filled pores, and carrier-mediated diffusion. We found that diffusion of oligosaccharides through the outer membrane was extremely rapid even at 0 °C[49], and this observation as well as the identical size limit for widely different kinds of compounds seemed to favor the aqueous pore mechanism. We sought a more definitive answer to this question through reconstitution studies, as described in the next section.

4.2. Reconstitution Studies

When the outer membranes are dissociated by detergents and then the detergents are slowly removed in the presence of Mg^{2+}, one observes the reformation of structures morphologically resembling the outer membrane[53]. These experiments established that the supramolecular structure of the outer membrane was ultimately determined by the structure and properties of the component molecules. However, they did not throw much light on the nature of interaction between the component molecules, or on the functions of individual components.

We carried out reconstitution experiments in order to determine the components that are responsible for the characteristic hydrophilic permeability of the outer membrane. Since both the hydrophilic permeability and the presence of LPS are unique attributes of the outer membrane, we first examined the possibility that LPS might be involved in the formation of pores. We prepared liposomes containing both LPS and phospholipids in the bilayer structure, by resuspending a dried film of phospholipids in an aqueous suspension of LPS, as described by *Kinsky et al.*[54]. These liposomes, bound by the mixed phospholipid-LPS bilayer were, however, as impermeable toward hydrophilic compounds as the liposomes made only of phospholipids[55]. These results led us to the alternative hypothesis that outer membrane proteins play an essential role in the formation of pores. This hypothesis was tested in our laboratory[56] by making liposomes in the presence of outer membrane proteins. For this purpose, the outer membrane proteins were extracted with the aid of detergents. Removal of detergents by extensive dialysis resulted in the precipitation of proteins, which were then recovered by centrifugation and resuspended in an aqueous buffer by sonication. Membrane vesicles were reconstituted by adding this protein suspension and an aqueous suspension of LPS to a dried film of phospholipids (Fig. 10). When the reconstitution medium contained both [^{3}H]-dextran and [^{14}C]-saccharose, both compounds were presumably present in intravesicular as well

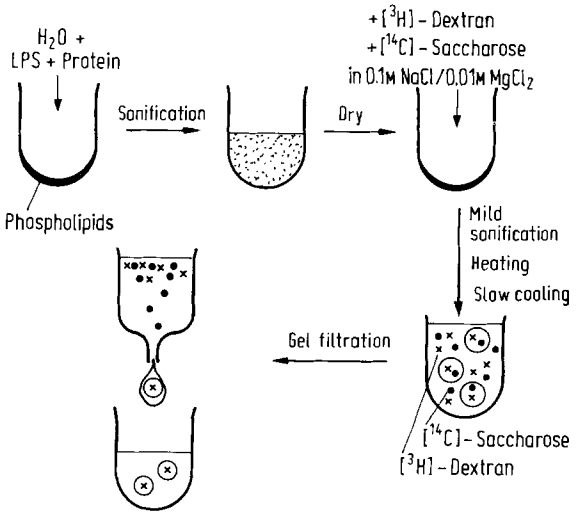


Fig. 10. Reconstitution of outer membrane vesicles. A dry film of phospholipids is resuspended with an aqueous suspension of LPS and proper proteins. After sonication to produce maximum dispersion and mixing, the mixture is dried as a film, and then resuspended in a salt solution containing [^{3}H]-dextran and [^{14}C]-saccharose. Heating and slow cooling of the suspension are carried out to ensure the maximal sealing of vesicles and the optimal rearrangement of membrane components. The vesicles, presumably containing both [^{3}H]-dextran and [^{14}C]-sucrose inside, are then applied onto a gel filtration column. They quickly become separated from the solutes in the extravesicular fluid. In addition, if the vesicle membrane is permeable to saccharose but not to dextran, [^{14}C]-saccharose will diffuse out of the vesicles during filtration, and the vesicles collected at the void volume will show a much higher $^3H/^{14}C$ ratio than the dextran-saccharose mixture originally added to the reconstitution system (see also Table 2).

as extravesicular space. When the vesicles were then separated from the medium by gel filtration through Sepharose 4B, a large portion of intravesicular [^{14}C]-sucrose diffused out through the protein-containing membrane during the filtration step, so that the $^3H/^{14}C$ ratio of the recovered liposome preparation was usually several times higher than the $^3H/^{14}C$ ratio in the initial reconstitution mixture. A control mixture lacking proteins produced liposomes essentially impermeable to saccharose, that is with hardly any increase in the $^3H/^{14}C$ ratio. In another control experiment, proteins from the red blood cell membranes of sheep were completely inactive in the production of saccharose-permeable pores. We conclude from these results that outer membrane proteins are essential in the formation of water-filled pores.

We then used partially purified preparations of outer membrane proteins for reconstitution, in order to identify the protein(s) involved in pore formation[57]. Treatment of *S. typhimurium* cell envelope with SDS at 37 °C leaves behind an insoluble complex that contains murein with covalently linked lipoprotein, as well as the major proteins of 34000—36000 daltons, *i.e.* the porins[58]. We found that the SDS-insoluble complex was much more active than the SDS-solubilized proteins in producing the pores. We then degraded the former with lysozyme and fractionated the products by gel filtration in SDS. This produced a protein aggregate containing only the porins from *S. typhimurium*[57] or from *E. coli* K12[59], and a similar oligomer composed only of the 36500 dalton porins from *E. coli* B[60], all of which were extremely active in producing pores in the reconstitution experiments (Table 2). *Inouye*[61] has proposed, on the basis of theoretical considerations, that oligomers of murein lipoproteins may contain aqueous channels in the center and thus produce pores by

Table 2. Result of a typical reconstitution experiment [a].

	[^{3}H]-Dextran [cpm]	[^{14}C]-Saccharose [cpm]
Activity in the reconstitution mixture	240000	260000
Activity in the vesicles after gel filtration		
Exp. I (without porin)	2400	2100
Exp. II (with porin oligomers, 10 μg)	3350	<30

[a] Membrane vesicles were reconstituted from 0.8 mg LPS and 0.8 mg phospholipids in the presence of [^{3}H]-dextran and [^{14}C]-saccharose, with or without porin oligomers [57]. Vesicles were recovered after gel filtration, which removed radioactive saccharides that were able to diffuse out through the vesicle membrane (see Fig. 10).

penetrating through the thickness of the outer membrane; our active complex, however, contained very few lipoproteins. In fact, the porin oligomer prepared from a lipoprotein-deficient mutant[14] of *E. coli* K12 was fully active[60]. Furthermore, aggregates containing mostly lipoproteins and little porin were only very weakly active in pore formation, and purified lipoprotein was completely inactive.

The pores produced by the addition of porins had the expected size, in that they allowed a free diffusion of saccharose and raffinose yet essentially excluded stachyose and larger oligosaccharides. The vesicles formed were also permeable to a wide variety of small, hydrophilic molecules, including galactose, glucosamine, glucose 1-phosphate, lysine, tryptophan, uridine, UMP, GDP, and polyethyleneglycol (600 daltons), but not to polyethyleneglycol (1540 daltons)[57]. Since complexes containing only one or three protein species can produce permeability to such a wide variety of substances, the mechanism of diffusion cannot be the facilitated diffusion that requires a specific carrier protein for each compound. This lack of specificity is indeed one of the strongest pieces of evidence suggesting the involvement of aqueous pores.

The channel-forming ability of the porin has recently been confirmed by a different approach. *Benz et al.*[62] added an extremely dilute (*e.g.* 0.5 ng/ml) solution of *E. coli* B porin to the aqueous solution in which a planar lipid bilayer membrane was bathed. Interestingly, the conductance increased in a stepwise manner, and the single incremental step of 1.7 nanosiemens (in 1 M KCl) was interpreted as resulting from the insertion of one molecule or oligomer of the porin into the membrane.

Reconstitution of hydrophilic pores has also been achieved by using outer membrane proteins of species other than *E. coli* or *S. typhimurium*[63,64]. A partial reconstitution from isolated phospholipids, LPS, and a small amount of outer membrane fragments has recently been performed by using components from *P. aeruginosa*[65]. Interestingly, the results suggest that the exclusion limit of *P. aeruginosa* pores is several thousand daltons, much higher than in the enteric bacteria.

4.3. Determination of Diffusion Rates with Intact Cells

If all the pores in the outer membrane are surrounded by porin molecules, the mutational loss of the porin is expected to be lethal. However, the loss of these proteins[11,13], or of all "major" proteins[12], did not produce any marked reduction in growth rates. The solution to this puzzle was provided in 1977 by studies utilizing two different methods of approach. Both of these methods enabled us to estimate the *rates* of

diffusion across the outer membrane, rather than the *equilibrium distribution* of solutes described previously (Section 4.1). In addition we gained new insights into the function of the outer membrane pores.

As described already, the diffusion rates across the outer membrane were too rapid to be measured with the equilibrium method described earlier. *Zimmermann* and *Rosselet*[66] recently devised an elegant method to measure these rates. They measured the rates of hydrolysis of β-lactam antibiotics (such as penicillins and cephalosporins) by intact cells as well as by broken cells of *E. coli*, containing a β-lactam-degrading enzyme, β-lactamase, in the periplasmic space. Thus, with intact cells the rate of diffusion across the outer membrane should be balanced, at the steady state, by the rate of hydrolysis in the periplasmic space. *Zimmermann* and *Rosselet*[66] made

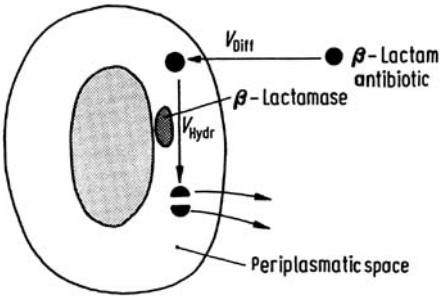


Fig. 11. Method of *Zimmermann-Rosselet* for the determination of outer membrane permeability. If we add substrates (*e.g.* β-lactam antibiotics) to intact bacterial cells that contain hydrolytic enzymes (*e.g.* β-lactamases) of known V_{max} and K_m in the periplasmic space, we can calculate the outer membrane permeability from the observed rates of hydrolysis. The efflux of the products of hydrolysis is expected to be much faster than the influx of the substrate—because of the smaller size of the products—and thus should have negligible effects on the kinetics at steady state.

a very important contribution in showing that the rates of hydrolysis by intact cells indeed followed this prediction and could be calculated by assuming that the diffusion and hydrolysis respectively followed Fick's law and Michaelis-Menten kinetics (Fig. 11). I should like to stress that this quantitative treatment is essential for the discussion of outer membrane permeability. For example, determination of "crypticity" (ratio of rates of hydrolysis in intact cells and in broken cells) at an arbitrarily chosen substrate concentration means very little, because the numerical values of "crypticity" can be altered freely, depending on the substrate concentration used[66].

We have followed the method of *Zimmermann* and *Rosselet* and determined the permeability coefficients of the outer membrane in various strains of *S. typhimurium*[67]. The results clearly show that the permeability of the outer membrane toward a hydrophilic β-lactam of 415 daltons, cephaloridine, decreases to less that 10% of that in the wild type in mutants with reduced levels of all three porins. Similar results were independently obtained with *E. coli* K12 by workers who approached the problem from the opposite direction, *i.e.* by examining membrane alterations in "cryptic" mutants. Intact cells of these mutants, studied by *Beacham et al.*[68], showed increased half-saturation (or Michaelis) constants (K_m) but unaltered maximal velocity (V_{max}) for the hydrolysis of nucleotides by periplasmic nucleotidases. When the outer membrane of these mutants was analyzed, it was found to have drastically reduced levels of porins[68].

In the approach described above, the inherent difficulty in the determination of diffusion rates across the outer membrane was solved by the use of enzymes that hydrolyzed substrates rapidly as they came into the periplasmic space. The prerequisite for this determination of outer membrane permeability is thus the efficient removal of diffusing substrates from the periplasmic space; only under these conditions will the overall rates of the process be determined predominantly by the diffusion rates across the outer membrane, and thus render the latter rates measurable. The removal of substrates can also be performed by active transport systems located in the cytoplasmic membrane. This forms the basis of the second approach to be described, *i.e.* the study of transport kinetics in intact cells. The diffusion rate (V) across the outer membrane is determined by Fick's law, and if we denote the substrate concentrations in the outside medium and in the periplasmic space by C_0 and C_p, respectively, then

$$V = P A (C_o - C_p)$$

where P and A are the permeability coefficient and the area of the membrane, respectively. The rate of active transport follows Michaelis-Menten kinetics, so that

$$V = C_p V_{max} / (K_m + C_p)$$

At steady state the two rates are equal, and thus we can eliminate C_p. This gives

$$V = \tfrac{1}{2}[V_{max} + P A K_m + P A C_o - \sqrt{(V_{max} + P A K_m + P A C_o)^2 - 4 C_o P A V_{max}}]$$

This equation looks rather unwieldy, but results of calculations using reasonable values of A, K_m, and V_{max} show that the decrease in outer membrane permeability (P) produces changes in the overall transport rate (V), changes suggesting an increased "K_m" value for the transport (K'_m) in intact cells without alteration in V_{max} (Fig. 12). This would suggest that the effect of porin deficiency on transport rates will become apparent only at low substrate concentrations (or high values of $1/C_o$). Furthermore, the effect will be difficult to detect even at low values of C_o, if the V_{max} of the active transport system (of the inner membrane) happens to be low.

Actually, mutants with the predicted change, *i.e.* increased "K_m" values for the transport of a number of substrates, were isolated some time ago by *von Meyenburg*[69] without the expectation of any outer membrane defect. These mutants were recently shown to be deficient in porins—in the 36.5 K porin in *E. coli* B/r and in both of the porins in *E. coli* K12[70]. Since the porin-deficient mutants have increased "K_m" for the transport of numerous compounds (various sugars, a sugar alcohol, a sugar phosphate, amino acids, a pyrimidine, and even inorganic anions like phosphate and sulfate)[73], this approach establishes the role of porins in the transmembrane diffusion of a very wide range of hydrophilic substrates. In addition, if we assume that the active transport systems in the cytoplasmic membrane have very high affinities (or low K_m values) for the substrate, we can estimate the minimal values of permeability coefficients for various substrates[74].

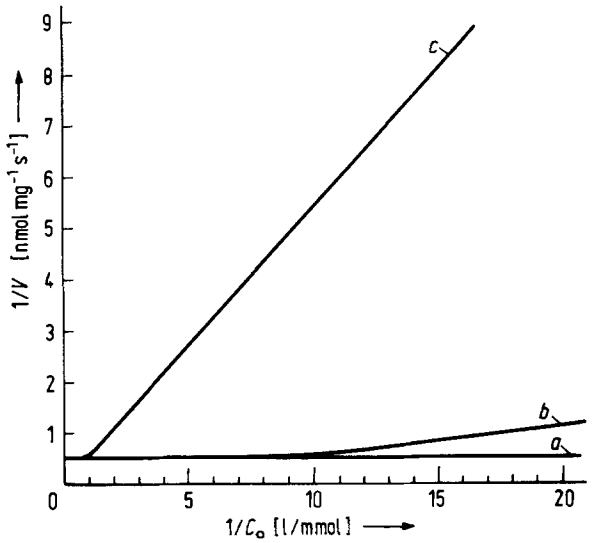


Fig. 12. Theoretically predicted behavior of transport systems in intact cells. Overall transport rates were calculated for different values of C_o (substrate concentration in the external medium), by assuming that the substrate first diffuses through the outer membrane with the permeability coefficient of value P, and then is transported actively by the underlying cytoplasmic membrane by a process characterized by the maximal rate (V_{max}) of 2 nmol/mg^{-1}/s^{-1} (based on dry weight), and the half-saturation (Michaelis) constant (K_m) of 1 μmol/l. The calculation was made for the P value of 1.4×10^{-2} cm/s (a "theoretical" value of permeability of *E. coli* outer membrane toward glucose [70]) (curve a, $K_m = 1.5$ μmol/l), and for P values corresponding to 1% and 0.1% of the value mentioned. The latter P values thus simulate situations in mutants producing 1% and 0.1% of the normal number of porins (curves b and c, $K'_m = 55$ and 550 μmol/l, resp.). It is seen that in mutants, the V_{max} of the overall transport process remains unchanged, but the apparent K'_m (*i.e.* the value of C_o giving the half-maximal rate of transport in intact cells) is increased. The plots are seen to follow straight lines except at very high values of C_o.

The transport studies and investigations with β-lactamase carried out in our laboratory have so far provided the following information:

(a) In contrast to the rate of diffusion of hydrophobic substances described in Section 3, the rate of diffusion of hydrophilic substances depends very little upon the temperature. Diffusion of a β-lactam antibiotic, cephaloridine, gave a Q_{10} value of about 2[71]; this low temperature dependence provides strong evidence for the permeation occurring through the water-filled pores.

(b) The most remarkable observation is the presence of a very large difference in permeability coefficients among permeable solutes. Thus, in wild type cells, the permeability coefficient of $\geq 1 \times 10^{-4}$ cm/s for lactose can be contrasted with a much lower coefficient for 6-aminopenicillanic acid (1.4×10^{-5} cm/s)[72], whose size (216 daltons) is actually smaller than that of lactose (342 daltons). We do not yet fully understand the factors that influence the rate of penetration through these pores, but a few parameters are already known to be important. The first factor is obviously the size of the solute molecule. In the "apparent transport K_m" experiments, the calculation of outer membrane P values on the basis of data on wild type cells gives only minimal values with a large margin of uncertainity. In contrast, the overall transport rates in intact cells of porin-deficient (*ompB*) mutants are essentially limited by the rates of diffusion through the outer membranes, especially at low values of C_o, and thus allow a fairly accurate calculation of P values[70]. Since the *ompB* gene is most probably a regulatory gene[73], the mutants are expected to produce smaller numbers of unaltered pores. Thus if we assume that hydrophilic solutes diffuse through the mutant outer membrane *via* the remaining porin channels, the data shown in Fig. 13 indicate clearly the effect of solute size. Furthermore,

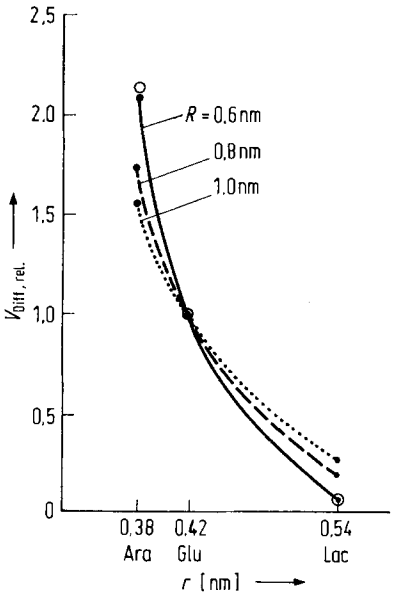


Fig. 13. Calculated and observed permeability toward solutes of various sizes. The calculated values (curves) were calculated by multiplying the free diffusion coefficients for arabinose (Ara), glucose (Glu), and lactose (Lac) by appropriate Renkin factors calculated for various pore sizes (hydration radii r see [75]). The observed permeability (○) was calculated from the "growth K_m" of porin-deficient (*ompB*) mutant CM7 on these carbon sources, and from the growth rate and growth yields (for details, see [70]). The relative diffusion rate $V_{diff,rel}$ serves as a measure of the permeability.

there is a reasonably good fit with the theoretical values calculated on the basis of the Renkin equation[74], which corrects for the hindrance caused by the collision of solutes of finite sizes with the rims of small pores, as well as for the viscous drag effect exerted by the pore wall.

The second factor is the hydrophobicity. Hydrophobic antibiotics cannot rapidly penetrate through the outer membrane of wild type *E. coli* or *S. typhimurium* even when their size is clearly below the exclusion limit of the pores[32]. This would suggest that the pores tend to exclude hydrophobic solutes,

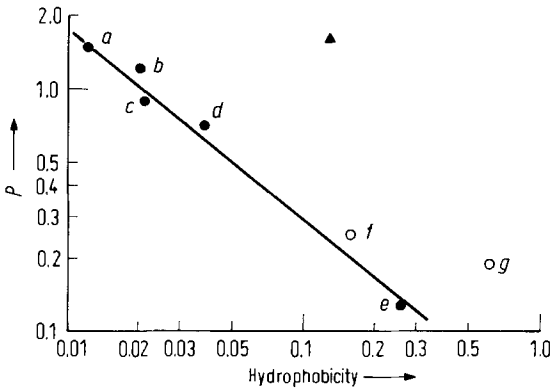


Fig. 14. Permeability (P, arbitrary units) of the pores as a function of hydrophobicity and charge. Rate of diffusion of β-lactam antibiotics across the outer membrane of *E. coli* (after [66]). The partition coefficients (as a measure of hydrophobicity) were determined in isobutanol/0.02 M phosphate buffer (pH 7.4) containing 0.9% NaCl, at 37°C. ●, monoanionic cephalosporins a: C 49288; b: C 49753; c: cephacetril; d: cephazolin, e: cephalothin; ▲, zwitterionic cephalosporin (cephaloridine), ○, monoanionic penicillins (f: ampicillin, g: benzylpenicillin).

an idea put to a direct test by *Zimmermann* and *Rosselet*[66]. They compared the outer membrane permeability to *E. coli* for a number of semisynthetic cephalosporin derivatives; their data (see Fig. 14) confirm the inverse correlation between hydrophobicity and transmembrane diffusion rates (through pores), at least for a series of monoanionic cephalosporins. At present it is not known why pores exclude hydrophobic molecules. An obvious possibility is that these hydrophobic antibiotics cannot penetrate into the pores because they form micelles. However, although these substances do indeed form micelles at very high concentrations, they seem to exist mostly as monomers at the concentrations used for permeability studies[71]. Perhaps the important thing to realize here is that the diameter of the pore is not much different from the diameter of solute molecules. Thus the walls of the pore are probably lined with hydrophilic or hydrogen-bonding structures, so that the transfer of hydrophilic solutes from bulk water to the interior of the pore can be achieved without the net breakage of many hydrogen bonds. In the "empty" pore, it is reasonable to expect that the structures on the wall are rather strongly hydrogen-bonded to water molecules in the pore, thus making the water in the channel more structured or more strongly hydrogen-bonded than the bulk water. Penetration of hydrophobic molecules into the pore will break this structure, and thus may be energetically unfavorable.

In this connection, the apparently larger pores found in *P. aeruginosa* may play a significant role in allowing the easier diffusion of hydrophobic molecules[65]. It is known that *P. aeruginosa* can grow on a number of organic acids and alcohols[76], and even on paraffinic hydrocarbons and camphor in the presence of a proper "degradative" plasmid[77]. Possibly a larger pore may permit the passage of hydrophobic molecules enveloped in a "cage" of structured water molecules, or even of micelles.

The third factor is the electrical charge. In the experiments of *Zimmermann* and *Rosselet*[66], the zwitterionic cephaloridine penetrated through outer membrane much faster than the monoanionic cephalosporins of comparable hydrophobicity (Fig. 14). It seems possible that the pore walls contain a number of anionic groups; in this connection we recall the observation that porins are the most acidic proteins found in the outer membrane, both in *E. coli*[58, 78] as well as in *S. typhimurium*[79]. However, a significant part of the resistance against anionic solutes may come from the fact that the periplasmic space contains many negatively charged macromolecules, and thus there exists a Donnan equilibrium favoring the exit of diffusible anions from the periplasmic space[51].

(c) These considerations help us understand the functions of porins in a physiological context. A very large number (about 10^5) of porins exist in a single cell. If we consider cells growing in a laboratory medium containing a typical concentration, say 0.2 %, of glucose, the porins are of course present in a large excess (perhaps 10^3-fold) over what is needed for the inflow of glucose at a rate needed for exponential growth at the doubling time of about 45 min (for calculation, see ref. [70]). But the production of these large numbers of porins is not wasteful, because they are needed under two conditions: Firstly, porins are needed for the diffusion of less permeable compounds. The Renkin equation predicts that the diffusion rates of disaccharide will be about 5 % of that of glucose. Hydrophobicity and electric charges will further reduce the diffusion rates by several orders of magnitude; this applies, for example, in some peptides that are a major source of nutrition for enteric bacteria in their natural habitat. It thus seems that for the diffusion of certain classes of compounds the presence of 10^5 copies of porins is indeed necessary. Secondly, the concentration of the nutrients is important. The passive diffusion rate is *proportional* to the concentration difference across the membrane. Thus although 10^5 copies of porins might seem an unnecessary excess in a medium containing 0.2 % (roughly 10^{-2} mol/l) glucose, all of these porins will become necessary if *E. coli* tries to keep growing at its maximal rate in the presence of only 10^{-5} mol/l glucose, apparently a condition *E. coli* is exposed to very frequently in its natural habitat[80].

In addition to the studies in our laboratory[70], other workers have found that porin-deficient mutants are less permeable to various nutrients and inhibitors such as Cu^{2+}, Ag^{+}, tetracycline, and chloramphenicol[81]. These results agree with the lack of specificity of porin channels observed in the reconstitution experiments, and suggest that most small, hydrophilic solutes cross the outer membrane through these channels (see, however, Section 5).

Both *E. coli* K12 and *S. typhimurium* LT2 synthesize more than one species of porins. Since the biosynthesis of the individual species is regulated by a specific set of environmental conditions[82], it seems possible that each species produces channels with slightly different properties from others. However, all reconstitution studies so far have indicated identical exclusion limits for the three species of *Salmonella* porins[83].

Inouye has proposed[61], on the basis of the amino acid sequence, that murein lipoprotein may form oligomers with a central channel, which would then serve as transmembrane pores. So far no experimental evidence favoring this hypothesis has been reported. Recently, by using a mutant lacking the lipoprotein[14], we have shown that the absence of this protein did not produce any reduction in the hydrophilic permeability of the outer membrane, measured by the diffusion of 6-aminopenicillanic acid[72].

4.4. Structural Basis of the Permeability toward Hydrophilic Molecules

We have seen that a special class of proteins, porins, make the outer membrane permeable to hydrophilic solutes. If these proteins form transmembrane channels, they should span the thickness of the membrane. Indeed, portions of the porins are exposed on the outside surface of the outer membrane, as seen from the binding of macromolecular labeling reagents[84], porin-specific bacteriophages[85] and antibodies[86]. At the same time the porins have a strong affinity toward the underlying murein layer[58, 87], and thus are believed to be exposed also on the inner surface of the membrane.

How are these proteins organized in the plane of the membrane? Porins solubilized in 0.1—0.2 % sodium dodecyl sulfate (SDS) at room temperature apparently exist as trimers, as revealed by cross-linking with bifunctional reagents[88] and by sedimentation equilibrium studies[89]. They seem to be organized as trimers also in the intact outer membrane, since cross-linking studies with cell envelopes produced predominantly dimers and trimers of porin[88].

These porin oligomers were "visualized" in the outer membrane by two techniques. Firstly, *Ueki et al.*[90] examined the small-angle X-ray scattering by oriented layers of intact outer membranes of *S. typhimurium*. The study revealed a series of in-plane reflections that appeared to correspond to regular protein aggregates of about 10 nm in diameter. A most interesting feature was the presence of a central electron-transparent area or a "hole" of about 5 nm in diameter. Since such reflections were absent in the outer membrane of a porin-negative mutant, these regular oligomers are formed only by the porins. Secondly, freeze-fracture electron microscopy revealed about 10^4 intramembranous "particles" on 1 μm^2 area of the concave fracture face of the outer membrane (see Fig. 7 and 8)[20-22]. From the total number of porin molecules per cell[58] and the surface area of an *E. coli* cell, one would expect about 10^4 porin trimers on 1 μm^2 area, and thus the majority of these particles are likely to correspond to porin trimers (or their complexes with LPS). Their size (8—10 nm) also agrees with the size of porin oligomers determined by X-ray scattering.

Does each monomer of porin contain a channel or does a channel get formed in the central space after the association of three subunits? A decisive answer is not available at present. So far it has not been able to reconstitute saccharose-permeable membranes by using monomeric porins[89]. On the other hand, some published results are at least consistent with the one-porin one-channel hypothesis. When the cell envelope of *E. coli* B is extracted with SDS at room temperature, murein sheets with hexagonally arranged oligomers of porin are left behind[58]. Because of this regular arrangement, *Steven et al.*[91] were able to use image-enhancement techniques in electron microscopy, and obtained the negatively stained picture suggesting that a trimer of proteins contains a central triplet of holes, each 2 nm in diameter. Although *Steven et al.* argued that these holes were probably occupied by lipoproteins, this sounds unlikely because the wall of the holes would then have to be hydrophobic and would repel the hydrophilic particles of the negative stains. If each of these holes corresponds to a channel, their size agrees very well with that predicted by the diffusion studies, *i. e.* about 1.2 nm in diameter (Section 4.3). Perhaps this triplet of channels could have appeared as a single large hole in the X-ray scattering study, because of the low resolution (about 2 nm) of the latter technique[90].

5. Specific Diffusion Processes

The discovery that some outer membrane proteins are involved in the specific transport of nutrients was made by *Bradbeer et al.*[92], when they found that a vitamin B_{12} binding protein, located in the outer membrane, is essential for the transport of this substrate into the cytoplasm. This discovery was rapidly followed by many other works describing various systems and defining their components (Table 3). Portions of the specific transporter proteins are expected to be exposed on cell surface, and indeed most of these proteins are used as "receptors" by various phages and colicins (Table 3).

We have observed in the previous section that the passive diffusion through porin channels is likely to become limiting if the solute has a large size or if the external concentrations of the solutes normally encountered are quite low, or if the rate of active transport is very high. We can thus expect that specific transport systems across the outer membrane will be needed for these cases, and it is gratifying to find that in all the cases listed in Table 3 one or more of the

Table 3. Outer membrane proteins involved in specific diffusion processes.

Facilitates the diffusion of:	Apparent mol. wt. of protein	Protein used as receptor by:	Ref.
Maltose and Maltodextrins	47000	λ	[93]
Ferrichrome	78000	T5, T1, Ø 80, colicin M	[94]
Fe^{3+}-enterochelin	81000	colicin B	[95]
Nucleosides	25000	T6, colicin K	[96]
Vitamin B_{12}	60000	BF23, E group colicins	[92, 97]

conditions above is satisfied. Thus iron-chelator complexes (ferrichrome, 740 daltons; Fe^{3+}-enterochelin, 746 daltons) as well as vitamin B_{12} (1357 daltons) are very large, and also exist in very low concentrations. Maltodextrin oligosaccharides are also large, and although maltose can diffuse through porin channels[93b] such diffusion becomes limiting for disaccharides if the external concentration falls below *ca.* 10^{-4} mol/l (see Section 4.3). Thus for the proper functioning of a maltose transport system, which has a very high affinity for maltose (K_{diss} of the periplasmic maltose binding protein is 2×10^{-7} mol/l for maltotriose[93b]) at low substrate concentrations, the porin channels are clearly insufficient. The presence of a specific protein for the transport of nucleosides which are not so large (less than 300 daltons) is somewhat unexpected, but is probably related to the fact that nucleoside transport is one of the most efficient transport systems in *E. coli* in terms of its high affinity combined with a very high velocity[80].

The maltose transporter, or the "λ-receptor", transports not only maltose but also maltotriose and possibly higher oligosaccharides[93b]. Since this protein shares several properties with porin[93c], it seems possible that it also acts essentially as a large pore with a discriminating mechanism in it. Consistent with this prediction is the observation that its presence allows the diffusion, albeit very slow, of glucose and lactose (but not of histidine) across the outer membrane of porin-deficient mutants[98]. Recently it was also shown that λ-receptor forms ion-permeable channels in planar lipid films[99]. The transport processes carried out by other specific transporter proteins may also involve pores, but little information is available on this point.

6. Penetration of Macromolecules

Under certain conditions, macromolecules can apparently cross the outer membrane barrier[100]. This situation is not correlated with any specific deficiency of the outer membrane components, but rather seems to occur whenever the stability of the outer membrane structure is decreased. It thus seems most likely that the "leakage" of this type occurs by the transient rupture and resealing of the membrane.

7. Conclusion

Owing to its location outside the cytoplasmic membrane, the outer membrane had to develop unusual permeability properties. Thus it is permeable to small hydrophilic molecules, and at least in *E. coli* and *Salmonella* essentially impermeable to hydrophobic molecules. Furthermore, it also had to develop specific diffusion mechanisms for exceptional compounds. We

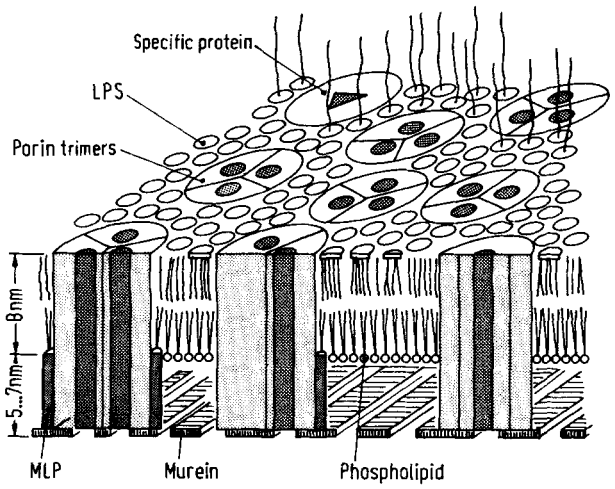


Fig. 15. Speculative model of the *E. coli* and *S. typhimurium* cell wall. Some features in this figure are highly speculative and have not been established experimentally: these include the assumptions that each porin molecule produces a channel, that murein lipoprotein is joined to the membrane only *via* its hydrocarbon chains, and that murein lipoprotein associates with porin. Spec. protein: protein which facilitates the diffusion of specific compounds; LPS: lipopolysaccharide; MLP: murein-lipoprotein.

now understand the structural basis of these permeability properties quite well at the molecular level. In fact, in terms of the correlation of structure with function, the outer membrane probably is the best understood among biological membranes. Since this membrane has a rather simple structure (Fig. 15) and a vast amount of data has already been accumulated on it, it seems likely that the outer membrane will remain a very useful object of study for the understanding of general principles of membrane structure and function[101].

The research in the author's laboratory has been supported by a U.S. Public Health Service research grant AI-09644 and an American Cancer Society research grant BC-20. I thank all my past and present coworkers who contributed ideas and hard work to this project, especially Taiji Nakae, Yoshiyuki Kamio, and John K. Smit.

Received: June 12, 1978 [A 269 IE]
German version: Angew. Chem. *91*, 394 (1979)

[1] a) *A. M. Glauert, M. J. Thornley*, Annu. Rev. Microbiol. *23*, 159 (1969); b) *J. H. Freer, M. R. J. Salton* in *G. Weinbaum, S. Kadis, S. J. Ajl:* Microbial Toxins. Vol. IV. Academic Press, New York 1971, Chapter 2.
[2] *T. Miura, S. Mizushima*, Biochim. Biophys. Acta *150*, 159 (1938); *193*, 263 (1969).
[3] *M. J. Osborn, J. E. Gander, E. Parisi, J. Carson*, J. Biol. Chem. *247*, 3962 (1972).
[4] *C. A. Schnaitman*, J. Bacteriol. *104*, 890 (1970).
[5] *G. F. Ames, E. N. Spudich, H. Nikaido*, J. Bacteriol. *117*, 406 (1974).
[6] a) *J. Uemura, S. Mizushima*, Biochim. Biophys. Acta *413*, 163 (1975); b) *W. Garten, I. Hindennach, U. Henning*, Eur. J. Biochem. *59*, 215 (1975); c) *B. Lugtenberg, J. Meijers, R. Peters, P. van der Hoek, L. van Alphen*, FEBS Lett. *58*, 254 (1975); d) *C. A. Schnaitman*, J. Bacteriol. *118*, 442 (1974).
[7] *V. Braun*, Biochim. Biophys. Acta *415*, 335 (1975).
[8] *H. Nikaido* in *L. Leive:* Bacterial Membranes and Walls. Marcel Dekker, New York 1973, Chapter 3.
[9] *O. Lüderitz, O. Westphal, A. M. Staub, H. Nikaido* in *G. Weinbaum, S. Kadis, S. J. Ajl:* Microbial Toxins. Vol. IV. Academic Press, New York 1971, Chapter 4.
[10] *T. Chai, J. Foulds*, J. Mol. Biol. *85*, 465 (1975).
[11] *J. K. Davies, P. Reeves*, J. Bacteriol. *123*, 96 (1975).
[12] *U. Henning, I. Haller*, FEBS Lett. *55*, 161 (1975).
[13] *M. Nurminen, K. Lounatmaa, M. Sarvas, P. H. Makela, T. Nakae*, J. Bacteriol. *127*, 941 (1976).
[14] *Y. Hirota, H. Suzuki, Y. Nishimura, S. Yasuda*, Proc. Nat. Acad. Sci. USA *74*, 1417 (1977).
[15] *A. Forge, J. W. Costerton, K. A. Kerr*, J. Bacteriol. *113*, 445 (1973).
[16] *P. Overath, M. Brenner, T. Gulik-Krzywicki, E. Schechter, L. Letellier*, Biochim. Biophys. Acta *389*, 358 (1975).
[17] *S. Rottem, M. Hasin, S. Razin*, Biochim. Biophys. Acta *375*, 395 (1975).
[18] *H. Nikaido, Y. Takeuchi, S.-I. Ohnishi, T. Nakae*, Biochim. Biophys. Acta *465*, 152 (1977).
[19] *D. Branton*, Proc. Nat. Acad. Sci. USA *55*, 1048 (1966).
[20] *A. P. van Gool, N. Nanninga*, J. Bacteriol. *108*, 474 (1971).
[21] *H. E. Gilleland, Jr., J. D. Stinnett, I. L. Roth, R. G. Eagon*, J. Bacteriol. *113*, 417 (1973).
[22] *J. Smit, Y. Kamio, H. Nikaido*, J. Bacteriol. *124*, 942 (1975).
[23] *K. Schleifer, O. Kandler*, Bacteriol. Rev. *36*, 407 (1972).
[24] However, the murein of *E. coli* strains that have been maintained in the laboratory for many years (and thus produce defective LPS [8]) can be degraded by treating intact cells with high concentrations of lysozyme (*D. S. Feingold, J. N. Goldman, H. M. Kurita*, J. Bacteriol. *96*, 2118 (1968)).
[25] *J. P. Robbie, T. H. Wilson*, Biochim. Biophys. Acta *173*, 234 (1969).
[26] *J. W. Payne, C. Gilvarg*, J. Biol. Chem. *243*, 6291 (1968).
[27] a) *R. J. Roantree, T.-T. Kuo, D. G. MacPhee, B. A. D. Stocker*, Clin. Res. *17*, 157 (1969); b) *R. J. Roantree, T.-T. Kuo, D. G. MacPhee*, J. Gen. Microbiol. *103*, 223 (1977).
[28] a) *S. Schlecht, G. Schmidt*, Zentr. Bakteriol. Parasitenk. Orig. *212*, 505 (1969); b) *G. Schmidt, S. Schlecht, O. Westphal, ibid. 212*, 88 (1969); c) *S. Schlecht, O. Westphal, ibid. 213*, 354 (1970).
[29] *S. Tamaki, M. Matsuhashi*, J. Bacteriol. *105*, 968 (1971).
[30] *L. Leive*, Biochem. Biophys. Res. Commun. *18*, 13 (1965); *21*, 290 (1965).
[31] *L. Leive*, Proc. Nat. Acad. Sci. USA *53*, 745 (1965).
[32] *L. Leive*, Ann. N. Y. Acad. Sci. *235*, 109 (1974).
[33] *H. Nikaido*, Biochim. Biophys. Acta *433*, 118 (1976).
[34] *J. F. Danielli* in *H. Davson, J. F. Danielli:* The Permeability of Natural Membranes. University Press, Cambridge 1952, Chapter 8.
[35] *P. Gustafsson, K. Nordstrom, S. Normark*, J. Bacteriol. *116*, 893 (1973).
[36] *R. Collander, H. Bärlund*, Acta Bot. Fenn. *11*, 1 (1933).
[37] *W. D. Stein:* The Movement of Molecules across Cell Membranes. Academic Press, New York 1967.
[38] *R. I. Sha'afi, G. M. Gary-Bobo, A. K. Solomon*, J. Gen. Physiol. *58*, 238 (1971).
[39] *W. R. Galey, J. D. Owen, A. K. Solomon*, J. Gen. Physiol. *61*, 727 (1973).
[40] a) *P. Mueller and D. O. Rudin*, Curr. Top. Bioenerg. *3*, 157 (1969); b) *A. D. Bangham*, Chem. Phys. Lipids *8*, 386 (1972).
[41] *J. Koplow, H. Goldfine*, J. Bacteriol. *117*, 525 (1974).
[42] *P. F. Mühlradt, J. R. Golecki*, Eur. J. Biochem. *51*, 343 (1975).
[43] *Y. Funahara, H. Nikaido*, unpublished results.
[44] *D. Romeo, A. Girard, L. Rothfield*, J. Mol. Biol. *53*, 475 (1970).
[45] a) *N. A. Roberts, G. W. Gray, S. G. Wilkinson*, Microbios *2*, 189 (1970); b) *S. W. Rogers, H. E. Gilleland, Jr., R. G. Eagon*, Can. J. Microbiol. *15*, 743 (1969).
[46] *N. C. Jones, M. J. Osborn*, J. Biol. Chem. *252*, 7405 (1977).
[47] *Y. Kamio, H. Nikaido*, Biochemistry *15*, 2561 (1976).
[48] *M. J. Maness, P. F. Sparling*, J. Infect. Dis. *128*, 321 (1973).
[49] *G. Decad, H. Nikaido*, J. Bacteriol. *128*, 325 (1976).
[50] A recent paper [51] concludes that the periplasmic space occupies a large fraction of total cell volume even in unplasmolyzed cells. The reason for this discrepancy is unknown.
[51] *J. B. Stock, B. Rauch, S. Roseman*, J. Biol. Chem. *252*, 7850 (1977).
[52] *T. Nakae, H. Nikaido*, J. Biol. Chem. *250*, 7359 (1975).
[53] a) *M. L. DePamphilis*, J. Bacteriol. *105*, 1184 (1971); b) *P. D. Bragg, C. Hou*, Biochim. Biophys. Acta *247*, 478 (1972); c) *K. Nakamura, S. Mizushima, ibid. 413*, 371 (1975).
[54] *T. Kataoka, K. Inoue, O. Lüderitz, S. C. Kinsky*, Eur. J. Biochem. *21*, 80 (1971).
[55] *H. Nikaido, T. Nakae*, J. Infect. Dis. *128*, S 30 (1973).
[56] *T. Nakae*, Biochem. Biophys. Res. Commun. *64*, 1224 (1975).
[57] *T. Nakae*, J. Biol. Chem. *251*, 2176 (1976).
[58] *J. Rosenbusch*, J. Biol. Chem. *249*, 8019 (1974).

[59] T. Nakae, Biochem. Biophys. Res. Commun. 71, 877 (1976).
[60] T. Nakae, Unpublished results.
[61] M. Inouye, Proc. Nat. Acad. Sci. USA 71, 2396 (1974).
[62] R. Benz, K. Janko, W. Boos, P. Läuger, Biochim. Biophys. Acta 511, 309 (1978).
[63] G. Decad, PhD Dissertation, University of California, Berkeley.
[64] K. Nixdorff, H. Fitzer, J. Gmeiner, H. H. Martin, Eur. J. Biochem. 81, 63 (1977).
[65] R. E. W. Hancock, H. Nikaido, J. Bacteriol. 136, 381 (1978).
[66] W. Zimmermann, A. Rosselet, Antimicrob. Agents Chemother. 12, 368 (1977).
[67] H. Nikaido-S.-A. Song, L. Shaltiel, M. Nurminen, Biochem. Biophys. Res. Commun. 76, 324 (1977).
[68] I. R. Beacham, D. Haas, E. Yagil, J. Bacteriol. 129, 1034 (1977).
[69] K. von Meyenburg, J. Bacteriol. 107, 878 (1971).
[70] P. Bavoil, H. Nikaido, K. von Meyenburg, Mol. Gen. Genet. 158, 23 (1977).
[71] H. Nikaido, P. Bavoil, E. Y. Rosenberg, unpublished.
[72] H. Nikaido, P. Bavoil, Y. Hirota, J. Bacteriol. 132, 1045 (1977).
[73] S. Ichihara, S. Mizushima, J. Biochem. (Tokyo) 83, 1095 (1978).
[74] E. M. Renkin, J. Gen. Physiol. 38, 225 (1954).
[75] S. G. Schultz, A. K. Solomon, J. Gen. Physiol. 44, 1189 (1961).
[76] R. Y. Stanier, N. J. Palleroni, M. Doudoroff, J. Gen. Microbiol. 43, 159 (1966).
[77] A. M. Chakrabarty, G. Chou, I. C. Gunsalus, Proc. Nat. Acad. Sci. USA 70, 1137 (1973).
[78] C. J. Schmitges, U. Henning, Eur. J. Biochem. 63, 47 (1976).
[79] G. F.-L. Ames, private communication.
[80] A. L. Koch, Adv. Microb. Physiol. 6, 147 (1971).
[81] a) J. F. Lutkenhaus, J. Bacteriol. 131, 631 (1977); b) E. C. R. Reeve, P. Doherty, ibid. 96, 1450 (1968); c) A. P. Pugsley, C. A. Schnaitman, ibid. 133, 1181 (1978).
[82] a) P. J. Bassford, Jr., D. L. Diedrich, C. A. Schnaitman, P. Reeves, J. Bacteriol. 131, 608 (1977); b) C. A. Schnaitman, ibid. 118, 454 (1974); c) K. Nakamura, S. Mizushima, J. Biochem. (Tokyo) 80, 1411 (1976).
[83] T. Nakae, J. Ishii, J. Bacteriol. 133, 1412 (1978).
[84] Y. Kamio, H. Nikaido, Biochim. Biophys. Acta 464, 589 (1977).
[85] D. B. Datta, B. Arden, U. Henning, J. Bacteriol. 131, 821 (1977).
[86] J. Smit, H. Nikaido, unpublished.
[87] Y. Hasegawa, H. Yamada, S. Mizushima, J. Biochem. (Tokyo) 80, 1401 (1976).
[88] E. T. Palva, L. L. Randall, J. Bacteriol. 133, 279 (1978).
[89] T. Nakae, J. Ishii, M. Tokunaga, J. Biol. Chem. 254, 1457 (1979).
[90] T. Ueki, T. Mitsui, H. Nikaido, J. Biochem. (Tokyo) 85, 173 (1979).
[91] A. C. Steven, B. ten Heggeler, R. Muller, J. Kistler, J. P. Rosenbusch, J. Cell Biol. 72, 292 (1977).
[92] J. C. White, P. M. DiGirolamo, M. L. Fu, Y. A. Preston, C. Bradbeer, J. Biol. Chem. 248, 3978 (1973).
[93] a) L. Randall-Hazelbauer, M. Schwartz, J. Bacteriol. 116, 1436 (1973); b) S. Szmelcman, M. Schwartz, T. J. Silhavy, W. Boos, Eur. J. Biochem. 65, 13 (1976); c) V. Braun, H. J. Krieger-Brauer, Biochim. Biophys. Acta 469, 89 (1977).
[94] a) V. Braun, H. Wolff, FEBS Lett. 34, 77 (1973); b) R. Wayne, J. B. Neilands, J. Bacteriol. 121, 497 (1975); c) K. Hantke, V. Braun, FEBS Lett. 49, 301 (1975); d) M. Luckey, R. Wayne, J. B. Neilands, Biochem. Biophys. Res. Commun. 65, 687 (1975).
[95] a) R. E. W. Hancock, K. Hantke, V. Braun, J. Bacteriol. 127, 1370 (1976); b) R. Wayne, K. Frick, J. B. Neilands, J. Bacteriol. 126, 7 (1976).
[96] K. Hantke, FEBS Lett. 70, 109 (1976).
[97] a) D. R. DiMasi, J. C. White, C. A. Schnaitman, C. Bradbeer, J. Bacteriol. 115, 506 (1973); b) S. F. Sabet, C. A. Schnaitman, J. Biol. Chem. 248, 1797 (1973).
[98] K. von Meyenburg, H. Nikaido, Biochem. Biophys. Res. Commun. 78, 1100 (1977).
[99] W. Boos, private communication.
[100] a) S. Lindsay, B. Wheeler, K. E. Sanderson, J. W. Costerton, K.-J. Cheng, Can. J. Microbiol. 19, 335 (1973); b) S. Tamaki, M. Matsuhashi, J. Bacteriol. 114, 453 (1973); c) H. Suzuki, Y. Nishimura, S. Yasuda, A. Nishimura, M. Yamada, Y. Hirota, private communication; d) R. A. Weigand, L. I. Rothfield, J. Bacteriol. 125, 340 (1976).
[101] Because of the limitation in space, many details and references could not be included in this review. For more details, the readers are referred to a more extensive review (H. Nikaido, T. Nakae, Adv. Microb. Physiol., in press).

A Model of Simple Liquids

By Werner A. P. Luck[*]

Dedicated to Professor Horst Pommer on the occasion of his 60th birthday

The intuitively clear hole defect model can be used for quantitative estimates and for understanding the properties of liquids. An ideal liquid is defined in analogy with an ideal gas and corrected for real liquids with hole defects. The good agreement permits an application of this approximation process to the understanding of some important material properties. The effective model fills a gap in the area of applied chemistry and of chemical teaching. It also leads to a correction factor for the failure of the theorem of corresponding states. The reasons for the applicability of such a simple model are demonstrated on the basis of the Lennard-Jones potential.

1. Introduction

One of the main problems of research and development in applied chemistry is the production of substances with predetermined properties (molecular engineering[1])—a problem for which the study of chemistry leaves one almost completely unprepared. For example, in dyestuffs research an average of 400 dyes are conceived, synthesized, and subjected to all-round testing before a new and better dyestuff is found; in pharmaceutical research the corresponding ratio is as large as 10000:1[1].

The yield of such an empirical process can be improved—if at all—only by a deeper understanding of the intermolecular forces in complicated systems. One example of this would be the structure of liquids, but its description with the aid of partition functions can hardly help the chemist.

The approximate description of the gaseous state by the "ideal gas equation" is generally recognized and used, although the model upon which this is based—of force-free point-size

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

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0350 $ 02.50/0

molecules—cannot describe liquefaction, diffusion, thermal conductivity, or viscosity. Why have there been so few attempts at describing liquids, although it is with liquids that the chemist must deal most often? Below it will be shown how simply a useful model of liquids can be developed.

2. Ideal and Real Liquids

2.1. The Ideal Liquid

To avoid complications, we begin with two limitations:
1) We shall deal with nonpolar or only weakly polar substances.
2) We shall discuss the saturation states of the coexistence of liquids and vapors.

It must be mentioned in connection with 1) that for polar parts of molecules orientation-dependent components of the interaction must also be taken into account, as has been demonstrated for the extreme example of water[2] and also for methanol and ethanol[3] with a very simple but effective orientation defect model; and in connection with 2) that deviations from saturation due to an increase of the pressure can easily be included.

Like the ideal gas, the ideal liquid can be defined on the basis of the variables of state volume V or density ρ and temperature T. The upper curves in Figure 1 show the liquid saturation densities ρ_l and the lower curves the corresponding gas densities ρ_v. At low values of T the following expression holds for nearly all substances:

$$\rho_l = \rho_0 - AT; \quad T < T_b \tag{1}$$

where T_b is the boiling point.

Eq. (1), which applies strictly at low temperatures, also has a physical significance at high temperatures: it represents the geometric locus of the sum $(\rho_l + \rho_v)$[4, 5]—a situation that again applies to nearly all substances and is generally known

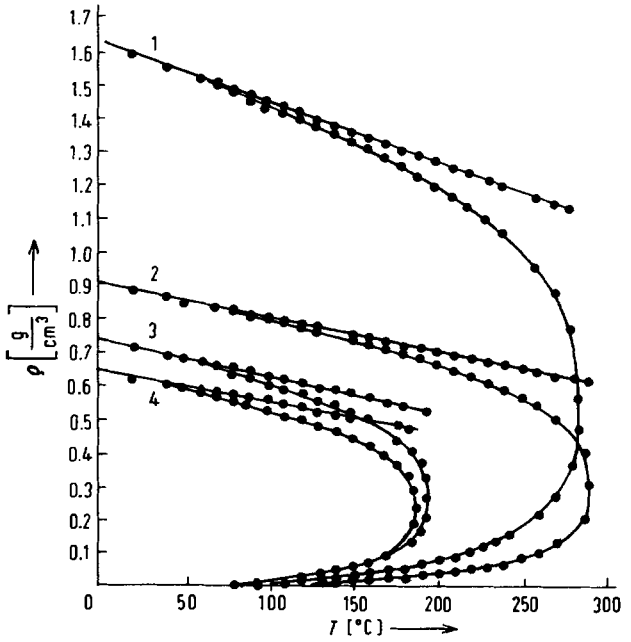


Fig. 1. Saturation densities: lower curves, vapor ρ_v; upper curves, liquid ρ_l; straight lines, $\rho_{id} = \rho_l + \rho_v$. 1, tetrachloromethane; 2, benzene; 3, diethyl ether; 4, 2-methylbutane.

for $(\rho_l + \rho_v)/2$ as the Cailletet-Mathias rule for testing critical characteristics (V_c, T_c).

We now define an ideal liquid by means of this straight line as a liquid whose volume, because of thermal oscillations about the equilibrium positions, increases with T in such a way that the relationship (1) applies exactly for its density $\rho_{id} = \rho_l + \rho_v$. While the ideal model gas corresponds the closer to reality the larger T/T_c becomes, the ideal model liquid thus defined approaches a real liquid the more closely the smaller is T/T_c.

2.2. The Real Liquid

Just as effective as the van der Waals corrections a and b for the gaseous state is the modification of the ideal model liquid by the assumption that hole defects appear in the real liquid with increasing T[4, 5]. We can give the number of hole defects for our model directly: the deviation of the density of the ideal liquid, which we have defined as $\rho_l + \rho_v$, from the density of the real liquid ρ_l is given exactly by ρ_v. Consequently, the hole-defect concentration in the model liquid must be equated with the concentration of molecules in the vapor. The fraction of hole defects is therefore determined by the expression

$$x_F = \frac{\rho_v}{\rho_l + \rho_v} \tag{2}$$

Figure 2 surveys the experimental values of x_F. A curve appears that applies to practically all organic compounds, but not to substances with low critical temperatures, such as He, Ne, and H_2. At T_c the value of x_F is 0.5, the number of

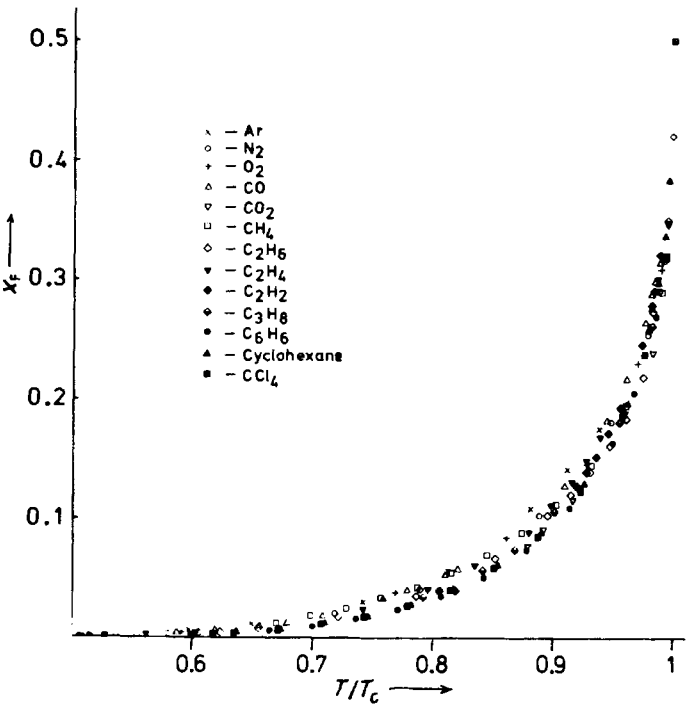


Fig. 2. Hole-defect concentration $x_F = \rho_v/(\rho_l + \rho_v)$.

hole defects in the liquid then being equal to the number of vapor molecules. The two phases have become indistinguishable.

Our model is in agreement with X-ray scattering data, which indicate that in liquids the distances between nearest neighbors increase only very slightly with increasing T, while the coordination numbers show a considerable decrease[6]. For example, for liquid argon at 149 K a mean distance between nearest neighbors of 5.27 Å would be expected on the basis of the density, while the X-ray scattering results show, in agreement with the hole model, a flat maximum of the pair distribution function at a distance of 4.1 Å; at T_c a coordination number of 6 is reached[6].

On the basis of the model, and in agreement with the X-ray results, we arrive at a simplified representation of a liquid (Fig. 3, left): a "crystal-like" structure, expanded at increased values of T and slightly distorted by the statistical oscillation volume; additional hole defects appear with rising T, their concentration being exactly equal to the vapor concentration.

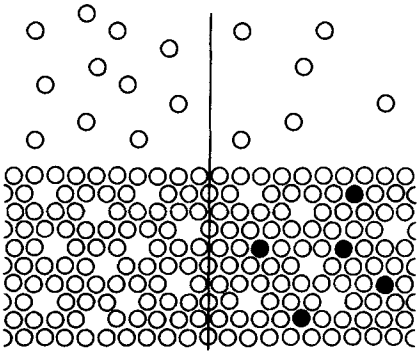


Fig. 3. Left: Hole defect model of a liquid: expanded crystal-like packing with the concentration of holes equal to the concentration of vapor. Right: model for *Raoult*'s law: dissolved particles having no intrinsic vapor pressure (black points) fill the holes and the vapor pressure of the liquid decreases in proportionality to the number of dissolved particles.

This model leads directly to *Raoult*'s law for the lowering of vapor pressure as a function of the concentration of dissolved foreign molecules. As in the thermodynamic derivation of this law, very laborious for most chemists, we presuppose that the dissolved molecules have no intrinsic vapor pressure. According to our model they will fill the holes in the liquid and therefore lower the vapor pressure proportionately. If the dissolved particles are much larger than the particles of the solvent, the well-known reduction in the lowering of the vapor pressure would be expected.

2.3. Zero-Point Density ρ_0

Figures 4 and 5 show, in reduced units, that the condition for the ideal liquid:

$$\frac{\rho_l + \rho_v}{\rho_c} = \frac{\rho_0}{\rho_c} - \left(\frac{\rho_0}{\rho_c} - 2\right)\frac{T}{T_c} \qquad (3)$$

is also satisfied for more complicated substances. The appreciable deviations in the case of H_2O and CH_3OH can be explained in terms of orientation defects[2] with lower density caused by the strong hydrogen bonding.

The slope of the straight lines represented by Eq. (3) is closely related theoretically and experimentally with the axial intercept ρ_0/ρ_c, because for $T/T_c = 1$, since $\rho_{v,c} = \rho_{l,c} = \rho_c$, we have: $(\rho_{v,c} + \rho_{l,c})/\rho_c = 2$.

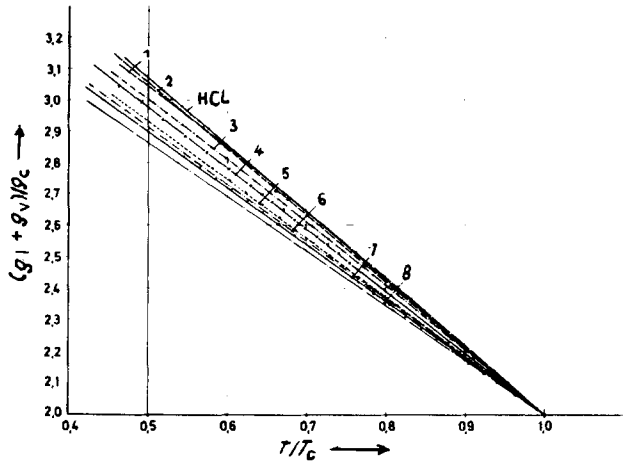


Fig. 4. Eq. (3) applies to HCl, but also for more complicated organic compounds such as 1, *n*-octane; 2, ethylamine; 3, *n*-heptane; 4, iodobenzene; 5, *n*-pentane; 6, dimethyl sulfide; 7, 2,3-dimethylbutane; 8, acetylene.

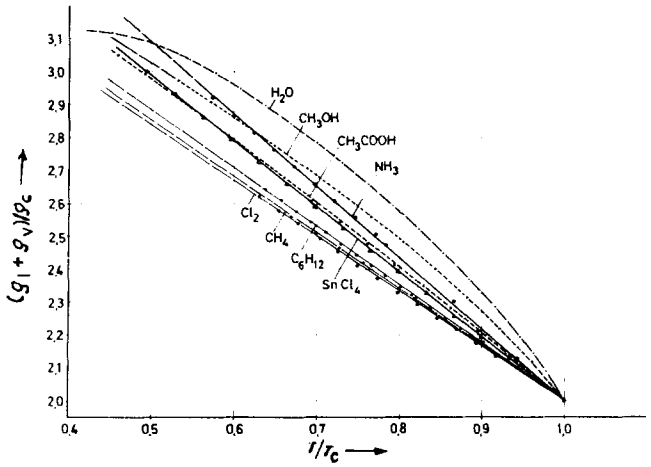


Fig. 5. Appreciable deviations from Eq. (3) occur only for substances with H-bonds.

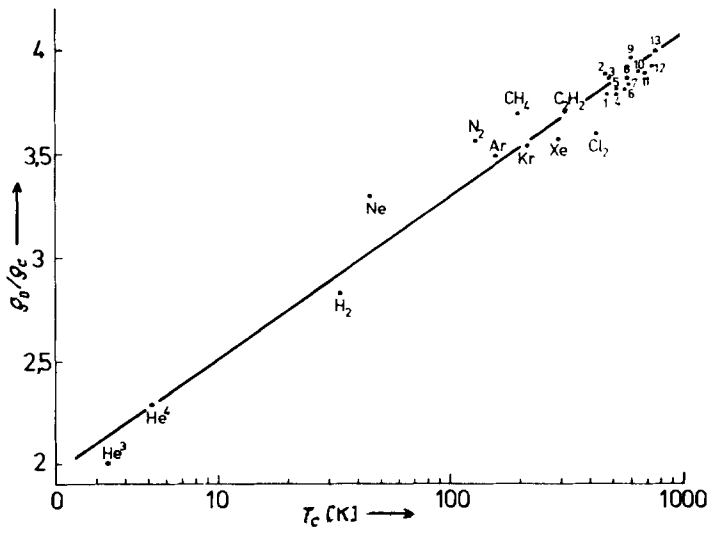


Fig. 6. Deviations from the theorem of corresponding states, ρ_0/ρ_c rises gradually with increasing values of the critical temperature (abscissa with logarithmic scale). 1, 2-methylbutane; 2, diethyl ether; 3, *n*-pentane; 4, dimethyl sulfide; 5, 2,3-dimethylbutane; 6, cyclohexane; 7, tetrachloromethane; 8, benzene; 9, tin tetrachloride; 10, chlorobenzene; 11, bromobenzene; 12, iodobenzene; 13, naphthalene.

Relation (3) does not correspond to the theorem of corresponding states; instead ρ_0/ρ_c rises slowly with T_c[7], *i.e.* with

the magnitude of the intermolecular forces[*] (Fig. 6). For organic vapors, whose critical temperatures T_c are generally lower than 500 K, $3.9 < \rho_0/\rho_c < 4$.

The van der Waals model with $V_c = 3b$ is most closely approached by H_2 with $\rho_0/\rho_c = 2.84$. In this case at T_c the mean distance of nearest neighbors $\bar{d}_c$ would be $\sqrt[3]{3}\,\bar{d}_0 = 1.44\,\bar{d}_0$, *i.e.* 1.44 times the closest packing. As Figure 7 illustrates, the mean distances $\bar{d}$ in the whole liquid range up to T_c are not very different from the distances in the crystal so that our model, in which the liquid below T_c is regarded as a close-packed melt, appears reasonable. In the hole model the distances of nearest neighbors would be even smaller than in Figure 7.

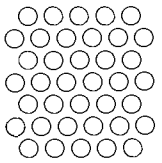


Fig. 7. Two-dimensional model of H_2 for mean particle separation $\bar{d}_c$ at the critical point.

The rise of the extrapolated zero-point density ρ_0/ρ_c with T_c is demonstrated in Figure 8 for noble gases with different

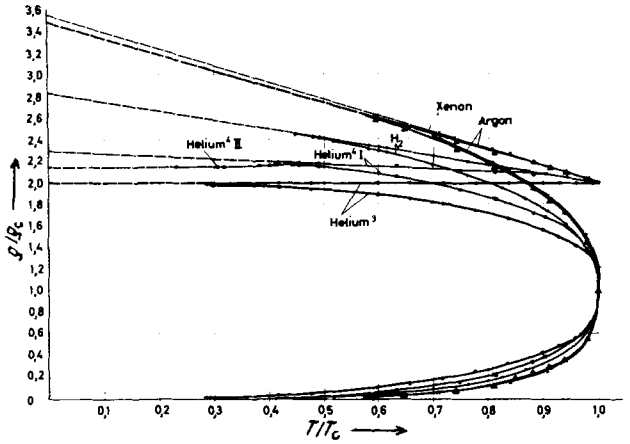


Fig. 8. $\rho/\rho_c = f(T/T_c)$; for ^{3}He and ^{4}He(II), $\rho_l + \rho_v$ is T-constant. Are there only holes, no vibration volumes?

T_c values. This shows the peculiarity that for the isotopes ^{3}He and ^{4}He(II) below the lambda point ρ_0/ρ_c is very close to 2 (for ^{3}He it is 1.9934). This means that the change in density of the ideal liquid $(\rho_l + \rho_v)$ is in this case almost zero. In our model this means that there are no oscillation volumes, and each rise in temperature merely causes an increase in the number of hole defects. A possible cause is the unusually high zero-point energy E_0 of the intermolecular degrees of freedom relative to the depth of the intermolecular potential $[(Z/2)(3/2)RT_c]$ for helium[9]:

	$3/2\,RT_c$ [cal/mol]	E_0 [cal/mol] [9]	$2E_0/Z$ [cal/mol]
^{3}He	10		
^{4}He	14	50—60	8.3—10

[*] This weak rise corresponds to the very similar rise of the critical coefficient $s = RT_c/P_cV_c$ with T_c and the small variation in $x_F(T/T_c)$ and $P\Delta V/RT_c$ with T_c [7].

In the last column E_0 has been corrected by the coordination number Z of nearest neighbors to value for the pair number $Z/2$ in order to be able to compare this value with the pair potential $(3/2)\,T_c$. Excitation of thermal oscillations in the intermolecular potential can therefore soon lead to a "dissociation" of aggregates.

3. Intermolecular Pair Potential

If the pair potential E_{pot} of the intermolecular forces and the arrangement of neighbors are known, it should in principle be possible to estimate the caloric properties of a liquid. However, can we estimate the pair potential for new substances?

The first and simplest indication of E_{pot} was the so-called Sutherland constant C, with which the temperature dependence of the gas-kinetic collision cross-section δ_T can be described:

$$\sigma_T^2 = \sigma_0^2\left(1 + \frac{C}{T}\right) \tag{4}$$

If two molecules are directly connected, then according to *Sutherland*[10]:

$$-C = \frac{2}{3R}E_{pot}; \quad -E_{pot} = \frac{3}{2}RC \tag{5}$$

For some substances, especially weakly polar ones, small deviations from the linearity of Eq. (4) are observed. We therefore redetermined the C values of all substances for which the gas-kinetic collision cross-sections are known in a sufficiently wide range of temperatures[11], and this as uniformly as possible in the neighborhood of T_c. As Figure 9 shows, the empirical relationship

$$C \approx 1.2\,T_c \tag{6}$$

was found for most substances. Consequently, according to Eqs. (5) and (6), the following relation is approximately valid:

$$-E_{pot} = \frac{3}{2}RC = 1.2\frac{3}{2}RT_c = f'\frac{3}{2}RT_c \tag{7}$$

This simple relationship permits estimation of the pair potential from T_c. Since, according to the Guldberg rule, the boiling point T_b is approximately equal to $2/3\,T_c$ and according to the Lorenz rule the melting point T_m is approximately equal to $2/3\,T_b = (2/3)^2\,T_c$, Eq. (7) shows the reason why substances can be very successfully characterized by T_b and T_m. With $3\,RT_c/2 = E_{kin}$ at T_c, Eq. (7) is reminiscent of *Kepler*'s laws of planetary motion, according to which a collision pair moves in a hyperbolic path for $|E_{kin}| > |E_{pot}|$ and in an elliptical path for $|E_{kin}| < |E_{pot}|$. Below T_c at sufficient density condensation to stable aggregates take place.

A factor with the order of magnitude of 1.2 frequently occurs in gas-kinetic derivations when the velocity distribution is neglected—as in the case of Eq. (5)[12].

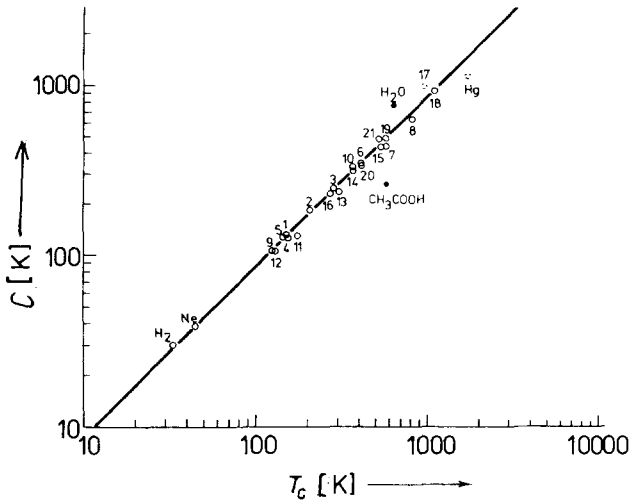


Fig. 9. Sutherland constant C and critical temperature T_c. The empirical relation $C \approx 1.2\,T_c$ holds for most substances. Consequently, T_c is a measure of the intermolecular pair potential. 1, Ar; 2, Kr; 3, Xe; 4, O_2; 5, F_2; 6, Cl_2; 7, Br_2; 8, I_2; 9, N_2; 10, H_2S; 11, NO; 12, CO; 13, CO_2; 14, COS; 15, CS_2; 16, SiH_4; 17, $HgCl_2$; 18, $HgBr_2$; 19, $SnCl_4$; 20, NH_3; 21, CH_3OH.

This estimation of E_{pot} from C and RT_c is supported by the fact that according to *van der Waals*

$$\frac{a}{3b} = \frac{a}{V_c} = \frac{9}{8} RT_c = 1.12\,RT_c$$

but empirically

$$\frac{a}{3b} \approx \frac{3}{2} CR$$

If T_c is unknown, its value can be estimated from T_b, T_m, or from group increments[7, 8].

4. Heat of Evaporation

On the basis of the hole model the heat of evaporation of a substance at constant volume, L_V, can be calculated. L_V is due to ΔH at constant pressure:

$$L_V = \Delta H - P\Delta V \tag{8}$$

For $T < T_b$, $P\Delta V = RT$. For $T > T_b$, ΔV must be calculated from measured densities; for organic vapors ΔV can be estimated from a (reduced) $P\Delta V/RT_c = f(T/T_c)$ diagram[7] or be determined by means of an approximate formula[7].

For L_V according to the hole model we have:

$$L_V = \frac{Zf}{2} R \left(\frac{3}{2} T_c - T\right)(1 - 2x_F) \tag{9}$$

Derivation: The potential energy between Z nearest neighbors is, according to Eq. (7):

$$-\frac{Z}{2} E_{pot} = \frac{3Z}{4} RT_c f'$$

At high temperatures and finite hole-defect concentrations, Z has to be corrected:

$$Z f'(1 - x_F)$$

In addition, the influence of more remote neighbors can be taken into account by a factor f'' (not exceeding 1.2[*])[2]. We combine the factors f' and f'' in f and write for the potential energy that is opposed to the forces of attraction on evaporation in vacuum:

$$\frac{3}{4} RT_c f Z(1 - x_F)$$

It must now be borne in mind that the molecular heat (molecular heat capacity) of all liquids is greater than that of the vapors because of intermolecular degrees of freedom. It has proved possible—insofar as experimental data are available—to express this heat content of the intermolecular degrees of freedom by the expression

$$\frac{fZ}{2}(1 - x_F)RT \tag{10}$$

in which for each pair of molecules an intermolecular degree of freedom is presumed. This component again becomes available on evaporation, and it must therefore be deducted from the potential energy in the calculation of L_V:

$$L_V' = \frac{Zf}{2} R \left(\frac{3}{2} T_c - T\right)(1 - x_F) \tag{11}$$

Comparison with experimental data shows good agreement for $T < T_b$, which becomes poorer at higher temperatures, where excessively high values are obtained. A value of L_V for evaporation in vacuum is calculated by means of Eq. (11); for $T > T_b$, however, the vapor pressure may rise to 100 atm and more, so that traces of intermolecular forces still remain in the real gas. On evaporation to the real gas state with a particle concentration x_F equal to the concentration of hole defects in the liquid this corresponds to a potential energy of the real vapor amounting to:

$$\frac{Zf}{2} R \frac{3}{2} T_c x_F$$

This component must be removed from Eq. (11) as unnecessary. In Eq. (11) we have deducted

$$\frac{Zf}{2} R\, x_F T$$

too much from the heat content of intermolecular degrees of freedom in the real gas, and this must therefore be added; altogether, we must subtract from L_V' the energy that would

[*] According to *Eucken*, f'' depends on the distance exponent n in $E_{pot} = f(1/r^n)$: $f''(n = 6) = 1.204$, and $f''(n = 12) = 1.01$ [12].

have to be exerted against intermolecular forces on transferring the real gas into vacuum:

$$\frac{Z}{2} fR\left(\frac{3}{2} T_c - T\right) x_F$$

In this way we obtain Eq. (9).

Testing: At low temperatures according to Eq. (9) the values of L_V correspond to a straight line whose intercept on the abscissa divided by the slope corresponds to a value of $3\,T_c/2$. This applies in all cases in which sufficient experimental data for L_V are available (Fig. 10). A magnitude of about 14 was to be expected for the product fZ[*]. We found the following values for fZ: $(C_2H_5)_2O$ 14.5, naphthalene 14.36, C_6H_5Cl 14.4, C_6H_5I 13.8, NH_3 13.8, C_6H_5Br 12.88, C_6H_6 12.82, CCl_4 12.4, and HCl 10.1. This is very good indeed. It means that our model can be used even for relatively large nonlinear molecules such as naphthalene, and even for polar molecules such as HCl.

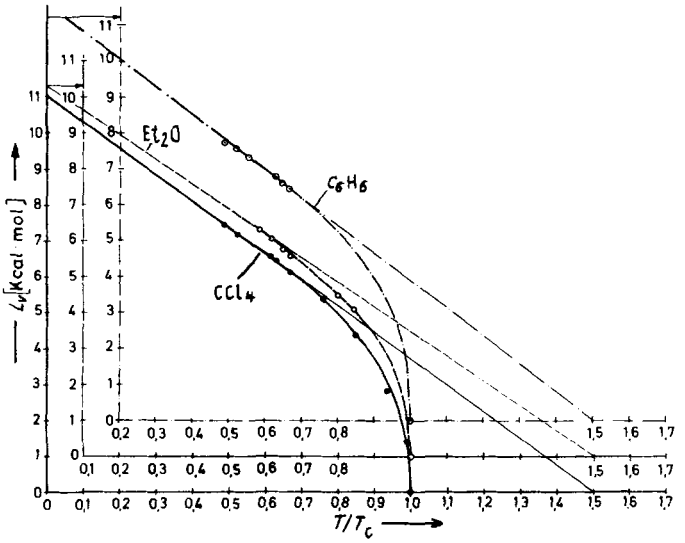


Fig. 10. Temperature dependence of the heats of evaporation L_V.

The straight lines required from Eq. (9) for low temperatures should intercept the abscissa for $L_V = 0$ at $3\,T_c/2$ (Fig. 10). The values of $L_V/(1-2x_F)$ also lie on the straight lines of Figure 10 within the accuracy of measurement of L_V. For nonpolar molecules we can therefore give: $12 < fZ < 14.5$. It is possible to determine the fZ very accurately, since it can be checked by two independent magnitudes—the slope and the intercept.

Figure 11 shows the interesting result that it is possible to understand deviations from the theorem of corresponding states on the basis of the factors fZ, which are a measure of the type of packing. The expression $L_V/fZ\,T = f(T/T_c)$ is generally valid. By measuring L_V at one temperature a value of fZ can be estimated for an unknown substance and thus the heat of evaporation can be given for all temperatures. In the range of error of 12 to 14.5, *i.e.* 20%, it is even possible to estimate heats of evaporation without making any measurement at all, provided that T_c is known or estimated with the aid of T_b.

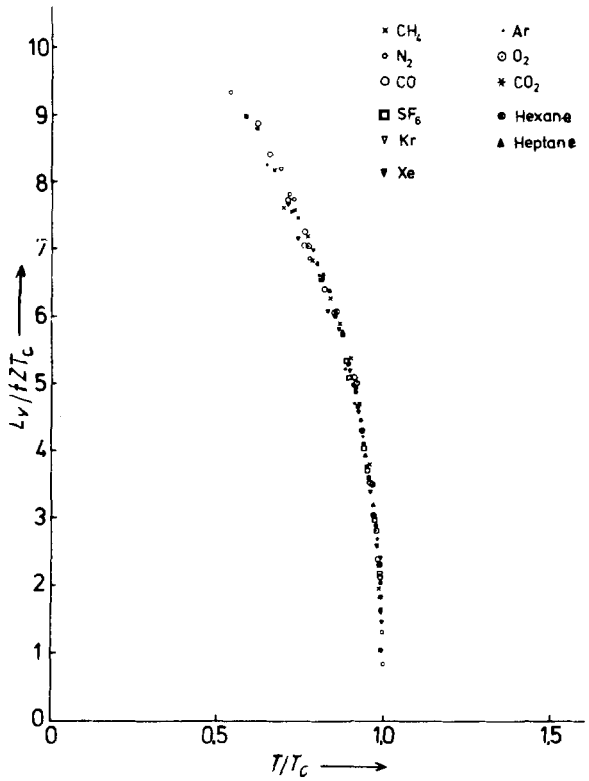


Fig. 11. $L_V/fZ\,T_c$ satisfies the theorem of corresponding states and is suitable for the estimation of unknown heats of evaporation L_V.

Eq. (9) leads not only to *Trouton*'s rule for L_V/T_b, or $\Delta H/T_b \approx 20$ cal/mol, but also explains the scatter round this value as again being due to the packing factor fZ. From Eq. (9) we obtain[5, 7] for

$$12 < fZ < 14.5$$
$$17 < \Delta H/T_b < 20$$

Deviations appear only in the cases of He, Ne, and H_2[7], which is explained by the relatively high zero-point energies E_0 of these elements; $17 < (\Delta H + E_0)/T_b < 20$ cal/mol[5].

5. Vapor Pressure Equation

The value of Eq. (9) can be demonstrated on the basis of two other facts, previously difficult to understand:

1) From the thermodynamic relation for the vapor pressure P:

$$\frac{\partial P}{\partial T} = \frac{\Delta H}{\Delta V} = \frac{L_V + P \cdot \Delta V}{T \cdot \Delta V} \tag{12}$$

it is possible to deduce as an approximation

$$\ln P = -\frac{\Delta H'}{RT} + \text{const} \tag{13}$$

in which $\Delta H'$ is constant over a wide range of T and is not identical with the T-dependent ΔH actually to be expected

[*] In the case of the closest packing of spheres, $Z = 12$. In the liquid state, because of the change in volume on melting, $Z = 0.8 \times 12 = 9.6$ and $9.6 \times f = 9.6 \times 1.2 \times 1.2 = 13.8 = fZ$.

$$\Delta H = \Delta H_0 + \int_0^T \Delta C_P \, dT$$

With

$$\Delta U_0 = \frac{3fZ}{4} RT_c \tag{14}$$

the heat of evaporation at $T=0$ it is possible to rearrange Eq. (9) in the following way:

$$L_V = \left(\Delta U_0 - \frac{fZR}{2} T\right)(1-2x_F) \tag{15}$$

In addition, the following relations hold (see eq. (2)):

$$(1-2x_F) = \frac{\rho_l + \rho_v - 2\rho_v}{\rho_l + \rho_v} = \frac{\rho_l - \rho_v}{\rho_l + \rho_v} \tag{16}$$

$$\Delta V = M\left(\frac{1}{\rho_v} - \frac{1}{\rho_l}\right) = M\frac{(\rho_l - \rho_v)}{\rho_l \cdot \rho_v} \tag{17}$$

It follows from Eq. (12) and Eqs. (14) to (17) that:

$$\frac{\partial P}{\partial T} = \left(\Delta U_0 - \frac{fZRT}{2}\right)\frac{(\rho_l - \rho_v)}{(\rho_l + \rho_v)} \cdot \frac{\rho_l \cdot \rho_v}{TM(\rho_l - \rho_v)} + \frac{P}{T}$$

$$= \left(\Delta U_0 - \frac{fZRT}{2}\right)\frac{\rho_l \cdot \rho_v}{(\rho_l + \rho_v)} \cdot \frac{1}{TM} + \frac{P}{T}$$

with $\rho_l \gg \rho_v$ and $\frac{\rho_l}{M} = \frac{1}{V_v} \approx \frac{P}{RT}$

$$\frac{1}{P}\frac{\partial P}{\partial T} = \frac{\Delta U_0}{RT^2} - \frac{fZR}{2RT} + \frac{1}{T}$$

$$\ln P = -\frac{\Delta U_0}{RT} - \left(\frac{fZ}{2} - 1\right)\ln T + \text{const} \tag{18}$$

$$\ln P \approx -\frac{\Delta U_0}{RT} + \text{const} \tag{19}$$

This corresponds to the proved Eq. (13), and shows that it contains ΔU_0, *i.e.* a T-independent magnitude.

From Eq. (18) we have also derived the improved empirical vapor-pressure equation due to *Kirchhoff*, *Hertz*, and *Dupré*[13] and to *Nernst*[14] with the characteristic summand $a \ln T$.

2) Empirically, a reduced vapor pressure equation

$$\ln \frac{P}{P_c} = g\left(\frac{T_c}{T} - 1\right) \tag{20}$$

has proved satisfactory; in this connection, *Nernst*[14] deduced the failure of the theorem of corresponding states on the basis of the material-dependent constant g.

If we write Eq. (19) for T_c and P_c and subtract this equation from the general equation (19), we obtain

$$\ln \frac{P}{P_c} = -\frac{\Delta U_0}{RT_c}\left(\frac{T_c}{T} - 1\right) \tag{21}$$

and ultimately, taking Eq. (14) into account,

$$\ln \frac{P}{P_c} = -\frac{3}{4} fZ\left(\frac{T_c}{T} - 1\right) \tag{22}$$

This is equivalent to Eq. (20) and shows that the substance-specific constant g is determined by the packing density fZ. The correction factor fZ for the theorem of corresponding states gives us a better insight into the properties of liquids.

6. Surface Energy U_σ

6.1. U_σ According to the Hole Model

Surface tension σ is defined as the energy necessary to increase a surface by 1 cm^2. Since the number of molecules per cm^2 is dependent on the material and the temperature, the molar surface energy σ_M must be used in discussions of structure[15, 16].

$$\sigma_M = N_A^{1/3} V^{2/3} \sigma \tag{23}$$

As isothermally measured work, σ_M is a free energy, and the surface enthalpy H_σ can be calculated from it by the Gibbs-Helmholtz equation:

$$H_\sigma = \sigma_M - T\frac{\partial \sigma_M}{\partial T} \tag{24}$$

In general, H_σ differs only very slightly from the surface energy U_σ.

Figure 12 shows that U_σ is independent of temperature for all substances which are not highly polar up to about $T/T_c < 0.9$. *Einstein*[17] erroneously concluded from this that the molecular heat at the surface is zero. Correctly stated, the difference between the molecular heats of the surface and of the interior of the liquid is zero. It follows from this that the loss of intermolecular degrees of freedom is compensated at the surface by translation.

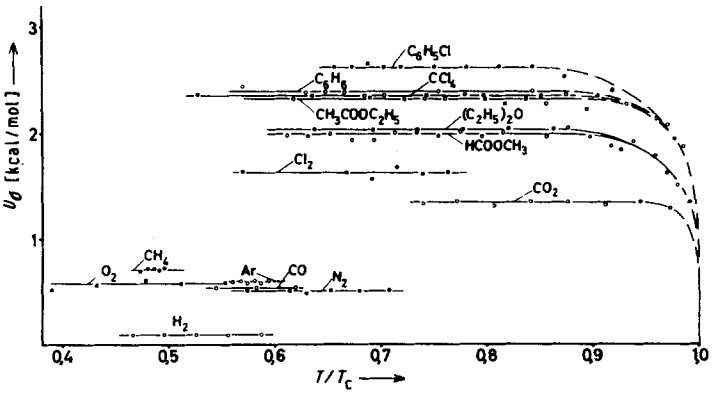


Fig. 12. The surface energy U_σ is T-constant for all nonpolar or weakly polar liquids up to about $T/T_c < 0.9$.

In earlier publications[15], the following relation, with an error of $\partial V^{2/3}/\partial T$

$$U'_\sigma = N_A^{1/3} V^{2/3}\left[\sigma - T\frac{\partial \sigma}{\partial T}\right]$$

was frequently used, and the good temperature constancy of U_σ was therefore overlooked.

If the coordination number at the surface is denoted by Z, then according to our model of a liquid one should expect:

$$U_\sigma = f(Z-X)\frac{3}{4}RT_c \tag{25}$$

Figure 13 confirms the good proportionality of U_σ and T_c over a very wide range of critical temperatures. In the case of substances with very low values of T_c the understandable deviation, amounting to $E_0/3$, again makes an appearance.

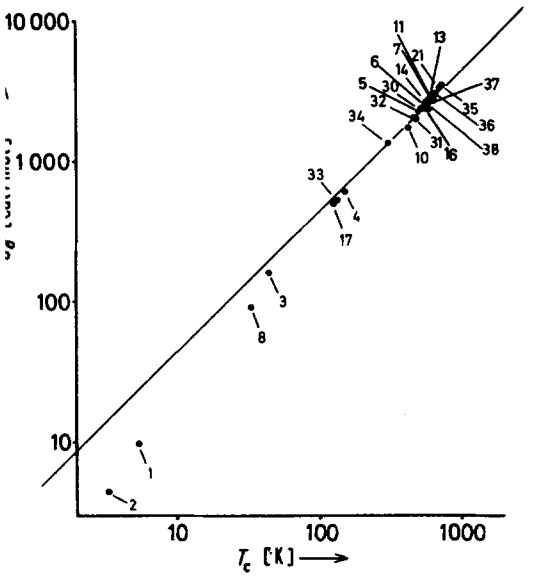


Fig. 13. The surface energy U_σ for $T/T_c < 0.9$ is proportional to T_c. 1, ^{4}He; 2, ^{3}He; 3, Ne; 4, Ar; 5, *n*-hexane; 6, benzene; 7, toluene; 8, H_2; 10, Cl_2; 11, *o*-xylene; 12, *m*-xylene; 13, *p*-xylene; 14, cyclohexane; 16, CCl_4; 17, N_2; 21, aniline; 30, ethyl acetate; 31, methyl formate; 32, diethyl ether, 33, CO; 34, CO_2; 35, *N,N*-dimethylaniline.

For most substances we obtain $fZ = 2.85$ from $4U_\sigma/3RT_c$[5]. In the case of closest spherical packing, we would have $X = 9$ and $Z - X = 3$. We can therefore estimate unknown surface tensions on the basis of the hole model:

$$\sigma_M = U_\sigma + T\frac{\partial\sigma_M}{\partial T} = 2.85\frac{3}{4}R(T_c - T) \tag{26}$$

and therefore σ as well from Eq. (23). In this way it is also possible to derive the empirical Eötvös rule, which gave a value fluctuating around 2.1 in place of $f(Z-X)\times 3/4 = 2.85\times 3/4 = 2.14$. Deviations from this rule can again be explained in terms of the packing density $(Z-X)$. In the case of substances with hydrogen bonds a maximum appears for $U_\sigma = f(T)$, which can be explained quantitatively by the orientation defect model[2, 18, 19].

6.2. The Temperature Dependence of U_σ for $T/T_c > 0.9$

According to the hole model, a temperature dependence of U_σ should be expected for $T/T_c > 0.85$ because of the factor $(1-2x_F)$. This term describes the experimentally found decrease in U_σ with rising temperature, but only approximately—it is too large. The influence of temperature can be better represented by a factor $(1-4x_F)$ in Eq. (25). The reasons for this are possibly a higher concentration of hole defects on the surface or a higher concentration of vapor in the neighborhood of the boundary layer.

6.3. *Stefan*'s Law

The so-called *Stefan*'s law was erroneously taken to mean that the expected ratio $L_V/U_\sigma = 2$ is valid. Values of 3 to 4 actually found for this quotient at room temperature have been explained incorrectly[15, 20].

According to Eqs. (9) and (25), the Stefan quotient is a function of temperature[5]:

$$\frac{L_V}{U_\sigma} = \frac{Z\left(\frac{3}{2}T_c - T\right)(1-2x_F)}{(Z-X)\frac{3}{2}T_c(1-4x_F)} \tag{27}$$

It is precisely this T function (27) and its limiting value

$$\lim_{T\to 0}\frac{L_V}{U_\sigma} = \frac{Z}{Z-X} = 4$$

which have been obtained experimentally.

7. Calculation of Enthalpy

To a second approximation it is also possible to attempt a calculation of the enthalpies H_v and H_l for the vapor and liquid under saturation conditions. This is easily possible on the basis of considerations that have already been discussed. A higher accuracy is achieved if it is borne in mind that the translational degrees of freedom are absent in the liquid state. We obtain astonishingly good agreement with formulas (28) and (29).

$$H_v = \frac{fZ}{2}\cdot\frac{3}{2}RT_c(1-x_F) + \frac{fZ}{2}RTx_F + \int_0^T C_V\,dT - \frac{3}{2}RTx_l + PV_v \tag{28}$$

The individual summands in Eq. (28) have the following significance:

1a: evaporation against potential energy at $T = 0$ K;
1b: summand 1a times x_F is absent in the real gas;
2: heat content of intermolecular degrees of freedom;
3: heat content of intramolecular degrees of freedom plus translation;
4: fall in the translational degrees of freedom due to association;
5: pressure-volume correction of the internal energy.

$$H_l = \frac{fZ}{2}\cdot\frac{3}{2}RT_cx_F + \frac{fZ}{2}RT(1-x_F) + \int_0^T C_V\,dT - \frac{3}{2}RT(1-x_F) + PV_l \tag{29}$$

The significance of the summands is analogous to the case of Eq. (28). In the fourth term the translational energy $3RT/2$ contained in the third term is deducted. At low values of

T, the first and the third summands are the largest for H_v, and the second summand for H_l. Eqs. (28) and (29), together with the straight lines of $L_V(1-2x_F)$ extrapolated to 0 K, give a sensitive delimitation of the range of error of fZ. It is possible to calculate directly all three quantities H_v, H_l, and L_V with one value of fZ.

In this way we obtain the heat of evaporation $L_V(T=0\,K)=1850$ cal/mol for argon with $fZ=8.18$, in good agreement with the value of 1840 cal/mol extrapolated by *Born* from the vapor pressure[22]. For carbon monoxide, with $fZ=9.525$, the heat of evaporation was found to be $L_V(T=0\,K)=1900$ cal/mol.

Figures 14 and 15 shows that Eqs. (28) and (29) describe well the results obtained by experiment[21]. As a rule, Eq. (29) gives somewhat low values for substances with low critical temperatures T_c such as argon and carbon monoxide. This can be corrected by the assumption that a translational degree of freedom is retained in liquid Ar and CO—an additional movement of aggregates taking place in phase appears plausible. In this case, the four summands in Eq. (29) must be replaced by the term $-2/2\times RT(1-x_F)$ and analogously in Eq. (28) by the term $-2/2\times RTx_F$.

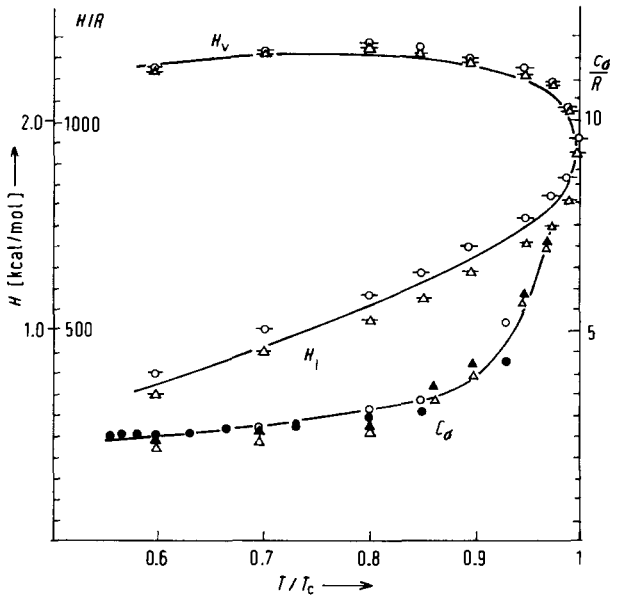


Fig. 14. Top: Enthalpies for saturation vapor H_v and saturated liquid H_l of argon; continuous curve: experimental values [21]; △, calculated according to Eqs. (28), (29), ○, calculated according to Eqs. (28), (29) with one "translational degree of freedom." Bottom: molar heats for saturated liquids; experimental [23]; ○, C_σ/R; ●, C_P/R; ▲, calculated according to Eq. (30); △, calculated according to Eq. (30) with one "translational degree of freedom".

Such effects already approach the limits of error of the model, which can be refined further by taking into account the zero-point energy, P, V corrections, *etc.* The correction introduced here for translation in the liquid becomes particularly appreciable in the case of the noble gases and substances with low molecular heats and without vibrational excitation. The necessity for this correction can also be seen from Eq. (9) for L_V. In the case of argon the straight line $L_V/(1-2x_F)$ intercepts the abscissa at somewhat higher values than 1.5 T/T_c since, because of the correction in Eq. (9), a factor of $T(Z/2(f)-$

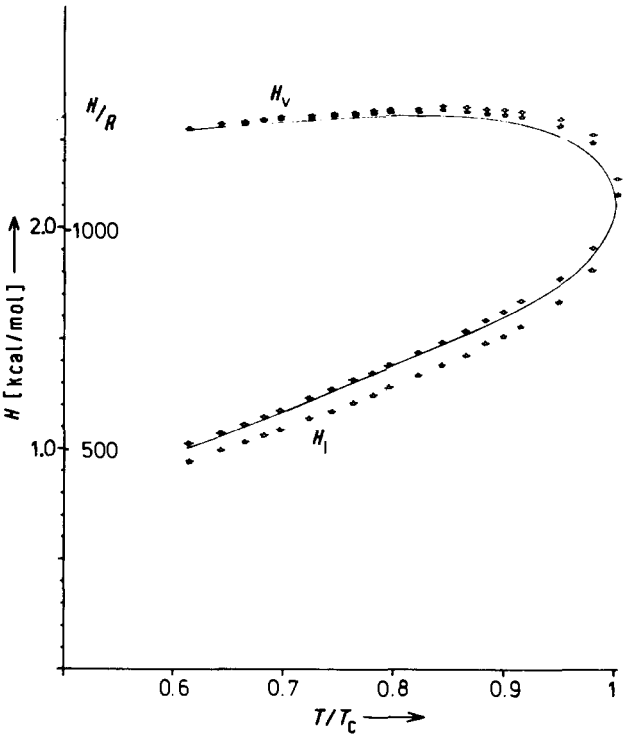


Fig. 15. H_v and H_l for carbon monoxide; continuous curve, experimental values [21]; △, calculated according to Eq. (28); ○, according to (29).

$^3/_2)R$ would be required [compare $L_V=H_v-H_l$ according to eq. (28), (29)].

8. Calculation of the Intermolecular Component of the Molecular Heat in the Condensed State

The molar heat C_σ on the saturation line for the internal energy U in the liquid state is expressed by means of Eq. (30):

$$C_\sigma=\frac{dx_F}{dT}R\left[\frac{fZ}{2}\frac{3}{2}T_c-\left(\frac{fZ}{2}-\frac{3}{2}\right)T\right]+$$
$$+R\left(\frac{fZ}{2}-\frac{3}{2}\right)(1-x_F)+C_{V,id} \quad (30)$$

where $C_{V,id}$ is the molar heat of the molecular degrees of freedom for the ideal gas. The translation has been corrected by the summand $R3(1-x_F)/2$ for the liquid. The factor after dx_F/dT corresponds to the straight line $L_V/(1-2x_F)$, see Section 5.

Figure 14 shows the values of C_σ/R calculated for argon by means of Eq. (30) and the experimental values given by *Rowlinson*[23]. In this case too we obtain better agreement between experiment and theory when we permit a "translational degree of freedom" in liquid argon. Values of dx_F/dT were taken from Figure 2.

In order to test the validity of formula (30) also for more complicated molecules with temperature-dependent molar heats of their ideal gas state, we have ourselves measured the molar heat of benzene along the saturation line in a *Calvet* adiabatic high-temperature calorimeter. The results are shown in Figure 16. In this case the agreement of experimental and calculated ($fZ=13.5$) values is again satisfactory.

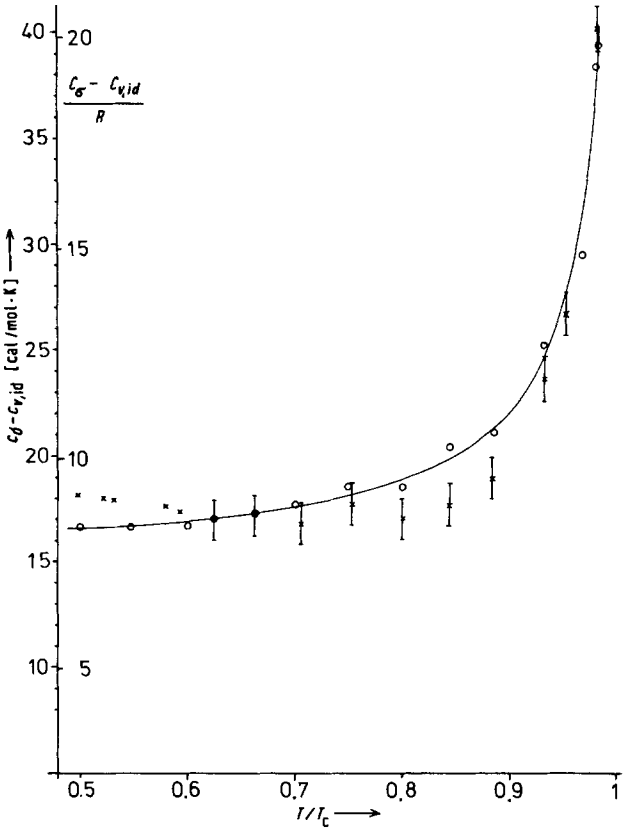


Fig. 16. Intermolecular component of the molar heat of liquid benzene under saturation conditions. Experimental: ×, according to *Rowlinson* [23]; *, own measurements. ○, calculated according to Eq. (30).

Deviations at low values of T/T_c may be due, *inter alia*, to some degree of displacement of the 20 vibrational frequencies, used for calculating $C_{V,id}$ by *Zeise*[24,25], by intermolecular forces, leading to a slight change in the oscillatory component of the molar heat. A correction for such second-order effects oversteps the accuracy of our approximate model. Originally we had hardly expected that the model, first tested on the heat of evaporation, could ever be applied to enthalpies and their differential quotients C_σ. These astonishing results could delude us into believing that the hole model is more than a mere empirical contrivance.

9. A One-Dimensional Lennard-Jones Model

The hole model described in the preceding sections is more informative than would have been expected on the basis of the simple assumptions. Why is this possible with a temperature-independent and therefore a distance-dependent pair potential? In the model, a T function is used with x_F only at high temperatures. According to *Lennard-Jones* the interaction potential varies with the intermolecular distance r in the following manner:

$$E_{pot} = 4\,\varepsilon_0 \left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6} \right] \tag{31}$$

$E(\sigma)=0$; ε_0 is the potential minimum at $r=1.22\,\sigma$ (here σ denotes not the surface tension but a definite distance)

To answer the question, let us consider a one-dimensional Lennard-Jones model with three particles on a straight line; we determine the sum of the Lennard-Jones potentials of two particles at a distance of $2r_0$ on a third particle lying between them at a distance of r from the midpoint of the line joining them; r_0 and r are measured in reduced and general units as multiples of σ. The parameters in the results of the calculation which are shown in Figure 17, are the

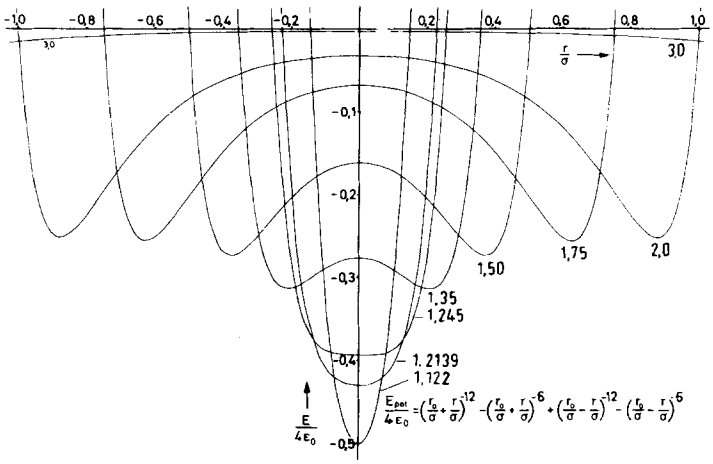


Fig. 17. One-dimensional Lennard-Jones model. Potential of the interaction of two outer particles with another particle between them on the line joining them. Parameters: distance r_0/σ of the outer particles from the center. Abscissa: Position of the middle particle in r/σ.

distances r_0/σ, the distances of the two outer particles from the center. The ordinate is the sum of the energies of interaction on the third particle in units of $4\,\varepsilon_0$. The most important results are summarized in Table 1.

Table 1. Minima of Figure 17 (see text).

r_0/σ	Corresponds in the case of CCl_4 to	Potential minimum	Minimum distance of outer particles
1.122	$T=0$ K	$-2\,\varepsilon_0$	$1.122\,\sigma$
1.2139	$T_m=0.445\,T_c$	$-1.72\,\varepsilon_0$	$1.122\,\sigma$
1.245		$-1.57\,\varepsilon_0$ (very flat)	1.2 to $1.245\,\sigma$
above 1.245		2 minima	
1.26	$T_b=0.63\,T_c$		
1.35	$T=0.83\,T_c$	$-1.25\,\varepsilon_0$	$1.14\,\sigma$
1.5	$T=0.97\,T_c$	$-1.088\,\varepsilon_0$	$1.13\,\sigma$
1.75	$T=T_c$	$-1.022\,\varepsilon_0$	$1.122\,\sigma$
1.8	$T>T_c$	$-1.016\,\varepsilon_0$	$1.122\,\sigma$
2	$T>T_c$	$-1.007\,\varepsilon_0$	$1.122\,\sigma$

Column 2 of Table 1 gives the temperatures for CCl_4 at which the mean separations calculated from the densities and the assumption $Z=12$ would correspond to the values of column 1. In the hole model the distances would be smaller: about $1.4\,\sigma$ for T_c and about $1.32\,\sigma$ for $T=0.83\,T_c$.

Table 1 is interpreted as follows. From about the boiling point T_b, above which the proportion of defects in the hole model becomes greater than 1%, two minima occur in the one-dimensional Lennard-Jones model. The distance of these minima to an outer particle corresponds, to within a few parts per thousand, to the distance for the minimum of the pair potential between two particles. This result explains the observation that in X-ray scattering diagrams the maximum for the nearest neighbors is practically independent of temperature and their distance is only slightly greater than the distance in the crystal. The position of that for second-nearest neighbors

from the X-ray data are T-dependent in agreement with the second minimum of Figure 17. The depth of the potential minimum is between the value ε_0 of the interaction with a nearest neighbor and the value $2\varepsilon_0$ for the interaction with two neighbors. The quotient of these energies corresponds to the number of hole defects. Consequently, the decrease of Z and T found by X-ray scattering becomes understandable. The depth of the potential minimum can be interpreted as if at a distance of 1.122σ a fraction of two molecules were to act instead of one neighbor. Since the hole model is independent of whether holes the size of complete molecules or several fractions of "molecular holes" are present, the two descriptions are equivalent. The potential depth at 1.12σ is naturally T-independent and for $Z=1$ it is always ε_0. The one-dimensional model of three "Lennard-Jones particles" would give a higher content of hole defects than our model. A two-dimensional model of six first nearest neighbors around a central molecule gives the following potential minima in reduced units (the corresponding distances r_0/σ are given in brackets): 1 (1.122); 0.859 (1.214); 0.78 (1.245); 0.585 (1.35) and 0.5 (1.42).

With increasing values of T/T_c the activation energy for migration between the two minima in Figure 17 would increase, but so would the mean thermal energy available for this purpose. Such migration is also in agreement with the unsymmetrical broadening of the pair distribution function in the direction of greater distances than the maximum of nearest neighbors. In addition, a relationship analogous to Eq. (7) applies[23]:

$$\varepsilon_0 = (1.25 \text{ to } 1.4)\, RT_c$$

According to *Rowlinson*[26], for polyatomic molecules the deviations from the central force field can be taken into account by a correction factor in the Lennard-Jones potential. The correction leads to a deeper potential minimum. It appears highly likely that the slight increase in fZ with molecular size in our hole model is caused by this circumstance. By means of this correction factor we can account for the influence of the effect on the thermal properties. The slight increase in quantities such as ρ_0/ρ_c, *etc.*, can probably be ascribed to the same cause.

Like chemical binding forces[27], the Lennard-Jones potential, with an attraction component proportional to $1/r^6$ and a repulsion component proportional to $1/r^{12}$, can also be ascribed to the superposition of the Coulomb potentials from point charges. *London*[28] interpreted his quantum-mechanically calculated dispersion forces on the assumption that in intermolecular interaction the symmetries resulting in the statistical mean are not decisive, but that even a single argon atom "senses" the approach of a second one as the action of point charges. Just as the Morse potential of the homopolar H_2 bond can be completely understood physically in terms of interactions between two dipoles[27], the dispersion forces can be explained by means of a quadrupole model. In Figure 18 the Coulomb interaction of two quadrupoles—as a model for He atoms—is compared with the Lennard-Jones potential. The inclination of the quadrupole with respect to the line joining the nuclei is derived from orientational quantization in the field of the second atom.

As can be seen from Figure 18, the mathematical course of the Lennard-Jones potential can be satisfactorily reproduced

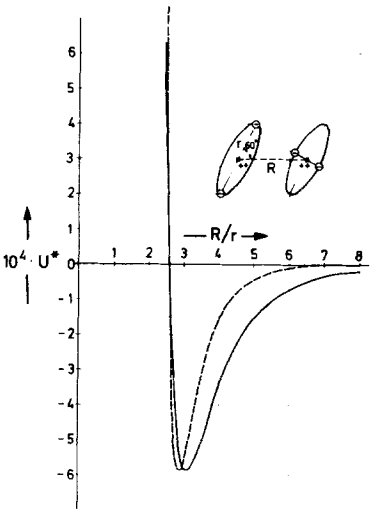


Fig. 18. – – – – –, Lennard-Jones potential; ————, Coulomb potential of two quadrupoles as a model for He-He interaction.

by a simple model of this kind. This supports *London*'s simple interpretation of the dispersion forces[28].

10. Melting Point

10.1. Cooperative Interpretation

A sharp melting point T_m can be explained only by cooperative mechanisms[29,30]. This means that the energy U_F required to generate a defect must depend on the defect concentration, *i.e.* on the degree of order $(1-x_F)$. The simplest case would be a linear relationship

$$U_F = U_{0F} + U_{1F}(1-x_F) \tag{32}$$

Bresler[29] has shown that with this equation and the formalism of statistical thermodynamics it is possible to obtain the T function for $(1-x_F)$ given in Figure 19. Under equilibrium

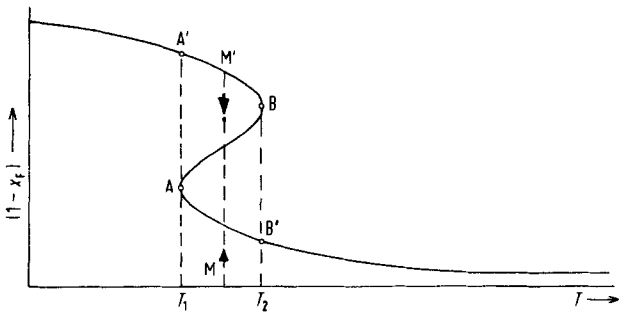


Fig. 19. Model for a sharp melting point in the defect model. The linear dependence of the defect production energy on the degree of order $(1-x_F)$ causes a jump-like change [29] in the degree of ordering at MM'.

conditions, therefore, $(1-x_F)$ would change in jump-like fashion at a temperature MM'. This would be the simplest explanation for a sharp melting point.

Our hole model with an interaction energy

$$E_{pot} = fZ\frac{R}{2}\frac{3}{2}T_c(1-x_F) \tag{33}$$

satisfies and specifies the idea of cooperative mechanisms. Where a defect is present at random the interaction energy is lower because of the smaller coordination number $Z(1-x_F)$. The probability of the occurrence of a second defect on further supply of heat energy is therefore shown by Eq. (33) to be higher in the neighborhood of a defect than in ordered defect-free regions.

10.2. Geometric Interpretation

According to an empirical rule due to *Lorenz*[31], the volume in the melt at T_m is:

$$V_m(T_m) = 1.2\, V_0(T=0\,K) \tag{34}$$

For a densest packing of spheres with $Z=12$, the separation of the (111) molecular planes should become greater by a factor $\Delta h = 1.061$[5] as the distance between the spheres increases as a consequence of the increase in vibration volume with T, so that the spheres of one (111) plane can slide over the gaps between the spheres in a neighboring plane without geometric hindrance[5] (see Fig. 7: direction of motion perpendicular to the plane of the drawing). This would correspond, in analogy with the Lorenz rule, to an increase in volume to $V=(\Delta h)^3\ V_0 = 1.194\ V_0$.

The 20 % increase in volume is due to equal extents—about 10 % each—to the sudden increase in volume at T_m and to the thermal expansion on going from T_0 to T_m.

In order to permit the (111) planes to slide freely over the neighboring planes in all directions (see Fig. 7: movement from left to right), an increase in the distance corresponding to an increase in volume to $V=1.84\ V_0$ is necessary[5]. In the hole model for most substances with $T_c > 200$ K: $3.7 < \rho_0/\rho_c < 4$. This corresponds at T_c with $x_F = 50$ % to $1.92 < V_{c,id}/V_0 < 2$.

10.3. In the Hole Model

The enthalpy rises more slowly in solids than H_1 in liquids. We can explain this by assuming that the intermolecular degrees of freedom are not completely excited in the solid state or that they are partly coupled by phase relationships[32] (lattice vibrations). Consequently, their number in the second summand of Eq. (29) should be put at less than $Z/2$. This idea can be illustrated directly under a microscope in the crystallization of monodisperse latices[33] with particle diameters of about 1 μm. The Brownian motion of individual latex particles becomes unrecognizable when they are superposed on an energetically favorable gap (Kossel step) of an aggregation.

In this model the heat of fusion essentially causes an increase in the number of independent intermolecular degrees of freedom (of the order of 50 % of Z). This also counters the objection that small aggregates with a crystal-like structure should melt below T_m according to *Gibbs-Thomson*. The region of ordering of the liquid differs from the solid not least by the fact that there are no phase relationships between its units, *i.e.* no lattice vibration.

10.4. In the One-Dimensional Lennard-Jones Model

The one-dimensional Lennard-Jones model discussed in Section 9 has the remarkable property that at a separation of the outer particles of $r_0 = 1.2444\,\sigma$, at which their two pair potentials intersect precisely at the point of inflection, a very flat minimum occurs with almost equal potentials for a certain range of distances (see Fig. 17). Above these distances the potential then splits into two minima. The range of distances of the deep flat potential minimum corresponds to a volume change of about 10 %.

11. Application to More Complicated Problems

11.1. The Supercritical Region

The hole model also permits semiquantitative answers to complicated questions. Thus, just above the critical point a reduction in the defect concentration is to be expected. In the range $T_c < T < 1.1\ T_c$ in the X-ray scattering for $V < V_c$ liquid-like maxima of the radial distribution curve are observed, which disappear at $V > V_c$[34]. Correspondingly, in the same range of T pronounced anomalies of the enthalpy and of the isotherms appear for $V < V_c$. *Eucken* pointed out the remarkable behavior of the molar heat in this temperature range[35]. Along the saturation line below T_c the molar heat has a ridge-sharp maximum in the P, T diagram, which clearly extends as an extrapolation of the saturation line to $1.1\ T_c$. In the same way as the melt can be described as the remainder of a disturbed crystal structure, the supercritical region $T_c < T < 1.1\ T_c$ for $V < V_c$ can be regarded as the residue of a disturbed liquid structure[36]. Because $(\partial P/\partial V)_{T_c} = 0$ or $(\partial V/\partial P)_{T_c} = \infty$, high density gradients may arise in the gravity field, which explains the pronounced tendency toward convection up to $1.1\ T_c$[36, 37].

11.2. Adsorption and Separation Processes

The estimation of the pair potential of intermolecular forces from RT_c is useful for the estimation of many material properties. Starting from the quantum-mechanical approximation that dispersion forces in mixtures depend on the geometric mean of the pair potentials of the components[28], properties of binary mixed systems can be derived from $R\sqrt{T_{c1}\,T_{c2}}$ or according to Eq. (7) from $R\sqrt{C_1 C_2}$ (see, for example, Table 2).

Table 2. Experimental dissociation energies of diatomic species in comparison with model data.

	ΔH [cal/mol] [38]	C_1	C_2	$R\sqrt{C_1 C_2}$ [cal/mol]
Hg_2	1600 ± 400	880	880	1760
HgKr	800	880	184	804
HgAr	600	880	130	670

Correspondingly, the heat of adsorption $\Delta H_{ad} \approx ZR/\sqrt{T_{c,A}\,T_{c,a}}$ is proportional both to the root of the critical temperature $T_{c,A}$ of the adsorbent and also to $T_{c,a}$ of the adsorbate, while, as already mentioned, when T_c is unknown it is instead possible to use T_b or, with lower accuracy, T_m (with a proportionality factor) in order to obtain an estimate. With the same adsorbent A, the magnitude $\Delta H_{ad}/\sqrt{T_{c,a}}$ or an equivalent quotient of T_b should be constant for various adsorbates a. Some examples of this are known:

1) Adsorption of gases on charcoal ($\Delta H_{ad}/R\sqrt{T_b}$) according to *Eucken*[39]: H_2 (275), N_2 (257), CO (265), CH_4 (260), C_2H_4 (260), C_2H_2 (290), CO_2 (287), NH_3 (287), CH_3OCH_3 (285) (cf. [40]).
2) Adsorption of gases on silica gel ($\Delta H_{ad}/R\sqrt{T_c}$) according to *Cremer* and *Prior*[41]: C_2H_4 (185), CO_2 (185), C_2H_2 (195), CH_2CHCl (191).

In some cases a proportionality between ΔH_{ad} and $T_{c,a}$, but not $\sqrt{T_{c,a}}$, has been reported[42–44]. This obviously relates to a multilayer adsorption, for which the interaction of the adsorbed molecules with one another is decisive[45].

Summarizing, it can thence be seen that in the case of a separation by adsorption, as for example in chromatography, the retention time may be expected to be proportional to $T_{c,a}$ or $T_{b,a}$ if highly polar substances and, in particular, those forming H-bonds are excluded. This fact came to light already in the pioneer investigations on gas chromatography by *Peters* and *Weil*[46] and by *Cremer* and *Müller*[47], in which the sequence of the retention times of a mixture of gases[47] $N_2 < C_2H_4 < C_2H_2$. This can be correlated with the sequence of the Sutherland constants N_2 (127) < C_2H_4 (283) < C_2H_2 (309).

Similar relationships are established with the results[48,49] of column chromatography, where the adsorbability generally agrees with the sequence of the melting points (T_m in °C), *e.g.*: 1,8-diphenyloctatetraene (225) > 1,6-diphenylhexatriene (194) > 1,4-diphenylbutadiene (152) > stilbene (124) > biphenyl (70). Since T_c and T_b increase approximately as the square root of the molecular weight (highly polar substances representing an exception), the adsorbability, and therefore the separation effect too, show a tendency to increase with molecular weight[50] or, in homologous series, with chain length[51,52].

When the adsorbents are changed[49], their adsorption capacity for the same adsorbate generally falls with their melting point, *e.g.*: Al_2O_3 (T_m = 2040 °C) > CrO_3 (1990) > ZnS (1900) > CaF_2 (1360) > $CaCO_3$ (1339).

Because of the high critical temperature and the high intermolecular energy of the adsorbents, the condition $L_V < L_p < \Delta H_{ad}$ is always satisfied, which explains the better separation effect of adsorption processes as compared with simple distillation (see Table 3).

Table 3. Comparison of the separation effect of distillation and adsorption on wood charcoal.

	L_P [cal/mol]	ΔH_{ad} [cal/mol]	$e^{-L_P(H_2)/RT}/e^{-L_P(N_2)/RT}$	$e^{-\Delta H_{ad}(H_2)/RT}/e^{-\Delta H_{ad}(N_2)/RT}$
H_2	220	2500	0.69 : 0.11 = 6.3	0.15 : 0.006 = 25
N_2	1330	4400		

11.3. Spectroscopy

The ordering principle of intermolecular effects based on the critical temperature applies for the most diverse material properties. Thus, the IR frequency shift $\Delta\nu$ observed by *Barnes et al.*[53] for HCl by the low-temperature matrix technique can be arranged according to the T_c values of the matrices used; $\Delta\nu$ is a measure of the interaction[54]. Similarly, the $\Delta\nu$ of the UV bands of benzene in various solvents[55] can be correlated with the T_c of the solvent. The solubility of gases in 2,2,4-trimethylpentane, investigated by *Wilhelm* and *Battino*[56], can also be explained in a simple manner on the basis of the T_c values of the gases. In all these applications, however, substances with extensive hydrogen bonding are excluded[2,3]. These will be described in a subsequent paper. Liquid metals must also be discussed separately.

At the end of the twenties, H. Mark and H. Meyer were the first to found a research team for the "molecular engineering" mentioned in the introduction, at the Ludwigshafen plant of IG Farben—later BASF AG. After the war, its reconstruction was entrusted to me by W. Reppe. This gave the initial impetus to the present study, and for this opportunity I am indebted to the research directors of BASF.

I am also grateful to the Deutsche Forschungsgemeinschaft for supporting further investigations, to W. Ditter for discussion contributions, and to M. Kuballa and G. Schietke for molar heat measurements.

Received: 8th December 1978 [A 268 IE]
German version: Angew. Chem. *91*, 408 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] *W. A. P. Luck*, Chem. Ing. Tech. *40*, 464 (1968).
[2] *W. A. P. Luck*, Discuss. Faraday Soc. *43*, 115 (1967); Z. Naturforsch. *B24*, 482 (1969); in *Luck:* Structure of Water and Aqueous Solutions. Verlag Chemie, Weinheim 1974; in *Schuster, Zundel, Sandorfy:* The Hydrogen Bond. North-Holland, Amsterdam 1976, Vol. III, pp. 1369–2423.
[3] *W. A. P. Luck*, Ber. Bunsenges. Phys. Chem. *72*, 365 (1968).
[4] *H. Eyring*, Z. Phys. Chem. *B4*, 283 (1936); *E. Cremer*, Z. Phys. Chem. *A193*, 287 (1944).
[5] *W. A. P. Luck, W. Ditter*, Tetrahedron *27*, 201 (1971).
[6] *A. Eisenstein, N. S. Gingrich*, Phys. Rev. *62*, 261 (1942); *D. G. Henshaw, ibid. 119*, 22 (1960).
[7] *W. A. P. Luck*, Ullmanns Encyklopädie der technischen Chemie, 4th Edit. Verlag Chemie, Weinheim 1972, Vol. I, p. 55.
[8] *J. O. Hirschfelder, R. B. Bird, E. L. Spotz*, Chem. Rev. *44*, 205 (1949); *L. I. Stiel, G. Thodos*, J. Chem. Eng. Data 7, 234 (1962).
[9] *K. Bennewitz, F. Simon*, Z. Phys. *16*, 183, 197 (1923); *F. Simon*, Nature (London) *133*, 529 (1934); *K. Clusius*, Angew. Chem. *56*, 241 (1943); *K. Clusius, K. Weigand*, Z. Phys. Chem. *B42*, 111 (1939); *W. Westphal:* Handwörterbuch der Physik. Springer Verlag, Berlin 1952, p. 126.
[10] *W. Sutherland*, Philos. Mag. *36*, 507 (1893).
[11] Landolt-Börnstein: Zahlenwerte und Funktionen, 6th Edit. Springer-Verlag, Berlin 1950, Vol. I/1, p. 369.
[12] *A. Eucken:* Lehrbuch der chemischen Physik. Akadem. Verlagsges., Leipzig 1944, Vol. II/1; Vol. II/2, p. 535.
[13] *K. Jellinek:* Lehrbuch der physikalischen Chemie. Enke Verlag, Stuttgart 1928, Vol. I, p. 875.

[14] *W. Nernst:* Theoretische Chemie, 15th Edit. Enke Verlag, Stuttgart 1926; Göttinger Nachrichten *1906*, 1.
[15] *K. L. Wolf:* Physik und Chemie der Grenzflächen. Springer-Verlag, Berlin 1957.
[16] *K. Schäfer:* Physikalische Chemie, 2nd Edit. Springer-Verlag, Berlin 1964.
[17] *A. Einstein*, Ann. Phys. (Leipzig) *4*, 513 (1901).
[18] *W. A. P. Luck*, Progr. Colloid Polym. Sci. *65*, 53 (1978).
[19] *W. A. P. Luck*, Chemie, Physikalische Chemie und Anwendungstechnik der grenzflächenaktiven Stoffe, Ber. VI. Int. Kongr. grenzflächenaktive Stoffe, Zürich 1972. Hanser-Verlag, München 1973, p. 83.
[20] *R. Grafe*, Nova Acta Leopold. *12*, 141 (1942).
[21] D'Ans-Lax: Taschenbuch für Chemiker und Physiker, 3rd Edit. Springer-Verlag, Berlin 1964.
[22] *F. Born*, Ann. Phys. (4) *69*, 473 (1922).
[23] *J. S. Rowlinson:* Liquids and Liquid Mixtures, 2nd Edit. Butterworths, London 1969.
[24] *H. Zeise:* Thermodynamik, Vol. III/1 Tabellen. Hirzel-Verlag, Leipzig 1954.
[25] Landolt-Börnstein: Zahlenwerte und Funktionen, 6th Edit. Springer-Verlag, Berlin 1961, Vol. II/4.
[26] Cf. [23], p. 270.
[27] *W. A. P. Luck*, Z. Elektrochem. *61*, 1057 (1957).
[28] *F. London*, Trans. Faraday Soc. *33 I*, 8 (1937).
[29] *E. Bresler*, Acta Physicochim. URSS *10*, 491 (1939).
[30] *J. Frenkel:* Kinetische Theorie der Flüssigkeiten. VEB Verlag Wissenschaften, Berlin 1957; Clarendon Press, Oxford 1946.
[31] *R. Lorenz*, Z. Anorg. Chem. *94*, 240 (1916).
[32] *R. Peierls*, Ann. Inst. Henri Poincare *5*, 177 (1935); Helv. Phys. Acta *7*, 81 (1934); *L. Landau*, Phys. Z. Sowjetunion *11*, 548 (1937).
[33] *W. A. P. Luck, M. Klier, H. Wesslau*, Ber. Bunsenges. Phys. Chem. *67*, 75 (1963); Naturwissenschaften *50*, 485 (1963); *W. A. P. Luck*, Phys. Bl. *23*, 304 (1967).
[34] *R. D. Spangler*, Phys. Rev. *46*, 698 (1934).
[35] *A. Eucken:* Lehrbuch der chemischen Physik. Akadem. Verlagsges., Leipzig 1948, Vol. II/1, p. 19.
[36] *W. A. P. Luck*, Ber. Bunsenges. Phys. Chem. *69*, 626 (1965).
[37] *J. Straub*, Chem. Ing. Tech. *39*, 291 (1967).
[38] Cf. [35], Vol. I, p. 404.
[39] Cf. [35], Vol. II/2, p. 1216.
[40] *O. Schmidt*, Z. Phys. Chem. *A 133*, 266 (1928).
[41] *E. Cremer, P. Prior*, Z. Elektrochem. *55*, 68 (1951).
[42] *W. Hene*, Dissertation, Universität Hamburg 1927; *H. Dohse, H. Mark* in: Hand- und Jahrbuch Chem. Physik. Akadem. Verlagsges., Leipzig 1933, Vol. 3/1/1, p. 11.
[43] *K. Peters*, Z. Phys. Chem. *A 180*, 79 (1937).
[44] *E. Cremer*, Österr. Chem. Ztg. *49*, 1 (1948).
[45] *W. A. P. Luck, E. Cremer*, Z. Elektrochem. *56*, 446 (1952).
[46] *K. Peters, K. Weil*, Z. Phys. Chem. *A 148*, 1 (1930).
[47] *E. Cremer, R. Müller*, Z. Elektrochem. *55*, 217 (1951).
[48] *G. Hesse:* Adsorptionsmethoden im Laboratorium. de Gruyter, Berlin 1943.
[49] *G. Hesse*, Chem. Ztg. *74*, 647 (1950).
[50] *H. G. Cassidy:* Adsorption und Chromatography (TOC V). Wiley-Interscience, New York 1951, pp. 110, 128.
[51] *A. Baum, E. Broda*, Trans. Faraday Soc. *34*, 797 (1938).
[52] *A. Baum, H. Mark*, Z. Phys. Chem. *A 180*, 392 (1937).
[53] *A. J. Barnes, H. E. Hallam, G. F. Shrimshaw*, Trans. Faraday Soc. *65*, 3159 (1969).
[54] *W. A. P. Luck* in *F. Franks:* Water—a Comprehensive Treatise, Vol. II. Plenum Press, New York 1973, p. 264.
[55] *K. Lauer, R. Oda*, Ber. Dtsch. Chem. Ges. *69*, 130, 141, 851 (1936).
[56] *E. Wilhelm, R. Battino*, J. Chem. Phys. *55*, 4013 (1971).

Circular Dichroism and Absolute Conformation: Application of Qualitative MO Theory to Chiroptical Phenomena[1]

By Günther Snatzke[*]

Although chiroptical methods have been used in chemistry for some 150 years, and the basic theory was developed by *Rosenfeld* 50 years ago, their success in determining absolute conformation rests mainly on empirical rules. Some of these can be proved theoretically; however, in the case of more complex molecules this is not yet always possible. In what follows, an attempt is made to bridge the wide gap between theory and empiricism: "qualitative MO-theory", which has already been successfully used to explain reaction mechanisms, the shape of molecules, or photoelectron spectra, can also be applied to circular dichroism (CD). In general we shall have to be content with a reasonable interpretation of the experimentally determined sign correlation, but even this will be of great value since it can yield general relations between the geometry of molecules and the sign of CD. Such relations become particularly important when only a few examples of a given chromophore are known. If first and second sphere of a molecule are achiral then sector rules can be put forward, and in other cases helicity or chirality rules.

1. Chiroptical Phenomena

Circular dichroism (CD) is nowadays the most frequently used chiroptical method [others involve *e.g.* measurement of optical rotation or optical rotatory dispersion, ellipticity, Raman-CID ("Raman Circular Intensity Differential"), CD in emission bands] and is defined as the difference of the molar decadic absorption coefficients $\Delta\varepsilon \equiv \varepsilon_L - \varepsilon_R$ for left and right circularly polarized light[2]. CD can therefore be observed only within absorption bands. These are mostly due to electron excitations in the VIS- or UV region of the spectrum, but the occurrence of CD within vibrational bands has also been experimentally proved[3]. In an unordered phase (*e.g.* solution, vapor), CD (a "Cotton effect") appears only when the respective molecules are chiral, *i.e.* if they are not congruent with their mirror image. However, this statement is not reversible:

[*] Prof. Dr. G. Snatzke
Lehrstuhl für Strukturchemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0363 $ 02.50/0*

although each molecule of a racemate is chiral, compensation precludes measurement of optical activity.

It is now our aim to correlate the *substance property CD* with the *geometric property chirality* (absolute conformation[*]) of the pertinent molecules.

2. Transition Moments in Electronic and CD Spectra

Light is well known to be electromagnetic radiation, whose electric field vector $\mathfrak{E}$ at each point oscillates at the frequency ν as a cosine function. "Allowed" (mostly $\varepsilon \geq 10^4$) excitation of a molecule by light is possible only if 1) the energy difference between the excited and the ground state is $E_a - E_g = \Delta E = h\nu$, and 2) the transition of the electron from the initial into the final orbital is associated with a charge migration, which leads to an electric dipole (transition moment $\vec{\mu}$)[4]. This is most readily established qualitatively by group theory: the direct product of the irreducible representations of the two orbitals engaged in the excitation must contain one component of the translation (T_x, T_y, T_z)[5]. A quantitative answer requires extensive calculations[6]; however, the following estimation will frequently suffice: The better the overlap between the respective orbitals, the larger will be ε. The following simple "recipe" yields both[7]: initial and final orbital are formally multiplied together; this procedure generally yields a multipole (*e.g.* a quadrupole Q). If the centers of gravity of positive and negative charge form a dipole then this excitation is electrically allowed and the line connecting the centers of gravity of the two charges yields the direction of the charge translation during excitation, *i.e.* the direction in which the excitation is "polarized". Examples of this formalism will be given in what follows.

The intensity of light absorption within a band can be described by the integrated absorption

$$\int_{\lambda_1}^{\lambda_2} \frac{\varepsilon(\lambda)}{\lambda} \mathrm{d}\lambda$$

better than by ε_{max}; it is essentially the area of the band[4]. If this experimentally accessible value is multiplied by

$$\frac{3hc \times 10^3 \ln 10}{8\pi^3 N_L} = 0.918 \times 10^{-38}$$

the "dipole strength" D is obtained, which according to theory is equal to the square of the electric transition moment $\vec{\mu}$

$$D = \mu^2 = \frac{3hc \times 10^3 \ln 10}{8\pi^3 N_L} \int_{\lambda_1}^{\lambda_2} \frac{\varepsilon(\lambda)}{\lambda} \mathrm{d}\lambda \qquad (1)$$

This equation (1) relates the measurable substance property "area of band" with the theoretically calculable molecular property "transition moment".

[*] The term "absolute conformation" is used here by analogy with "absolute configuration": The conformation of a molecule is known if we know the magnitudes and relative signs of all torsion angles. If we also know which one is positive, and which one is negative, we have then determined the "absolute conformation".

CD can only occur within an absorption band if the electron excitation is associated not only with a charge translation $(\vec{\mu})$ but also with a charge rotation; the electron thus formally has to be excited along a helical path[6, 8]. Each rotation of electric charge around an axis is equivalent to a circular current, which according to *Biot-Savart* creates a magnetic field proportional to the area enclosed by the path of the point charge; this magnetic field can in our case be described by a magnetic transition moment $\vec{m}$[9]. Once again both methods mentioned for $\vec{\mu}$, *viz.* group theory and formal orbital multiplication, yield the approximate magnitude and direction of $\vec{m}$ during an excitation.

The integral circular dichroic absorption is a better quantitative measure for CD than $\Delta\varepsilon_{max}$

$$\int_{\lambda_1}^{\lambda_2} \frac{\Delta\varepsilon(\lambda)}{\lambda} \mathrm{d}\lambda$$

i.e. essentially the area under the CD curve; multiplication of this experimentally accessible value by

$$\frac{3hc \times 10^3 \ln 10}{32\pi^3 N_L} = 0.229 \times 10^{-38}$$

(for theoretical reasons this factor is only one fourth of the factor for D), one obtains the "rotational strength" R, which also can be obtained by calculation[10]:

$$R = \mu m \cos(\vec{\mu}, \vec{m}) = \frac{3hc \times 10^3 \ln 10}{32\pi^3 N_L} \int_{\lambda_1}^{\lambda_2} \frac{\Delta\varepsilon(\lambda)}{\lambda} \mathrm{d}\lambda \qquad (2)$$

The occurrence of CD thus not only requires that the transition be associated with an electric $(\vec{\mu})$ and a magnetic $(\vec{m})$ moment but also precludes orthogonality of these moments; $\vec{\mu}$ and $\vec{m}$ must have components in the same direction. If the angle between $\vec{\mu}$ and $\vec{m}$ is acute (extreme case: parallel arrangement), eq. (2) shows the CD to be positive; if the angle is obtuse (extreme case: antiparallel arrangement) then the CD is negative. We thus obtain the sign of the CD provided we can determine the mutual relative orientation of $\vec{m}$ and $\vec{\mu}$ for a transition.

3. Classification of Chromophores; g Values

Absorptions which are not associated with a transition moment $\vec{\mu}$ should not be observable in spite of meeting the condition $\Delta E = h\nu$. That they can still occur (albeit with relatively small ε) is attributable mainly to modification of the symmetry of the chromophore by non-totally-symmetric vibrations, the forbidden transition then "stealing" intensity from an allowed transition[4]. The order of magnitude of $\vec{\mu}$ for an electric dipole allowed transition is one Debye ($\mu_D = 10^{-18}$ cgs units), and that of $\vec{m}$ for a magnetically allowed transition is one Bohr magneton ($\mu_B = 0.927 \times 10^{-20}$ cgs units); $\vec{m}$ can also be "stolen" from other transitions *via* vibrations if necessary. As shown by group theory, $\vec{\mu}$ and $\vec{m}$ can have components in the same direction only in the case of chiral chromophores; to a zero approximation CD can therefore only occur in

such cases. *Moscowitz*[11] therefore divides chiral molecules into two classes, *viz.* those which contain an inherently chiral chromophore (class I) and those whose chromophore is locally achiral but is perturbed by its chiral surroundings (class II).

W. Kuhn has introduced the wavelength-dependent g value[12] for the characterization of optically active compounds by means of the definition

$$g = \frac{\Delta\varepsilon(\lambda)}{\varepsilon(\lambda)} = 2\frac{\varepsilon_L - \varepsilon_R}{\varepsilon_L + \varepsilon_R} \tag{3a}$$

(the conventionally measured ε value is an average value $\varepsilon = (\varepsilon_L + \varepsilon_R)/2$), or as a number characterizing the whole band[10]:

$$g^I = 4R/D \tag{3b}$$

From (1) and (2) it follows that

$$g^I = 4\mu m \cos(\vec{\mu},\vec{m})/\mu^2$$

and is therefore of the order of magnitude $g^I \approx m/\mu$; for allowed bands of substances, whose molecules belong to *Moscowitz*'s class I, the g^I value is therefore approximately

$$1\,\mu_B/1\,\mu_D \approx 10^{-2}$$

For molecules of class II $g^I < 10^{-2}$ (mostly $\approx 10^{-4}$) for a given transition if it is electrically allowed but magnetically forbidden; however, the value is $> 10^{-2}$ (mostly between 5×10^{-3} and 10^{-1}) if the transition is magnetically allowed and electrically forbidden. The magnitude of the g value is therefore a good means of identifying the type of a transition[8].

From the practical point of view, it proved convenient to further subdivide class II[13]. To this end the molecule is divided into spheres; the chromophore itself forms the first sphere, and any ring possibly incorporating the chromophore forms the second one. Groups or rings connected with this make up the third sphere, *etc.* Accordingly, molecules with a chiral first sphere belong to *Moscowitz*'s class I. It turned out for practically every chromophore that the chiral sphere nearest to the chromophore mainly determines the sign and magnitude of the Cotton effect. A few apparent exceptions[14] can be explained if the chirality of the chiral sphere nearest to the chromophore is quite small while that of the following one is very large.

If we know the exact geometry of a molecule, as well as the chromophore and electron excitation responsible for a band, then the electric and the magnetic transition moment can be calculated, and thus also the CD. However, such calculations involve enormous expenditure and their results depend on the chosen approximation (sometimes this even applies to the sign!). Of the many relevant publications only a few may be cited here[15-26]. In many cases, however, general predictions about CD can also be obtained with the aid of simple MO arguments, an approach adopted *e.g.* with great success in interpreting photoelectron spectra[27]. This "elementary" procedure depends upon which chiral sphere is nearest to the chromophore, and uses the formal multiplication method mentioned in Section 2 for determining $\vec{\mu}$ and $\vec{m}$. When using this procedure it must be born in mind that the signs of the phases within each lobe of an MO (*e.g.* $\Psi_1 = \pi$ or $\Psi_2 = \pi^*$ of an olefin, Fig. 1) have no physical meaning; only their relative distribution is important. They are therefore not indicated by + or −, but by hatching or non-hatching. The meaning of the product $\Psi_1 \otimes \Psi_2$ (only real MOs are considered) within the common region of space (orbitals actually extend to infinity, but the value of Ψ decreases rapidly with the distance from the nucleus) is that of an electron density (or electron probability) function; where $\Psi_1 \otimes \Psi_2$ is positive the charge is negative, and *vice versa*[7]. This determines the direction of the transition moment $\vec{\mu}$ (from the positive to the negative pole), which of course still depends on the arbitrary initial choice of the relative phase signs in Ψ_1 and Ψ_2. The signs of the charges acquire significance only after correlation with the direction of $\vec{m}$.

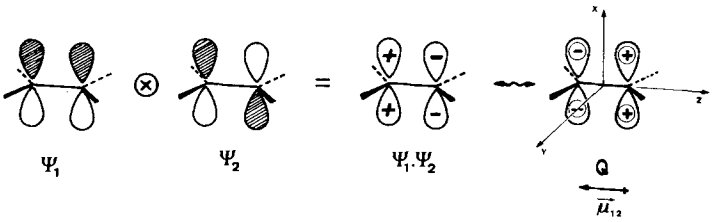


Fig. 1. Determination of the transition moments for a $\pi_x \rightarrow \pi_x^*$ transition. The two p-AOs which make up the MOs occupy practically the same space; overlap is optimal. The electron density distribution created by this transition is described [4, 7] by the product function $\Psi_1 \otimes \Psi_2$; it is obtained by formal multiplication of the orbital functions. A negative charge corresponds to a positive electron density and a deficit of electrons (during the excitation), and a positive charge to a negative one. $\Psi_i \otimes \Psi_2$ therefore describes a quadrupole Q (right), whose signs oppose those of $\Psi_1 \otimes \Psi_2$. In the quadrupole drawn the two partial dipoles add up to a dipole $\vec{\mu}_{12}$ along the z axis, whose direction depends on the (arbitrary) choice of the phase signs within the lobes of the orbitals, and which has no physical significance (energy transfer from the photon to the molecule is possible if the electric field vector $\mathfrak{E}$ points in the $(+z)$- or in the $(-z)$ direction). No charge rotation results, however ($\vec{m} = 0$).

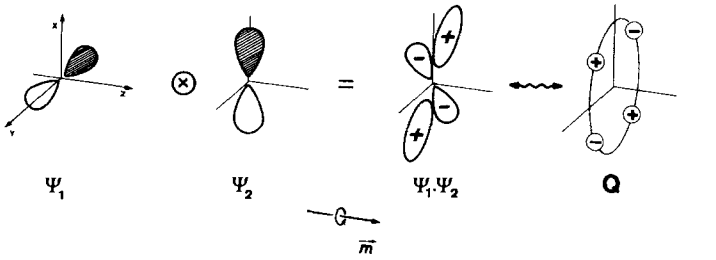


Fig. 2. Determination of the transition moments for a $p_y \rightarrow p_x^*$ transition. The overlap is much smaller than for the case shown in Fig. 1. The quadrupole Q obtained in analogous manner does not correspond to a dipole, since the two partial dipoles compensate each other for symmetry reasons; therefore $\vec{\mu}_{12} = 0$. On the other hand, electron charge is rotated during this excitation; the "right-hand rule" indicates the direction of the associated magnetic transition moment $\vec{m}$, which, however, again depends on the (arbitrary) choice of the signs of the orbital lobes.

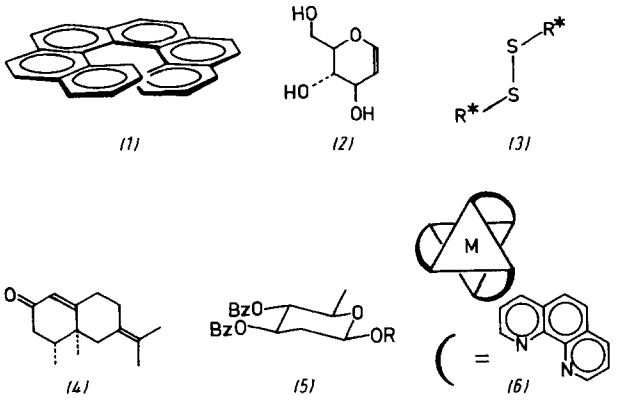
The magnetic transition moment $\vec{m}$ is generally associated with the appearance of an electrical quadrupole Q, and Figure 2 shows the relation between the two for the case $\Psi_1 = p_y$ and $\Psi_2 = p_x$. The orbital lobes of Ψ_1 are rotated through the smaller angle in such a way relative to those of Ψ_2 that like phase signs become superimposed, and this determines the direction of $\vec{m}$ according to the right-hand rule[*] (Fig. 2). Formal multiplication yields four regions of alternating signs for the product $\Psi_1 \otimes \Psi_2$ separated by nodal planes; the signs

[*] This rule states: If the 2nd through 5th finger of the right fist follow the movement of the orbital lobes then the thumb points in the direction of $\vec{m}$.

of the four "poles" of this quadrupole Q (essentially of its (x,y) component) again follow by sign inversion (Fig. 2, right). Thus if the sign pattern of Q is known, then the direction of $\vec{m}$ follows from Figure 2 provided it is known which of the two orbitals Ψ_1 and Ψ_2 is the initial orbital and which is the final one.

4. The Chiral First Sphere

Typical examples are hexahelicene *(1)*, glycals like *(2)*, chiral disulfides *(3)*, noncoplanar conjugated enones *(4)*, chiral dibenzoates *(5)*, or octahedral complexes with three bidentate ligands *(6)*. Two types may be recognized: those in which the σ skeleton of the chromophore, and therefore also at least one of the two MOs involved in the excitation, may be chiral [*(1)–(4)*], and those in which two or more achiral chromophores are in a chiral mutual arrangement and so



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

close together that, according to the exciton theory[8, 28–31], the excitation cannot be localized in one individual chromophore [*(5)*, *(6)*, but also polymers with periodically ordered structure such as the α- or β form of proteins; base-stacked forms of nucleic acids]. In the case of C_2-symmetry of the whole chromophore, the signs of the CD can be determined by a general rule given by *Hug* and *Wagnière*[32]. This is possible even for such complex chromophores as *(1)*; however, it requires an exact identification of the transitions for the many bands in the spectrum. An "elementary" treatment seems not very reasonable for *(1)*.

In glycals such as glucal *(2)*, the enol ether system has to be regarded as the chromophore, and is isoelectronic with the allyl anion. On incorporation into a dihydropyran ring, this chromophore cannot be arranged in a single plane, and crystal structure analysis of several such compounds shows that the deviation from coplanarity is either equally distributed over the C=C and the C—O bond, or that the latter is "softer" and its twist is therefore larger than that of the former[33, 34]. Figure 3a shows the HOMO and LUMO of the allyl anion. In comparison, the symmetry is somewhat perturbed for an enol ether and for π^0 a small electron density appears also on the central atom [C(1) of *(2)*][35]; however, the MO picture is only insignificantly changed. For example, if we assume a negative torsion angle $\omega_{C(5)-O-C(1)-C(2)}$ in *(2)* as drawn in Figure 3b then formal multiplication of Ψ_g with Ψ_a gives a picture of the kind shown in Figure

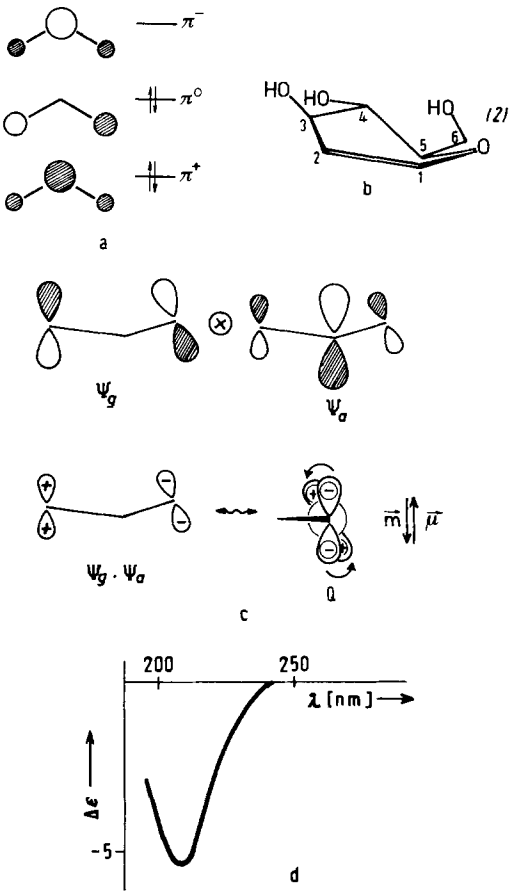


Fig. 3. The inherently chiral enol ether chromophore. a) The three MOs of the isoelectronic allyl anion; b) favored conformation of D-glucal *(2)*; c) chirality of the initial ($\Psi_g = \pi^0$) and final MO ($\Psi_a = \pi^-$), product of the two, and resulting quadrupole Q. The charge translation ($\vec{\mu}$) is in this case associated with a charge rotation ($\vec{m}$); the two partial dipoles are not parallel as in Fig. 1, but oblique to each other. The arrangement describes a left-handed screw; $\vec{m}$ and $\vec{\mu}$ are thus antiparallel and the CD is therefore negative. d) CD of D-glucal in acetonitrile.—Any other choice of the phase signs of the MOs must, of course, also lead to a left-handed screw for this transition.

3c: the centers of gravity of the positive charges lie on a line which is oblique to the line connecting the centers of gravity of the negative charges. If, in the course of excitation, electron charge is translated, say, from the oxygen towards C(2), then according to Figure 3c a concomitant charge rotation around the connecting line O—C(2) occurs. According to the right-hand rule $\vec{m}$ is therefore antiparallel to $\vec{\mu}$ ("the excitation takes place along a left-handed screw"), and the CD for this band should be negative, as has indeed been found for several D-glycals around 195—210 nm[36].

This example also demonstrates another point: the measured CD of a glycal reveals the sign of the torsional angle $\omega_{C(5)-O-C(1)-C(2)}$; the *absolute conformation* of the enol ether moiety is therefore derivable. In order to infer from this the *absolute configuration* we have first to correlate configuration and conformation. This can be done, *e.g.* by conformational analysis, discussion of NMR spectra, or resorting to X-ray diffraction analysis. In our example of glucal *(2)* the absolute conformation of the ring is determined from the negative CD (Fig. 4). A simple conformational analysis, which is in agreement with the X-ray analysis of similar products[34], shows that the absolute conformation found is compatible only with the D-configuration of glucal. *The absolute configura-*

tion can thus be determined from the CD only indirectly, not directly.

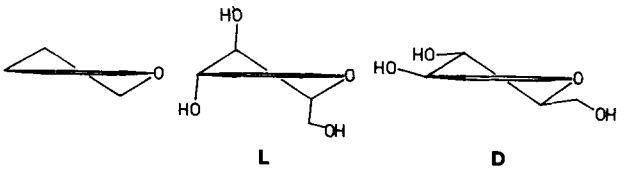


Fig. 4. Left: conformation of the helical dihydropyran ring of a glycal, as derived from the CD (cf. Fig. 3). Center and right: stereoformulae for L- and D-glucal with this conformation of the ring. It is the energetically least favored one for the L-form (all substituents axial), the most favored one for the D-form (all substituents equatorial).

For disulfides such as *(3)* the preferred conformation[37] is that in which the torsional angle around the S—S bond is approximately 90°. In order to understand their CD we have first to discuss the thioethers. The HOMO is shown by several calculations[22] to be the n_x orbital (Fig. 5); in the

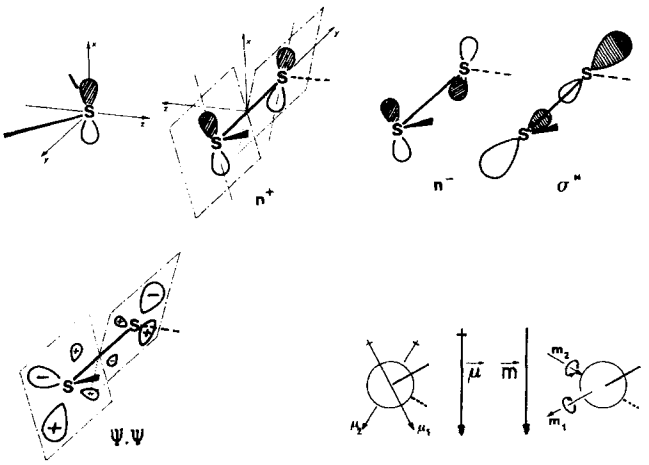


Fig. 5. The chiral disulfide chromophore. Top, HOMO of a thioether chromophore [22]; center, its two possible combinations n^+ and n^-, and LUMO of the disulfide [16]. A chiral conformation with positive torsion angle (<90°) was chosen. n^- contains (perpendicular to the S—S bond) one nodal plane more than n^+ and therefore has a higher energy than n^+. Bottom left, formal MO multiplication ($n^- \otimes \sigma^*$). An octupole is obtained, which consists of two quadrupoles. Because of the (albeit slight) overlap of the (mainly) p_x-AO on one S atom with the p_y-AO on the other S atom the "inner" poles are smaller than the "outer" ones; the partial dipoles no longer compensate each other (as was the case in Fig. 2). Bottom right, resulting direction of the electric and magnetic transition moments on S-1 and S-2, and their respective sum moments $\vec{\mu}$ and $\vec{m}$. These are parallel to each other, and a positive torsion angle (<90°) of the C—S—S—C chromophore therefore leads to a positive CD for the absorption band at longest wavelengths. Another choice of the phase signs of the involved MOs might change the direction of the individual transition moments, but not the mutual orientation of the sum moments; they always remain parallel for the chosen absolute conformation.

case of disulfides, these respective orbitals on the two S atoms have to be combined because of mutual overlap, and for a torsion angle $\omega_{C-S-S-C} < 90°$ the n^+-MO is energetically favored over n^-, which has one nodal plane perpendicular to the S—S bond; the latter is therefore the HOMO for the disulfide chromophore[16]. The LUMO is σ^* of the S—S group. Formal multiplication of HOMO and LUMO yields an octupole (Fig. 5), whose charges are, however, "outside" larger than "inside"; in spite of partial compensation there thus arises an electric transition moment $\vec{\mu}$, which points in the $(-x)$ direction if the signs of HOMO and LUMO are chosen in the given manner. Furthermore, on each of the two S atoms electronic charge is rotated around the bond leading to the next C atom, and the directions of the corresponding local magnetic transition moments $\vec{m}_1$ and $\vec{m}_2$ follow from the right-hand rule; their sum vector $\vec{m}$ is arranged parallel to $\vec{\mu}$. For a positive torsional angle $\omega_{C-S-S-C} < 90°$ a positive CD is thus predicted for the band at longest wavelengths[16], as is also found experimentally[38]. The next band, corresponding to the $n^+ \rightarrow \sigma^*$ transition, then shows a negative Cotton effect for the same absolute conformation of the C—S—S—C chromophore, as can be derived analogously. If the torsion angle is larger than 90°, then $\vec{\mu}$ and $\vec{m}$ for the band at longest wavelengths (now formally $n^+ \rightarrow \sigma^*$) are arranged in the manner just derived for the second transition, and the sign of the CD must therefore be negative. This has also been confirmed experimentally[39].

For $\omega_{C-S-S-C} = 90°$ the orbital energies of n^+ and n^- are equal; the orbitals are degenerate and the two CD bands of opposite sign compensate each other. The inherent chiral CD contribution is thus zero in spite of the chiral arrangement of the C—S—S—C moiety; of course, a weak CD from approximations of higher order still remains. Improved calculations do not change this picture in principle; the degeneracy may

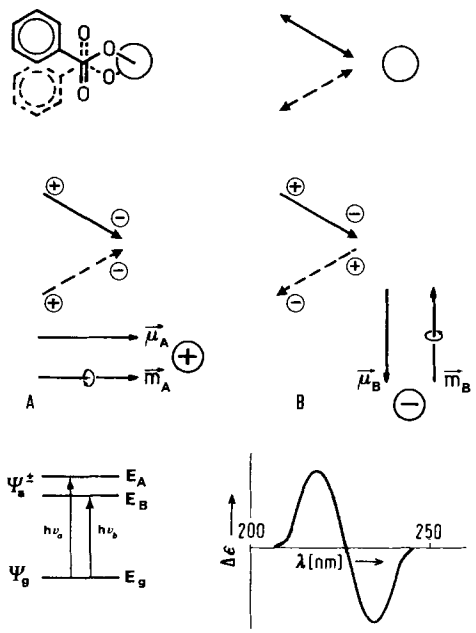


Fig. 6. Coupled oscillators: The chiral dibenzoate chromophore. Top left, preferred conformation of the benzoate groups of a 1,2-glycol dibenzoate [42]. The chosen absolute conformation is characterized by a negative torsion angle. Top right, relative orientation of the strong electric transition moments (CT transition) of the two benzoate chromophores. Center, the two possible combinations (A and B) of the mutually inclined transition moments. A, the total electric transition moment is oriented along the C_2 axis of the dibenzoate chromophore; the charge rotation created by the combined action of the two partial moments corresponds to a right-handed helix. $\vec{\mu}_A$ and $\vec{m}_A$ are therefore parallel, and the corresponding CD is positive. (The charge rotation can be recognized very simply by envisaging the total $\vec{\mu}$ as the axis of a cylinder, and the two individual $\vec{\mu}$ as tangents to this same cylinder.) B, the electric total transition moment is perpendicular to $\vec{\mu}_A$ (and lies in the plane of the figure), the magnetic transition moment $\vec{m}_B$, obtained as for A, is oriented antiparallel to $\vec{\mu}_B$, and the CD of the corresponding band is therefore negative. Bottom, relative energies of the two excited states: for A the two poles of same signs are closest to each other, and the overall interaction is therefore repulsive. For B the total interaction is attractive, and the energy of the combination A is therefore higher than of the combination B; accordingly, λ_A is smaller than λ_B. The resulting "CD couplet" is negative; its branch at longer wavelengths is negative, and that at shorter wavelengths positive. In analogous manner, a positive couplet is obtained for an absolute conformation with positive torsion angle [30, 40].

just appear at angles $\omega_{C-S-S-C}$ somewhat larger or smaller than 90°, depending *e.g.* on the bond angle Θ_{C-S-S}[16].

Dibenzoates likewise contain an inherently chiral chromophore[30,40]. Benzoates have a very intense absorption band around 230 nm, corresponding to a "charge-transfer transition" ("conjugation band" between benzene ring and COOR moiety), whose $\vec{\mu}$ is thus very large. The direction of $\vec{\mu}$ is only insignificantly inclined to the bond between the benzene ring and the C of the ester moiety (approximately 6.5° in the plane of the whole system), and thus lies approximately parallel to the C—O bond of the alcohol moiety[41], if the preferred conformation[42] of the benzoate group is assumed (see Fig. 6). For a dibenzoate of a 1,2-cyclohexanediol the torsional angle between these bonds is either about 60° (e-e, e-a, a-e) or somewhat smaller than 180° (a-a); the first three arrangements are therefore chiral, and the latter is approximately achiral. According to the exciton theory[23,29], in the case of chromophores which are closely adjacent to each other (they need not be identical as in our example) the site of excitation—first or second chromophore—cannot be localized (this would violate *Heisenberg*'s uncertainty principle).

If we designate the "local" orbitals in the ground state as Φ_{ig} ($i=1, 2$), and those in the corresponding excited state as Φ_{ia}, then of course only a single ground state exists for the whole molecule ($\Psi_g=\Phi_{1g}\cdot\Phi_{2g}$), whereas the excited state is degenerate, because it can result on excitation within chromophore 1 ($\Phi_{1a}\cdot\Phi_{2g}$) or within chromophore 2 ($\Phi_{1g}\cdot\Phi_{2a}$). As always in such cases, these two states interact, leading to a splitting of energy levels ($N^{\pm}$ are normalizing factors; (4) is valid for two like chromophores):

$$\Psi_a^{\pm}=N^{\pm}(\Phi_{1a}\cdot\Phi_{2g}\pm\Phi_{1g}\cdot\Phi_{2a}) \qquad (4)$$

As easily proved by calculation, $\vec{\mu}$ for the two transitions $\Psi_g\rightarrow\Psi_a^+$ and $\Psi_g\rightarrow\Psi_a^-$ is given by the sum of the two "local" transition moments for $\Phi_{1g}\rightarrow\Phi_{1a}$ and $\Phi_{2g}\rightarrow\Phi_{2a}$; each of the two possible relative phase relations (A and B in Fig. 6) must be chosen once. Coupling of the two moments $\vec{\mu}$ leads then to parallel (A) and antiparallel (B) arrangement of $\vec{\mu}$ and $\vec{m}$, and the sign of the CD is immediately derived therefrom (in the present case: $\Delta\varepsilon$(A) positive, $\Delta\varepsilon$(B) negative). Because $h\nu_i=E_{ia}-E_g$ ($E_{ia}=E^+$ or E^-) the position of the bands is solely determined by the energy in the excited state.

However, the relative magnitudes of E_A and E_B cannot always be estimated so easily as in the example of dibenzoates. Figure 6 shows that the most important interaction (*viz.* that between the "poles" separated by the shortest distance) is repulsive for combination A and attractive for B if the torsion angle $\omega_{O-C-C-O}$ is negative. A therefore has higher energy, and B lower energy, $h\nu_A>h\nu_B$, or $\lambda_A<\lambda_B$. The negative Cotton effect (B) is therefore at longer wavelength, and the (equally large) positive one (A) at shorter wavelengths; for this absolute conformation a "negative couplet"[28,43] arises. This result is in agreement with experiment. However, the two benzoate groups need not be linked to adjacent C atoms in order to apply the method of "coupled oscillators" (also called[30,40] the "exciton chirality method"). Although this method is very valuable for the determination of absolute conformation, it must nevertheless be confined to those cases in which both transition moments are large, the position of the individual transition moments is well known, and the "geometric factor"[28] (relative energy difference between A- and B coupling) can be derived unequivocally from the geometry of the molecule.

5. The Achiral First Sphere

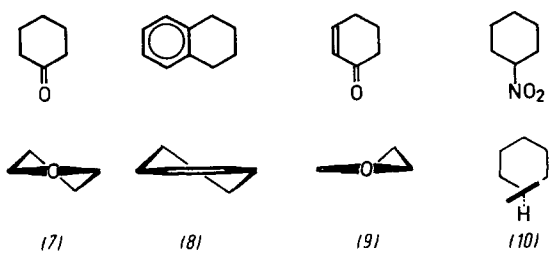
In order for CD to occur in a given electron transition of molecules in which the first sphere is achiral, one has to "steal" from some other transition the missing transition moment lying in the direction of the present one. This second transition can be in the same chromophore ("intrachromophoric"), or in another one ("interchromophoric", *e.g.* a $\sigma\rightarrow\sigma^*$ transition within a C—C or C—H bond). Perturbation theory of first or second order then describes how the two transition moments are to be mixed. In the case of "static coupling" it is assumed that this mixing of MO states of different symmetry, which should be forbidden, can be brought about by the chiral positive residual field of the nuclei not fully shielded by their electrons[6,28]. In case of "dynamic coupling" this mixing is effected by induced multipoles (dipoles, quadrupoles, octupoles, ...) in other chirally arranged bonds of the molecule as a result of the electronic rearrangement which takes place in the chromophore on excitation[6,28].

In both cases the expression for the rotational strength R contains several terms, some of which describe a possible exciton interaction if the transition in question is associated with a strong electric transition moment. Others are of the form of products $\mu\cdot m\cdot\cos(\vec{\mu},\vec{m})$ ("optical factor"[28]), which have to be multiplied by a "geometric factor". The energies of the orbitals involved contribute to this geometric factor, as does the exchange energy between them, which, of course, must also depend on the geometry of the molecule. This will be explained in more detail in Section 8 taking the $n\rightarrow\pi^*$ band of oxo compounds as example.

The fact that groups or bonds close to the chromophore cause the most effective perturbation justifies the special significance of the chiral second sphere. Nevertheless, groups which are more distant may still provide an exceedingly large contribution to the CD, if a fully antiperiplanar (zig-zag shaped and coplanar) through-bond connection exists between them and the chromophore[44].

6. The Chiral Second Sphere

Figure 7 illustrates a few examples[2] [*(7)—(10)*] of chirality of the second sphere. Experience shows that in such cases



(7) *(8)* *(9)* *(10)*

Fig. 7. Examples for a chirality of the second sphere [2a]. All absolute conformations depicted give rise to a positive CD for the specified transitions: $n\rightarrow\pi^*$ band of a cyclohexanone *(7)* in twist form; B_{2u} band of a tetralin *(8)*; $n\rightarrow\pi^*$ band of a conjugated cyclohexenone *(9)* with coplanar arrangement of C=O and C=C; $n\rightarrow\pi^*$ band of an axial nitrocyclohexane *(10)*.

the contribution of the third (fourth, ...) sphere generally influences only the magnitude of the CD to a slight extent, but does not affect its sign. For a new chromophore it therefore suffices to examine the correlation between the CD sign and the absolute conformation of the ring for a few selected examples. A line of contiguous bonds within the second sphere is, by the way, not essential; the importance of the second sphere is mainly to fix the torsional angle around the bond between the chromophore and the next chirally arranged bond. (The mechanism of this chiral perturbation will be discussed in Section 7.)

7. The Chiral Third Sphere

Now chromophore and "skeleton" are locally achiral; only on suitable substitution (often with achiral groups) does the whole molecule become chiral (*e.g.* chirally substituted cyclohexanone in chair form). An algebraic treatment of this case has been published by *Ruch*[45] and two general solutions have been given for the chirality functions (and thus also for the rotational strength). For our purpose only the second one is important. According to this, each chirality function (χ) can be built up as a sum of simpler ones (ω), which are valid for chiral molecules of the same type in which the maximum number of identical ligands is present. This maximum number is called the "chirality order o". The number of atoms in general positions which are connected by the symmetry elements of the skeleton (*i.e.* which belong to the same "transitivity area") is *n*.

The difference $(n-o)$ can only be 1, 2, or 3, and the chirality functions for these three cases are

$$\chi_1 = \sum\omega(i); \quad \chi_2 = \sum\omega(i,j); \quad \chi_3 = \sum\omega(i,j,k)$$

The indices i, j, and k refer to symmetry equivalent ligand sites in the skeleton. The functions $\omega(i)$ thus depend only on the substituent at a single ligand site, $\omega(i,j)$ on two, and $\omega(i,j,k)$ on three substituents. Figure 8 demonstrates the

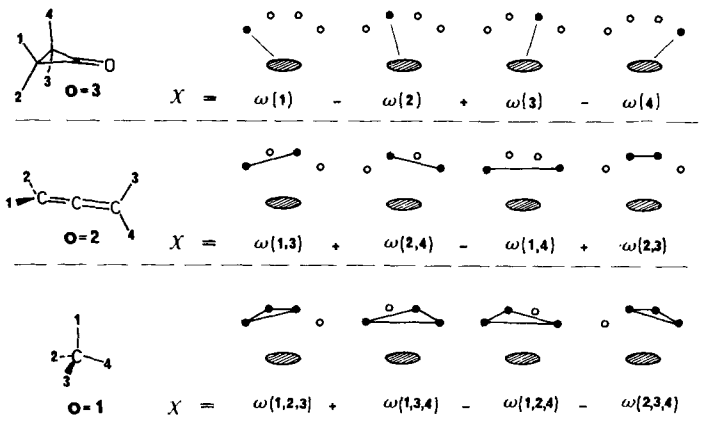


Fig. 8. Chirality functions χ for three molecules each having four ligands per transitivity area. The chirality functions ω refer to the corresponding chiral molecules with the maximal number of like ligands. The hatched area represents the chromophore, the four circles the ligands. Filled circles belong to those ligand sites which appear in the chirality functions ω. Top, carbonyl chromophore (*e.g.* in cyclopropanone), local C_{2v} symmetry, chirality order o = 3. Center, allene chromophore, local D_{2d} symmetry, chirality order o = 2. Bottom, asymmetric C atom as chromophore, local T_d symmetry, chirality order o = 1.

determination of o for three examples with $n=4$: for an asymmetric C atom as chromophore not even two ligands may be identical, and the chirality order is therefore o = 1; for allenes o = 2, and for cyclopropanones even three ligands may be identical and a chiral molecule is still obtained: o = 3. The chirality functions χ are also given in Figure 8, as well as their graphic interpretation. Only in the case of $(n-o)=1$ may specific increments appear for individual substituents; these are the functions $\omega(i)$ themselves, whereas in the other examples several terms $\omega(i,j)$ or $\omega(i,j,k)$ will change their values on replacement of one substituent by a new one. We may therefore expect a general sector rule to be valid only for the case $(n-o)=1$; in the other cases we can at best look for "special" sector rules, which are applicable, however, only when we keep one or two of the remaining substituents constant.

Having convinced ourselves, according to *Ruch*[45], that a sector rule may be valid at all for the chromophore in question then the simplest ("symmetry-determined") one can be found according to *Schellman*[46] by making the mirror planes of the chromophore into nodal planes of the sector rule (a nodal plane separates two adjacent sectors, within which the contributions to the CD have opposite signs for substituents arranged symmetrically with respect to each other; ligands lying within a nodal plane, make no contribution to the CD). We accordingly expect a "planarity rule" for an ester, a quadrant rule for a ketone, an octant rule for an olefin, a rule with 24 sectors for a benzene derivative, *etc.* To these nodal planes, however, must still be added "orbital-determined" nodal surfaces; these are nodal surfaces for the orbitals involved in the excitation, and they may be curved or even closed (finite) surfaces. These MO-determined nodal surfaces may of course be different for different transitions within one and the same chromophore. Their number can also depend on the type of approximation one is using. For example, the symmetry-determined quadrant rule for the 300 nm band of a ketone has to be extended to an octant rule to account for that nodal surface of the π^* orbital which cuts the C=O bond perpendicularly; if the n-orbital is also delocalized, then even more nodal surfaces have to be introduced[2,15]. The determination of the sign within different sectors will be described in what follows for the carbonyl and the benzene chromophore. Depending on the approximation used, intra- or interchromophoric terms may proponderate; the signs may therefore not always be predicted unequivocally.

8. The n→π* Band of Saturated Carbonyl Compounds

The n→π* transition in the carbonyl chromophore is correlated, according to Figure 2 (n-orbital = $p_{O,y}$; π^*-orbital = $N(p_{O,x}-p_{C,x})$, with a magnetic transition moment $\vec{m}$ in the direction of the C=O bond; a μ_z has to be "stolen" from another transition. In the intrachromophoric case, this can be, *e.g.*, the π→π* transition (*z*-allowed according to Fig. 1), a Rydberg transition[47], or a σ→σ* transition from the C=O bond; in condensed phase the π→π* transition is the most probable one. In formaldehyde itself there is no a_2-type normal vibration[5,47] which could lead to intensity stealing from such a *z*-allowed transition; however, the chiral

environment of the chromophore may lead to mixing of orbitals or states because of the lowering of the overall symmetry. Some time ago *Wagnière*[48] compared different mechanisms of such mixing; first-order perturbation theory leads to a quadrant rule, and only on incorporation of suitable d-orbitals or more prominent delocalization does the experimentally found octant rule[49] result.

For an electrically forbidden transition, the exciton terms mentioned in Section 5 may be dropped in the approximative formula for the rotational strength, and there remain the following four terms (first-order perturbation theory)[6, 15, 23, 28]:

$$R = T_1 + T_2 + T_3 + T_4 =$$

$$= \frac{2}{h} \frac{\nu_{0,k} \cdot V_{0,a(1);0,k(2)}}{\nu_{0,k}^2 - \nu_{0,a}^2} \cdot \mu_{0,k}(2) \cdot m_{0,a}(1) \cdot \cos(\vec{\mu},\vec{m})$$

$$+ \frac{1}{h} \frac{V_{a,b(1);0,0(2)}}{\nu_{0,b} - \nu_{0,a}} \cdot \mu_{0,b}(1) \cdot m_{0,a}(1) \cdot \cos(\vec{\mu},\vec{m}) \qquad (5)$$

$$+ \frac{1}{h} \frac{V_{0,b(1);0,0(2)}}{\nu_{0,b}} \cdot \mu_{a,b}(1) \cdot m_{0,a}(1) \cdot \cos(\vec{\mu},\vec{m})$$

$$+ \frac{1}{h} \frac{V_{0,a(1);0,0(2)}}{\nu_{0,a}} \cdot |(\vec{\mu}_{a,a}(1) - \vec{\mu}_{0,0}(1))| \cdot m_{0,a}(1) \cdot \cos(\Delta\vec{\mu},\vec{m})$$

In these formulae the subscript 0 refers to the ground state, a to the n→π* state of the carbonyl, b to another excited state in the same chromophore, and k to an excited state in the "perturbing chromophore" (*e.g.* a C—C bond arranged chirally with respect to the C=O group). The meaning of the interaction energy V is illustrated graphically in Figure 9, $m_{0,a}$ (1) is z-allowed, and its order of magnitude is the Bohr magneton μ_B.

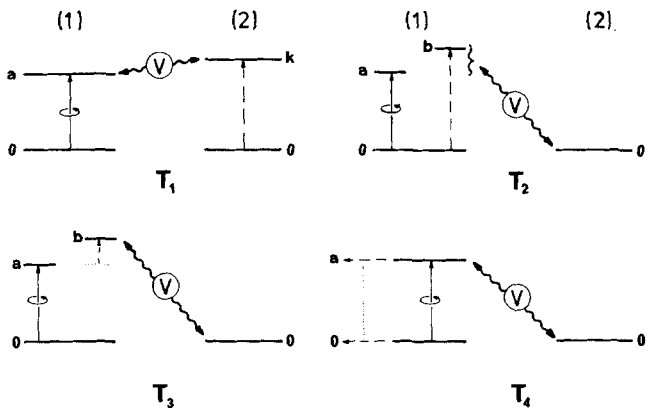


Fig. 9. Illustration of interaction energies V resulting from first-order perturbation calculations for the four terms T_1 to T_4 of eq. (5) [23]. (1) and (2) refer to two different chromophores in the same molecule (*e.g.* 1: C=O group, 2: C—C bond), 0 is the (common) ground state of the molecule; a and b characterize excited states of chromophore 1, and k an excited state of chromophore 2.

In the first term we need an electric transition moment in the z-direction from another chromophore; that may be a σ→σ* transition within a C—X bond. For the second term we have to obtain a μ_z from the carbonyl chromophore itself, and the energetically nearest excited (not Rydberg) state is the π→π* state. The third term may be neglected, as for this a transition from the first into another still higher excited state of a_2 symmetry is required; because of the denominator $\nu_{0,b}$, which is then quite large, the geometric factor will become relatively small. The fourth term contains a contribution from the difference of the permanent dipole moments for the first excited ($\vec{\mu}_{aa}$) and the ground-state ($\vec{\mu}_{00}$) of the carbonyl chromophore; this term is also of a lower order of magnitude than the first or the second.

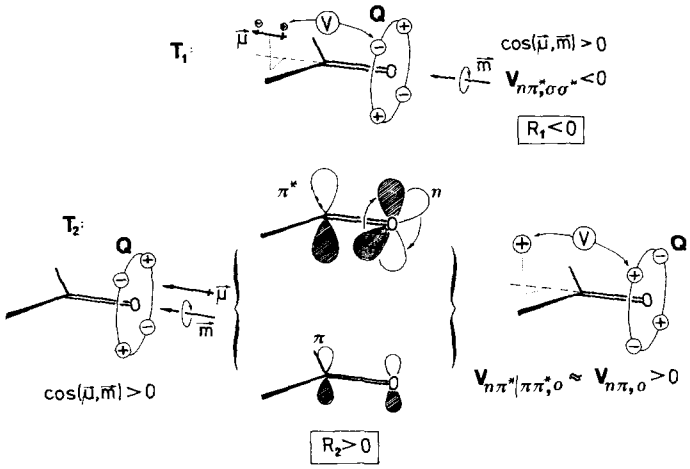


Fig. 10. Determination of the signs of the terms T_1 and T_2 in equation (5). Top, T_1. The transition 0→a of the carbonyl chromophore 1 is associated with a magnetic moment $\vec{m}$, and the transition 0→k in a C—C bond (chromophore 2) with an electric moment $\vec{\mu}$. For a C—C bond in the upper left back octant the direction of $\vec{\mu}$ was chosen arbitrarily such that it is parallel to that of $\vec{m}$ (also chosen arbitrarily). The "optical factor", $\cos(\vec{\mu},\vec{m})$ is therefore positive. The overall interaction of Q with $\vec{\mu}$ is attractive (for the correlation between Q and $\vec{m}$, cf. Fig. 2), the interaction potential V ("geometric factor") is negative, and the product of the two [$\cos(\vec{\mu},\vec{m})$ and V] is also negative. This "interchromophoric" interaction leads to a negative contribution to the CD, contradicting the experimentally found octant rule. Any other choice of the direction of the two transition moments gives the same result. Bottom, T_2. $\vec{m}$ is associated with the n→π* transition of the carbonyl chromophore; $\vec{\mu}$ is taken from the π→π* transition of the same chromophore ("intrachromophoric" interaction). Again both are chosen parallel to each other, and the optical factor is therefore positive. For instance, if we hatch the left lobe of the n orbital on oxygen, then the relative phase signs for π and π* result as given at the bottom (center; cf. also Fig. 1 and 2). According to theory, V is proportional to the energy between the perturbing partial charge and the quadrupole obtained by multiplication of the n- and π orbital (not π*!). The overall interaction of Q (bottom right) with a positive charge is repulsive, and V is therefore positive. $\cos(\vec{\mu},\vec{m}) \times V$ is also positive; a positive charge in the upper left back octant therefore gives a positive contribution to the CD. T_1 describes an octant rule, and T_2 a quadrant rule. The signs of the contributions to the CD also depend upon the sign of the perturbing charge.

The signs of the terms T_1 and T_2 are derived in Figure 10; if the positive residual charges of the nuclei which are not completely screened by their electrons[6, 15] are chosen as the chiral perturbation of the skeleton then a quadrant rule with the correct sign is obtained from T_2. The term T_1 does indeed yield an octant rule, but with the wrong signs. Clearly, the second term T_2 is the leading one. The experimentally established octant rule would also be obtained by admixture of 3d orbitals[15a]; however, their energy might differ too much[50]. Recent calculations which also account for delocalization of the n orbitals lead to the correct octant rule without any need for contributions from such d orbitals[15b-e].

Second-order perturbation theory[4, 7, 51, 52] also yields an octant rule with the right signs (Fig. 11). According to the general rules for interaction of orbitals we can undertake this mixing step by step. First of all, the mixing can be supposed to be caused by the energetically closest chiral orbital, a σ-MO from the C—C bond next to the chromophore (chiral second sphere!). As its energy is lower than that of π and n, we

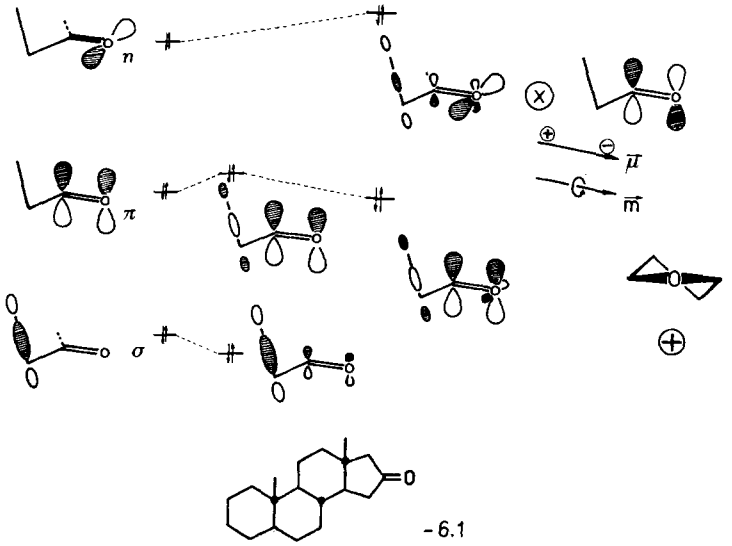


Fig. 11. Second order perturbation for ketones with chiral second sphere (mixing of MOs). The admixture (forbidden for symmetry reasons in formaldehyde) of π character to the n orbital of the carbonyl can be caused by a neighboring, chirally arranged σ bond. As the energy of a C—H bond is lower than of a C—C bond, σ_{C-C} governs the interaction. Its phase signs have again been chosen arbitrarily (top center). Instead of "localized" orbitals the suitable combination of "canonical" p_x- and p_y-AOs could also have been used. Since n- and π-MO have higher energies than the σ-MO, the latter is admixed to the first one in such a way that the energetically unfavored combination is obtained for the slightly modified MOs n″ and π″. The overlap between the σ-MO and the n- as well as the admixed π-MO is therefore negative, and this is the way the relative phase signs for the orbitals have been drawn. Whatever phase signs are chosen for the π*-MO, according to Fig. 1 and 2 a parallel arrangement of the two transition moments will always result, and a positive CD will therefore arise for the given absolute conformation of the chiral moiety C—C—C=O. In a twist form of a cycloalkanone this same arrangement appears twice, whence the mentioned rule could be derived. The CD of a 16-oxo steroid, with absolute conformation of ring D enantiomeric to this one, is accordingly strongly negative (−6.1) [2].

have for this purpose always to use the energetically less favored combination with σ. If we choose for the σ orbital the phase signs as given in Figure 11, then the unfavored combination for the admixture of the π- with the n orbital will have a nodal plane perpendicular to the C_α—C(=O) bond; the unfavored combination with the n-MO itself is that with negative overlap. As shown by Figure 11, the σ orbital of the chiral C—C bond thus induces the relative signs for the n- and the admixed π orbital lobes. Whichever phase signs we choose for π*, the product $n'' \otimes \pi^*$ in each case leads to a small $\vec{\mu}$, which is parallel to $\vec{m}$; the CD of the absolute conformation given in Figure 11 (CD of the second sphere) is therefore positive. This is the CD sign which has been found experimentally for (7) (Fig. 7)[2, 53]; the conformation of ring D of a 16-oxo steroid is the mirror image. This perturbation mechanism leads to a kind of octant rule, although the exact position of the third "orbital-determined" nodal surface cannot be derived from this simple picture. For a coplanar arrangement ($\omega = 180°$ in Fig. 11) the interaction for both possible choices of the phase signs of the admixed π orbital is of course identical, and there is no preferred orbital lobe sign. A similar situation arises for the n orbital at $\omega \approx 90°$. In the range $120° < \omega < 150°$ (deviation from coplanarity approximately 30—60°) the perturbation may be expected to reach a maximum, and this explains the particularly large Δε values for twist forms[53] of cycloalkanones. More exact calculations[54] give the same result.

The farther away the perturbing chiral bond is from the chromophore, the smaller will be its influence. An exception is seen, however, in the fully antiperiplanar train of bonds between perturbing group and chromophore[44], mentioned in Section 5; the influence of β-situated axial substituents of a cyclohexanone upon the CD, which is contrary to the general octant rule, can also be explained in this way (Figure 12). This bond comes very close to the n- and its admixed π orbital, and thus induces the relative phase signs in the manner considered above. Once again, it does not matter how the phase signs for the π* orbital are chosen: product formation leads for the given geometry to an antiparallel arrangement of $\vec{\mu}$ and $\vec{m}$; the CD is thus negative and hence in agreement with the experimental values[55] found for such groups.

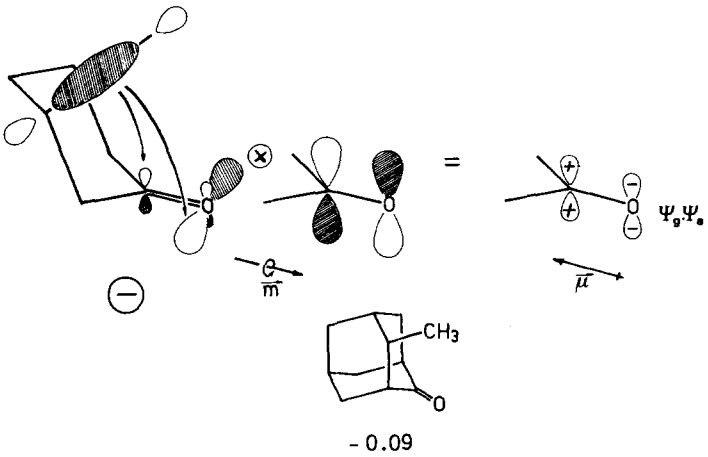


Fig. 12. The antioctant contribution of a β-axial substituent on a cyclohexanone [55]. The corresponding σ bond is very close to the MOs of the carbonyl chromophore; the relative phase signs—and therefore the relative directions of $\vec{m}$ and $\vec{\mu}$—are obtained analogously to Fig. 11. The two transition moments are antiparallel to each other for the absolute configuration chosen; the contribution to the CD is therefore negative. "Axial" 4-methyl-2-adamantanone is cited as an example. That the methyl group does not appear in a front octant follows from more detailed calculations, according to which the third nodal surface exhibits a concave curvature towards the oxygen [15e].

Perturbations through space can come from "poles" (*e.g.* the positive residual charges of nuclei not completely screened by their electrons; "one-electron theory"), or from dipoles induced in other bonds by electron excitation in the chromophore ("polarizability theory"), or from transition dipoles in such bonds, which can supply the missing electric transition moment. If we wish to apply *Coulomb*'s law we cannot, of course, investigate the interaction between a charge and an orbital lobe, but again only that between a charge and dipoles or quadrupoles. For this we have to know the relative energies of the excited states which can interact with each other. This is particularly easy for the 300 nm band of a saturated ketone as this corresponds to the excitation from the ground state into the lowest excited singlet state S_1 ($n\pi^*$). Whatever state S_i we use for the production of a μ_z, it must always have higher energy than S_1; that one of the two new states which differs only slightly from S_1 is the energetically favored one, S^+ (Fig. 13). This gives the recipe for the induction of the charge signs as a result of Coulomb interaction: we have to use the attractive and not the repulsive combination of the charges.

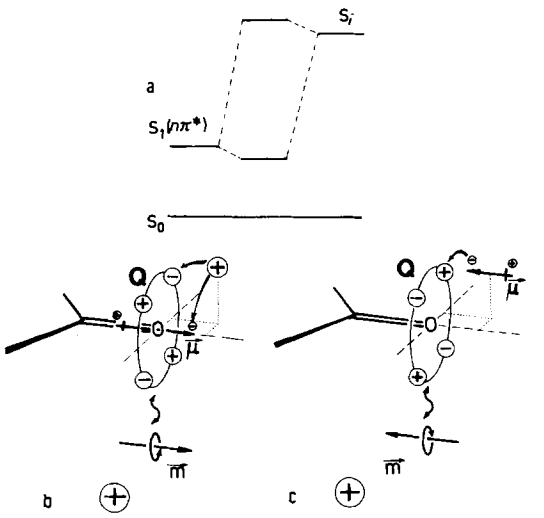


Fig. 13. Second-order perturbation theory for ketones with chiral third sphere (mixing of excited states). The chiral environment intra- or extra-chromophorically admixes an excited state S_i (always of higher energy), which is associated with an electric transition moment $\vec{\mu}$ along the same coordinate, with the first excited singlet state S_1 ($n\pi^*$), which is associated with a magnetic transition moment. a) The slightly modified first excited singlet state is here the energetically favored combination of S_1 and S_i; the interaction of a perturbing group must therefore be of the same sign for S_1 as for S_i (for instance, the energetically favored combination is used on both occasions). b) the ($\pi\pi^*$) state can supply the missing $\vec{\mu}$, which lies along the C=O bond, intrachromophorically. If a (*e.g.* positive) charge is present in the upper right front octant, and we choose the energetically favored combination between transition dipole and -quadrupole, then we obtain the signs for the individual poles as given in the Figure. According to Fig. 2 this corresponds to a parallel arrangement of $\vec{\mu}$ and $\vec{m}$; the CD is positive. Thus the correct sign for an octant rule is obtained. In this derivation a change of the sign of the charge does not lead to inversion of the sign of the contributions [which is in agreement with the experiment [75]] and one could just as well have used one pole of a dipole (induced by the excitation) instead of one isolated charge. c) The missing $\vec{\mu}$ could, *e.g.*, also be taken interchromophorically from a ($\sigma\rightarrow\sigma^*$) state of a C—C bond. Again the energetically favored combination between this transition dipole and the transition quadrupole has to be considered, from which a parallel orientation of $\vec{\mu}$ and $\vec{m}$ results according to Fig. 2, *i.e.* a positive contribution to the CD. Hence this contribution also yields an octant rule with correct signs.

If $\vec{\mu}$ is "stolen" intrachromophorically by admixture of the ($\pi\pi^*$) state, then μ_z and m_z are collinear; the parallel and the antiparallel arrangement have the same energy. The more favored interaction then always has to refer to one of the residual charges mentioned, or to a (possibly induced) dipole: for instance, if there is a positive pole present in the upper right front octant (Fig. 13b) not too close to the z axis, then it determines the sign pattern in the quadrupole Q and in the dipole $\vec{\mu}$ according to *Coulomb*'s law in such a way that the poles at the smallest distance from the perturbing pole must be negative. Figure 2 then reveals a parallel arrangement of $\vec{\mu}$ and $\vec{m}$; the CD is positive. An octant rule results once again, and its signs are those found experimentally. If the n orbital is delocalized, then additional (smaller) quadrupoles are also formed around the C of the C=O group, around the two C_α atoms, *etc.*, creating additional "enclaves" of opposite sign in a few restricted regions. Such "enclaves" have indeed been proposed by *Bouman* and *Lightner*[15e] on the basis of improved CNDO/S calculations.

Interchromophoric interaction can also be utilized to produce a $\vec{\mu}$; this latter should then come from a $\sigma\rightarrow\sigma^*$ excitation within a C—C bond near to the chromophore. If this transition dipole lies, *e.g.*, parallel to the $(-z)$ axis in the upper right front octant (Fig. 13c), then according to Figure 13a that charge pattern within the quadrupole Q must be favored which (in combination with the facts of Figure 2) leads to parallel arrangement of $\vec{\mu}$ and $\vec{m}$; again the correct sign for an octant rule is predicted. In this case, however, the interaction energy also depends to some extent on the orientation of the dipole and not only on the coordinates of its center. Improved calculations give more complex pictures for such interactions[15c].

This simple approximation procedure for finding a new sector rule (including the corresponding signs) can in general readily be applied, if one considers those transitions which are magnetically allowed but electrically forbidden (*e.g.* $n\rightarrow\sigma^*$ transitions of episulfides and thioethers[56], $n^-\rightarrow\pi^*$ transitions of pyrazines[57]). A general recipe can be formulated in the following way[56] (cf. Figure 14): if a band is caused by a

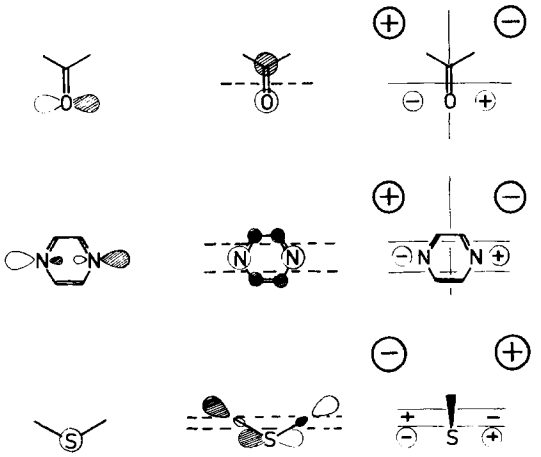


Fig. 14. Generalized rule for the CD in the case of $p_x\rightarrow p_y$ transitions. Top, $n\rightarrow\pi^*$ transition of a carbonyl compound; center, $n^-\rightarrow\pi_4^*$ transition of a pyrazine; bottom, $n\rightarrow\sigma^*$ transition of a thioether. Left, initial orbital; center, final orbital; right, generalized sector rule. The signs of the contribution in the proximity of the initial orbital are constant; on going towards the back sectors, each crossing of a nodal surface inverts the sign. The signs of contributions in the back sectors found experimentally are drawn larger. Notice that the plane of the C—S—C chromophore has to be placed perpendicular to the plane of the paper for setting up the rule.

transition which (at least to a large extent if LCAO-MOs are used) can be characterized by $p_y\rightarrow p_x$ (coordinate system as in Fig. 2), then the sign pattern in the proximity of the initial orbital in the four front sectors ($z>0$) is dissignate[58], *e.g.* as given in Figure 14. The signs in the other sectors are found by reversal for each crossing of a nodal surface. Figure 14 shows this for the octant rule of saturated ketones, for the rule mentioned for the $n^-\rightarrow\pi^*$ transition of pyrazines, and for the rule of the 240 nm band of thioethers. If the n orbital is delocalized further, *e.g.* by considering the p orbitals of corresponding symmetry at the C atom of the carbonyl group as well as at both C_α atoms, then according to this recipe an additional nodal surface perpendicular to the carbonyl plane is obtained, as has been described by *Pao* and *Santry*[15b] as the result of a more sophisticated calculation.

9. The $n\rightarrow\pi^*$ Band of Conjugated Carbonyl Compounds

The $n\rightarrow\pi^*$ band of conjugated carbonyl compounds appears approximately between 330 and 350 nm, since the HOMO

and the LUMO approach each other as a result of interaction between the π systems of C=O and C=C[4]. Figure 15 shows

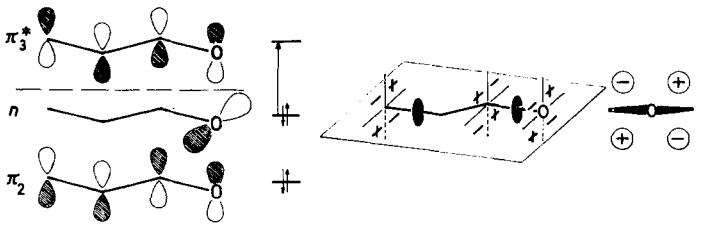


Fig. 15. Conjugated enone with coplanar arrangement of the C=C—C=O chromophore. The signs obtained according to Fig. 13 for the contributions to the CD of a ligand in a front octant, where the MOs for a saturated and a conjugated ketone are similar, are shown in the middle drawing. The signs of the contributions change on each crossing of a nodal surface; this will happen twice on proceeding to sectors lying farther back, as the final orbital π_3^* has two nodal surfaces. In the back sectors the sign pattern given on the right will therefore result [59, 60].

the symmetry properties of the two highest filled orbitals (π_2 and n) and that of the LUMO. While π^* of the saturated ketone has only one nodal plane, π_3^* of a conjugated ketone contains two nodal surfaces, and according to the generalized rule[56] the sign pattern has to change twice on going from the oxygen in the $(-z)$ direction. Thus a rule is obtained for the back octants which opposes the rule for saturated ketones. This has been proved experimentally[59] and is also obtained by a more sophisticated calculation[60].

However, this rule can only be applied when the enone moiety is completely or nearly coplanar. If it is more severely twisted around the central bond, as very often happens on incorporation into a ring system, then we are dealing with a chiral first sphere, for which only the final and not the initial orbital is chiral. The simple multiplication procedure is therefore inapplicable (at least as long as the n orbital is not extensively delocalized). On the other hand, the method of admixing of π character with the n orbital, as used for saturated ketones, gives the correct result if we make the obvious assumption that the chiral part of π_2 is the most effective perturber and will therefore determine the phase signs of the n orbital (Fig. 16). Formal multiplication by

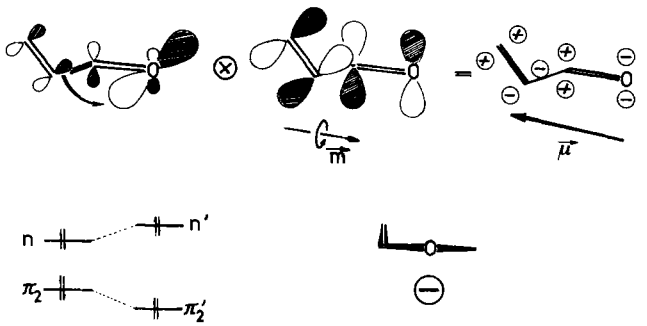


Fig. 16. The CD within the n→π* band of non-coplanar conjugated enones. The missing electric transition moment for the magnetically allowed n→π* transition can again be obtained by admixture of some π_2 character to the n orbital. As π_2 is itself chiral and lies energetically lower than the n-MO, the energetically unfavored combination of phase signs has to be used for n' (as in Fig. 11); participation of σ-MOs is no longer necessary. If one deliberately chooses the signs for π_2 as shown on the left, the phase signs for the n-orbital will follow. Whatever signs are used for the final orbital π_3^*, $\vec{m}$ and $\vec{\mu}$ will always be arranged (nearly) antiparallel to each other when the absolute conformation corresponds to that in the figure. The experimentally well-supported rule which follows from this is given on the bottom right [13].

the LUMO (the choice of signs within the orbital lobes around the oxygen is again arbitrary) yields an antiparallel arrangement of $\vec{\mu}$ and $\vec{m}$ according to Figure 16 for absolute conformation of the nonplanar enone system shown; the CD is thus predicted to be negative, and this is also found experimentally[13].

A completely analogous approach for ketones having a three-membered ring (cyclopropane or oxirane) "conjugated" with the carbonyl and in a chiral arrangement again gives the correct results[61] if the Walsh orbitals of the three-membered ring are used (Fig. 17).

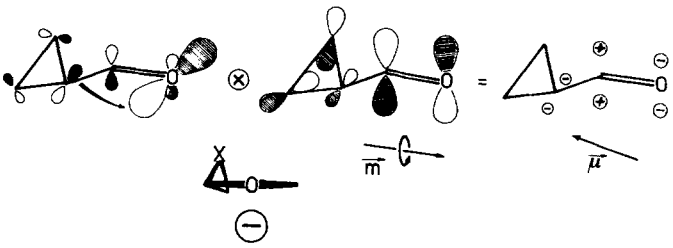


Fig. 17. The CD of the n→π* band for a chirally arranged three-membered ring (cyclopropane or oxirane ring) in "conjugation" with the C=O group. As in Fig. 16 the p-AO from π_2 at C_α determines the phases of the n orbital; this is accomplished here by the same p-AO from the Walsh orbital of the three-membered ring. For the given absolute conformation, an (approximately) antiparallel orientation of $\vec{m}$ and $\vec{\mu}$ results. The rule obtained, which again complies with experience [61], is illustrated below.

10. CD of Benzene Derivatives

The three known absorption bands of benzene around 260 (α-), 200 (p-), and 185 nm (β band) are generally[4] ascribed to π→π* transitions from the degenerate HOMOs into the likewise degenerate LUMOs, and belong in the D_{6h} point group of benzene to the representations B_{2u}, B_{1u}, and E_{1u}, respectively. An E_{2g} assignment has also been proposed for the p band[62]. *Allen* and *Schnepp*[63] have shown by comparison of the UV- and CD spectra of 1-methylindan (vapor state) that these three bands are accompanied by two additional band systems around 217 and 195 nm, for which E_{1g}- and E_{2g} symmetry have been proposed. Solution spectra sometimes also show these additional bands but in most cases they are rather indistinct. In the following, only the CD within the α band is discussed in detail.

11. CD of the α Band of Benzene

In the case of benzene, the transition into the B_{2u} state is forbidden electrically as well as magnetically. Only if additional molecular vibrations which lower the D_{6h} symmetry are excited in the electronically excited state will a small transition moment appear. The α band of benzene therefore shows a very pronounced vibronic fine structure; the 0-0 transition does not appear. The D_{6h} symmetry of the π system can, however, also be perturbed by substitution. Conjugation with π- or p electrons, as well as hyperconjugation with σ bonds, therefore also creates a small electric transition moment, and hence the UV spectrum of toluene is found to contain one fine structure series, which commences at the 0-0 transition, and at least one other one corresponding to that of benzene. For both series of chirally substituted benzene

derivatives, the pertinent magnetic transition moments have to be "stolen"; the signs of the corresponding Cotton effects therefore do not have to be identical. This further complicates the CD spectra within the α band. Moreover, "hot" bands may also appear; these are bands for which one normal vibration is already excited in the electronic ground state. Yet another rule may be valid here. We therefore suggest that the position of the 0-0 transition be calculated first (*e.g.* by using suitable estimates[64,75]) and this partial CD band consulted only for stereochemical correlation.

For chirally monosubstituted benzene derivatives and for tetrahydronaphthalenes and isoquinolines we have published[66] empirical sector rules for the α- and p bands. Although the skeleton of a monosubstituted benzene belongs to the C_{2v} point group, it is general practice to characterize the MOs and the transitions by the corresponding irreducible representations of benzene itself (D_{6h} symmetry). Such a monosubstitution confers upon the transition into the B_{2u} state (α band) a small electric moment in the plane of the ring perpendicular to the Ph—R bond: a small magnetic moment arises perpendicular to the plane of the ring[64,65]. According to *Allen* and *Schnepp*[63] a state of E_{1g} symmetry is energetically adjacent to the B_{2u} state, and is associated with a magnetic transition moment in the plane of the ring[5], as is necessary for the occurrence of CD. The α band can therefore intrachromophorically gain the $\vec{\mu}$ from the B_{2u} and the $\vec{m}$ from the E_{1g} state. Such an E_{1g} state corresponds to a $\pi\rightarrow\sigma^*$ (or $\sigma\rightarrow\pi^*$) transition; however, the double degeneracy of initial and final orbital render prediction of the sign of the Cotton effects very difficult in the case of a chiral second sphere (similar to that shown in Figure 11 for ketones). The experimentally found sector rule for contributions of a chiral third sphere, which is supported by theoretical calculations[17a], can, however, again be readily explained (Fig. 18). A (*e.g.* positive) "residual charge" will—in similar manner to that discussed for ketones (cf. Fig. 13)—again mix the two transition moments (*i.e.* $\vec{\mu}$ and that component of $\vec{m}$ which is parallel or antiparallel to it), thus determining the relative sign patterns for the dipole and the quadrupole. The experimentally found sign, and therefore the direction of $\vec{m}$, for the CD of the α band is obtained only on excitation from the π- into the σ* orbital[63]. Since, however, the weight of interchromophoric contributions to the same CD is unknown, the treatment shown in Figure 18 should be understood only as a suggestion to make this CD plausible; during recent years we have therefore focused our attention on changes arising in the CD on additional achiral substitution of the benzene ring[67]. According to *Platt*[64], the magnitude of the electric transition moments induced in benzene by substitution can be described quantitatively by "q-values", which are tabulated for numerous ligands[64,65]. In the case of multiple substitution, individual moments still have to be added vectorially even if these substituents are achiral, such as OH, OCH_3, alkyl, which are very often present in natural products. This substitution can drastically change the direction of the overall moment, so that sign inversion may also be observed for the CD bands in homochirally analogous series. For instance, the CD is negative within the α band of estradiol and of its 3-*O*-methyl ether but positive for the corresponding acetate.

We have tried[67] several different empirical formulae in order to correlate the induced magnetic transition moment

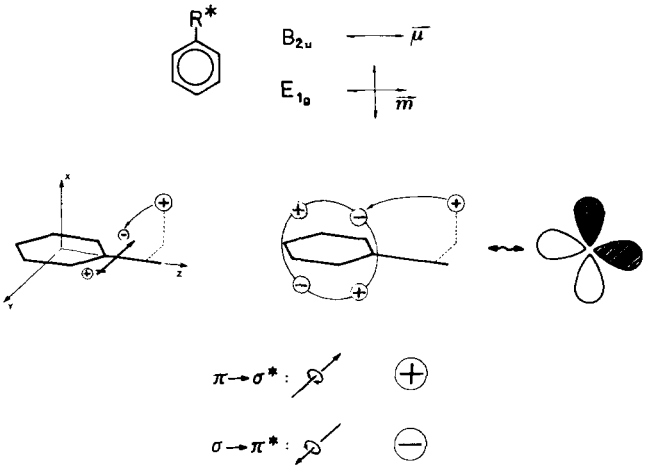


Fig. 18. CD of the α band of benzene derivatives with a chiral substituent (intrachromophoric mechanism). Top, introduction of a group R* yields a (weak) electric transition moment in the given direction for the B_{2u} band. The energetically closest [63] state has E_{1g} symmetry; with this is associated a magnetic transition moment in the plane of the ring. Center, relative signs of $\vec{\mu}$ and the transition quadrupole. This transition quadrupole corresponds to a sign pattern of the orbital lobes as given on the right. For a $\pi\rightarrow\sigma^*$ transition $\vec{m}$ and $\vec{\mu}$ are parallel, and the CD is positive; for a $\sigma\rightarrow\pi^*$ transition $\vec{m}$ and $\vec{\mu}$ would be antiparallel, and the CD negative. The positive CD found for the given absolute conformation corresponds to a preferred contribution of the $\pi\rightarrow\sigma^*$ transition to the E_{1g} state.

$\vec{m}$ [which must be coplanar with the present electric transition moment $\vec{\mu}$] with the molecular structure, and to this end we have synthesized a great number of model compounds. Occasional sign inversion is found experimentally if benzene derivatives already containing a chiral substituent are further substituted by an achiral group in a *p*-, *m*-, or *o* position. This change of sign depends on the type (and therefore, on the q value) of both groups, and on their relative position. In Table 1 these "sign patterns" are given for three series.

Table 1. Sign of the CD within the α band of mono- and disubstituted benzene derivatives R*—Ph' with one chiral substituent. Ph' stands for phenyl and toluyl. Top, α-D-glucosides; center, bornanyl derivatives; bottom, isoborneol derivatives.

	R*	R* CH_3	R* CH_3	R* CH_3
HO, HO, HO, HO, O, OPh'	+	+	+	+
Ph'	+	−	+	−
OH, Ph'	+	−	+	+

The results can be described by a simple model, which leads to the following formulae:

$$R_p = R^* \left[1 + (1-\gamma)\frac{q}{q^*} - \gamma\left(\frac{q}{q^*}\right)^2\right]$$

$$R_m = R^* \left[1 - \frac{1+\beta}{2}\frac{q}{q^*} + \beta\left(\frac{q}{q^*}\right)^2\right] \qquad (6)$$

$$R_o = R^* \left[1 - \frac{1-\alpha}{2}\frac{q}{q^*} - \alpha\left(\frac{q}{q^*}\right)^2\right]$$

R^*: rotational strength of the chirally monosubstituted benzene; R_p, R_m, and R_o: rotational strengths of the products with additional achiral substituent in *p*-, *m*-, or *o* positions; q* and q: the q values for the chiral and achiral groups, respectively. The parameters α, β, and γ which characterize the *o*-, *m*- and *p* substituent, obey the restriction $0 \leq \gamma \leq \beta \leq \alpha \leq 1$. With the exception of a few *o*-substituted derivatives, whose conformation has most probably changed, all known CD data can be described correctly by using a value of about 0.7 for all these parameters. From the identical (positive) signs reported for L-phenylalanine and L-tyrosine we formerly[66] concluded that the above-mentioned parameters approach their lower limiting value on separation of the chirality center from the benzene ring by one CH_2 group. We found, however, that the CD of L-phenylalanine is negative in organic solvents; these amino acids therefore behave like our analogous model compounds[67].

Equations (6) thus do not describe the CD directly, but only the influence of additional achiral substituents (sign inversion or not). Similar influences were also found for tetralins and tetrahydroisoquinolines[66, 67]. However, a recent publication[68] presents a calculation which seems to indicate no influence of additional (achiral) substituents for such compounds. In this paper, the orientation of the coordinate system was kept constant in spite of different substitution by having the *z* axis coincide with the C_2 axis of the non-aromatic ring regardless of the substitution type; this can only lead to the cited result! *Sagiv*[69] gives a description of the CD

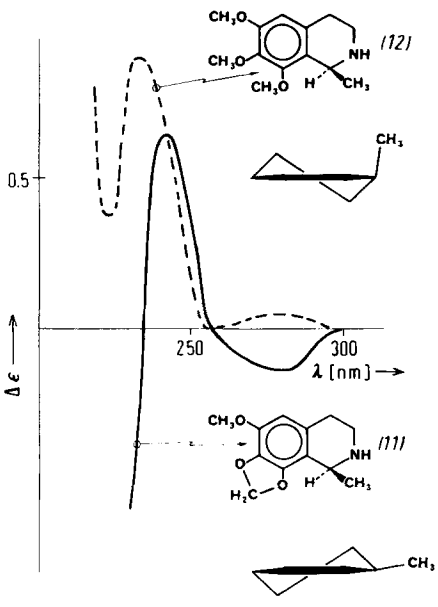


Fig. 19. The CD above 220 nm of (−)-anhalonine *(11)* and (+)-*O*-methylanhalonidine *(12)* of same absolute configuration. The projections given under the formulae are valid for the crystalline state as well for solution, and are performed along the C_2 axis of the ring system (from the benzene ring towards the piperideine ring).

of benzene derivatives resembling our own treatment, in which the additional substitution of the chromophore by achiral groups also plays an important rôle.

An inherent weakness of these rules for the Cotton effects of chirally monosubstituted benzene derivatives lies in the fact that the preferred conformation of the chiral side chain is not always known; for tetralins and tetrahydroisoquinolines the situation is very often much simpler, although—as in all other cases—the CD can give only the absolute conformation and not the absolute configuration. Figure 19 strikingly illustrates this fact: (−)-anhalonine *(11)* and (+)-*O*-methylanhalonidine *(12)* have the same absolute configuration but opposite rotations at the NaD line and also Cotton effects of opposite signs within the bands at longest wavelengths[70]. The reason becomes clear from X-ray data[70]: the methyl group is arranged quasi-equatorially in *(11)* but quasi-axially in *(12)*; *(11)* and *(12)* therefore have opposite ring helicities in spite of their identical absolute configuration. This conformational difference must also persist in solution, as proved by CD.

12. Future Prospects

As a rule, the empirical correlations between absolute conformation and Cotton effect gained by comparison of a great number of CD spectra can now be understood relatively well—with the aid of sophisticated calculations in favorable cases, and frequently already on the basis of simple qualitative MO considerations—even though the sign cannot always be predicted unequivocally. Nevertheless, combination of empirical rules and theoretical interpretation can reveal—if only *post festum*—valuable general regularities, from which one at least can derive the limits of applicability and even explain occasional exceptions. The qualitative MO consideration applied here will continue to be of value in the near future because *ab initio* calculations are much too expensive—especially for more complicated molecules—and all semi-empirical methods make several assumptions and use approximations. Although such semi-empirical methods do yield numbers and not only qualitative results, one can generally only rely on trends and not on these absolute values. This qualitative treatment can also be refined without difficulty, *e.g.* by incorporation of configurational interaction[76].

Apart from "classical" CD measurements in the range from about 180 to 800 nm, other methods have been developed in recent years whose general applicability cannot yet be foreseen. Thus the range of measurement was extended to below 140 nm[63, 71] and into the IR[3], and CD recorded in emission[72] and CID in Raman scattering[73]. Furthermore, chiral guest molecules in appropriate nematic mesophases can cause a transition to cholesteric phases of preferred helicity[74], and the chiroptical data of the host phase in the IR permit conclusions to be drawn about the absolute configuration of the guest molecules. In this case, it is not the chiral environment of a chromophore which is investigated, but rather the conformation of the whole molecule. Both this method and CID ("circular intensity differential") may perhaps in the future yield valuable results supplementing classical chiroptical methods for the determination of absolute configuration.

I would like to thank my many enthusiastic co-workers at Bonn and Bochum, as well as many colleagues in Germany and abroad for the synthesis of model compounds, supply of valuable samples, and many fruitful discussions, Mr. E. Kirmayr and Ing. U. Wagner for careful measurements, as well as the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for generous financial support.

Received: June 12, 1978 [A 270 IE]
German version: Angew. Chem. *91*, 380 (1979)

[1] Circular Dichroism, Part 72.—Part 71: *G. Tóth, O. Clauder, S. S. Yemul, G. Snatzke*, J. Chem. Soc., in press.
[2] a) Definitions and fundamentals are compiled, *e.g.*, in *F. Ciardelli, P. Salvadori:* Fundamental Aspects and Recent Developments in ORD and CD. Heyden, London 1973; b) the most detailed recent survey of the applications of chiroptical methods has been authored by *M. Legrand, M. J. Rougier* in *H. B. Kagan:* Stereochemistry, Fundamentals and Methods. Vol. 2. Thieme, Stuttgart 1977, p. 33.
[3] See, *e.g., G. Holzwarth, E. C. Hsu, H. S. Mosher, T. R. Faulkner, A. Moscowitz*, J. Am. Chem. Soc. *96*, 251 (1974); *L. A. Nafie, T. A. Keiderling, P. J. Stephens, ibid. 98*, 2715 (1976).
[4] See, *e.g., H. H. Jaffé, M. Orchin:* Theory and Applications of Ultraviolet Spectroscopy. Wiley, New York 1962; *J. N. Murrell:* The Theory of the Electronic Spectra of Organic Molecules. Methuen, London 1963.
[5] Concerning the application of group theory to spectroscopy, cf., *e.g., J. M. Hollas:* Die Symmetrie von Molekülen. de Gruyter, Berlin 1975. A highly useful collection of formulae is given by: *J. A. Salthouse, M. J. Ware:* Point Group Character Tables and Related Data. Cambridge University Press, Cambridge 1972.
[6] The theory of CD is presented in detail by *D. J. Caldwell, H. Eyring:* The Theory of Optical Activity. Wiley, New York 1971; cf. also *A. D. Buckingham, P. J. Stiles*, Acc. Chem. Res. 7, 258 (1974); *J. A. Schellman*, Chem. Rev. *75*, 323 (1975).
[7] Simple calculations are given in, *e.g., E. Heilbronner, H. Bock:* Das HMO-Modell und seine Anwendung. Verlag Chemie, Weinheim 1968. Formale MO multiplication is mentioned by *H. Labhart:* Einführung in die Physikalische Chemie. Teil V, Molekülspektroskopie. Springer, Berlin 1975.
[8] Cf. also, *e.g., F. S. Mason*, Quart Rev. *17*, 20 (1963).
[9] Cf. also, *e.g.*, the description of optical activity by *W. Kauzmann:* Quantum Chemistry. Academic Press, New York 1957.
[10] *W. Moffitt, A. Moscowitz*, J. Chem. Phys. *30*, 648 (1959).
[11] *A. Moscowitz*, Tetrahedron *13*, 48 (1961); *A. Moscowitz, K. Mislow, M. A. W. Glass, C. Djerassi*, J. Am. Chem. Soc. *84*, 1945 (1962).
[12] *W. Kuhn*, Trans. Faraday Soc. *46*, 293 (1930).
[13] *G. Snatzke*, Tetrahedron *21*, 413, 421, 439 (1965); *G. Snatzke, F. Snatzke* in [2a], p. 173.
[14] See, *e.g., R. K. Hill, J. W. Morgan*, J. Org. Chem. *33*, 927 (1968).
[15] Ketones: a) *A. Moscowitz*, Adv. Chem. Phys. *4*, 67 (1962); b) *Y.-H. Pao, D. P. Santry*, J. Am. Chem. Soc. *88*, 4157 (1966); c) *E. G. Höhn, O. E. Weigang, Jr.*, J. Chem. Phys. *48*, 1127 (1968); d) *T. D. Bouman, A. Moscowitz, ibid. 48*, 3115 (1968); e) *T. D. Bouman, D. A. Lightner*, J. Am. Chem. Soc. *98*, 3145 (1976).
[16] Disulfides: *J. Linderberg, J. Michl*, J. Am. Chem. Soc. *92*, 2619 (1970); *J. Webb, R. W. Strickland, F. S. Richardson, ibid. 95*, 4775 (1973); *D. B. Boyd*, Int. J. Quantum Chem.: Quantum Biol. Symp. No. *1*, 13 (1974).
[17] Benzene: a) *H. Dickerson, F. S. Richardson*, J. Phys. Chem. *80*, 2686 (1976); b) *O. Červinka, M. Král, P. Malon*, Collect. Czech. Chem. Commun. *41*, 2406 (1976).
[18] Conjugated dienes: *E. Charney*, Tetrahedron *21*, 3127 (1965); *J. S. Rosenfield, E. Charney*, J. Am. Chem. Soc. *99*, 3209 (1977).
[19] Allenes: *D. Haase, E. Ruch*, Theor. Chim. Acta *29*, 247 (1973); *H. Dickerson, S. Ferber, F. S. Richardson, ibid. 42*, 333 (1976).
[20] Lactones: *F. S. Richardson, N. Cox*, J. Chem. Soc. Perkin Trans. II *1975*, 1240; *F. S. Richardson, W. Pitts, ibid. 1975*, 1276.
[21] Azides: *C. Djerassi, A. Moscowitz, K. Ponsold, G. Steiner*, J. Am. Chem. Soc. *89*, 347 (1967).
[22] Thioethers: *J. S. Rosenfield, A. Moscowitz* in [2a], p. 41; *S. Hagishita, K. Kuriyama*, J. Chem. Soc. Perkin Trans. II *1974*, 686.
[23] Biopolymers: *I. Tinoco, Jr.*, Adv. Chem. Phys. *4*, 113 (1962); *P. M. Bayley, E. B. Nielsen, J. A. Schellman*, J. Phys. Chem. *73*, 228 (1969); *R. W. Woody*, J. Chem. Phys. *49*, 4797 (1968); *I. Tinoco, Jr., R. W. Woody, D. F. Bradley, ibid. 38*, 1317 (1963).
[24] Pyridine: *C.-Y. Yeh, F. S. Richardson*, J. Chem. Soc. Faraday Trans. II *72*, 331 (1976).
[25] Ethylene: *A. F. Drake, S. F. Mason*, Tetrahedron *33*, 937 (1977).
[26] Inorganic complexes: *e.g. S. F. Mason, R. H. Seal*, Mol. Phys. *31*, 755 (1976); *C.-Y. Yeh, F. S. Richardson*, Inorg. Chem. *15*, 682 (1976).
[27] *H. Bock*, Angew. Chem. *89*, 631 (1977); Angew. Chem. Int. Ed. Engl. *16*, 613 (1977); *J. W. Rabalais:* Principles of Ultraviolet Photoelectron Spectroscopy. Wiley, New York 1977; *C. R. Brundle, A. D. Baker:* Electron Spectroscopy. Vol. I. Academic Press, London 1977.
[28] *J. A. Schellman*, Acc. Chem. Res. *1*, 144 (1968).
[29] *A. S. Dawydow*, Zh. Eksp. Teor. Fiz. *18*, 210 (1948).
[30] *N. Harada, S.-M. Lai Chen, K. Nakanishi*, J. Am. Chem. Soc. *97*, 5354 (1975).
[31] Cf. *U. Nagai*, Kagaku no Ryoiki *31*, 28 (1977).
[32] *G. Wagnière, W. Hug*, Tetrahedron Lett. *1970*, 4765; Tetrahedron *28*, 1241 (1972).
[33] *E. Thom, A. T. Christensen*, Acta Crystallogr. *B 27*, 794 (1971).
[34] *V. Rogić, Ž. Ružić-Toroš, B. Kojić-Prodić, N. Pravdić*, Acta Crystallogr. *B 33*, 3737 (1977).
[35] See, *e.g., I. Fleming:* Frontier Orbitals and Organic Chemical Reactions. Wiley, London 1976, p. 44.
[36] *T. Sticzay, V. Bílik, Š. Kučař*, Chem. Zvesti *24*, 203 (1970) and our own measurements.
[37] See, *e.g., P. H. Laur* in *A. Senning:* Sulfur in Organic and Inorganic Chemistry. Vol. III. Marcel Dekker, New York 1972, p. 91.
[38] *M. Carmack, L. A. Neubert*, J. Am. Chem. Soc. *89*, 7134 (1967); *R. M. Dodson, V. C. Nelson*, J. Org. Chem. *33*, 3966 (1968); *G. Claeson*, Acta Chem. Scand. *22*, 2429 (1968).
[39] *U. Ludescher, R. Schwyzer*, Helv. Chim. Acta *54*, 1637 (1971).
[40] *M. Koreeda, N. Harada, K. Nakanishi*, J. Am. Chem. Soc. *95*, 266 (1974).
[41] *J. Tanaka*, Nippon Kagaku Zasshi *79*, 1114, 1379 (1958).
[42] Cf., *e.g.*, the X-ray structure analysis of a sugar tribenzoate: *F. W. Lichtenthaler, T. Sakakibara, E. Oeser*, Carbohydr. Res. *59*, 47 (1977).
[43] *G. Haas, P. B. Hulbert, W. Klyne, V. Prelog, G. Snatzke*, Helv. Chim. Acta *54*, 491 (1971).
[44] *G. P. Powell, J. Hudec*, Chem. Commun. *1971*, 806; *M. T. Hughes, J. Hudec, ibid. 1971*, 805; *M. R. Giddings, E. E. Ernstbrunner, J. Hudec*, J. Chem. Soc. Chem. Commun. *1976*, 956.
[45] *E. Ruch, A. Schönhofer*, Theor. Chim. Acta *10*, 91 (1968); *19*, 225 (1970); *E. Ruch*, Acc. Chem. Res. *5*, 49 (1972); Angew. Chem. *89*, 67 (1977); Angew. Chem. Int. Ed. Engl. *16*, 65 (1977).
[46] *J. A. Schellman*, J. Chem. Phys. *44*, 55 (1966).
[47] *D. C. Moule, A. D. Walsh*, Chem. Rev. *75*, 67 (1975).
[48] *G. Wagnière*, J. Am. Chem. Soc. *88*, 3937 (1966).
[49] *W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, C. Djerassi*, J. Am. Chem. Soc. *83*, 4013 (1961).
[50] *M. V. Vol'kenshtein, M. P. Kruchek*, Opt. Spektrosk. (Russian) *9*, 243 (1960).
[51] *N. D. Epiotis, W. R. Cherry, S. Shaik, R. L. Yates, F. Bernardi*, Top. Curr. Chem. *70*, 1 (1977).
[52] *M. J. S. Dewar, R. C. Dougherty:* The PMO Theory of Organic Chemistry. Plenum Press, New York 1975.
[53] *C. Djerassi, W. Klyne*, Proc. Natl. Acad. Sci. USA *48*, 1093 (1962).
[54] *E. E. Ernstbrunner, M. R. Giddings, J. Hudec*, J. Chem. Soc. Chem. Commun. *1976*, 953.
[55] *G. Snatzke, B. Ehrig, H. Klein*, Tetrahedron *25*, 5601 (1969); *H. J. C. Jacobs, E. Havinga, ibid. 28*, 135 (1972).
[56] *P. Welzel, I. Müther, K. Hobert, F.-J. Witteler, T. Hartwig, G. Snatzke*, Justus Liebigs Ann. Chem. *1978*, 1333.
[57] *G. Snatzke, Gy. Hajós*, Heterocycles *5*, 299 (1976); in *B. Pullman, N. Goldblum:* Excited States in Organic Chemistry and Biochemistry. Reidel, Dordrecht 1977, p. 295.
[58] *W. Klyne, D. N. Kirk*, Tetrahedron Lett. *1973*, 1483.
[59] *W. Nagata, Y. Hayase*, J. Chem. Soc. *C 1969*, 460.
[60] *K. Kuriyama*, footnote in [59], p. 461.
[61] *K. Schaffner, G. Snatzke*, Helv. Chim. Acta *48*, 347 (1965); *C. Djerassi, W. Klyne, T. Norin, G. Ohloff, E. Klein*, Tetrahedron *27*, 163 (1965); *M. Legrand, R. Viennet, J. Caumartin*, C. R. Acad. Sci. *252*, 2378 (1966).
[62] Cf., *e.g., P. B. Visscher, L. M. Falicov*, J. Chem. Phys. *52*, 4217 (1970).
[63] *S. D. Allen, O. Schnepp*, J. Chem. Phys. *59*, 4547 (1973).
[64] *J. R. Platt*, J. Chem. Phys. *17*, 484 (1949); *19*, 263 (1951).
[65] *J. Petruska*, J. Chem. Phys. *34*, 1120 (1961); *P. E. Stevenson*, J. Mol. Spectrosc. *15*, 220 (1965).
[66] *G. Snatzke, P. C. Ho*, Tetrahedron *27*, 3645 (1971); *G. Snatzke, M. Kajtár, F. Werner-Zamojska, ibid. 28*, 281 (1972); *G. Snatzke, M. Kajtár, F. Snatzke* in [2a], p. 148.
[67] *H. Dorcal-Mathelier, Badruddin, J. Hollweg, A. Steinmetz, U. Rudolph*, Dissertationen, Universität Bochum 1975, 1976, 1975, 1976, and 1979, respectively.
[68] *J. Cymerman Craig, S.-Y. C. Lee, R. K. P. Chan, I. Y.-F. Wang*, J. Am. Chem. Soc. *99*, 7996 (1977).
[69] *J. Sagiv*, Tetrahedron *33*, 2315 (1977).
[70] *A. Brossi, J. F. Blount, J. O'Brien, S. Teitel*, J. Am. Chem. Soc. *93*, 6248 (1971).

[71] O. Schnepp, S. Allen, E. F. Pearson, Rev. Sci. Instrum. 41, 1136 (1970); W. C. Johnson, Jr., ibid. 42, 1283 (1971); E. S. Pysh in B. Pullman, N. Goldblum: Excited States in Organic Chemistry and Biochemistry. Reidel, Dordrecht 1977, p. 409.
[72] See, e.g., D. H. Turner, I. Tinoco, Jr., M. Maestre, J. Am. Chem. Soc. 96, 4340 (1974); H. G. Brittain, F. S. Richardson, ibid. 98, 5858 (1976).
[73] Cf., e.g., L. D. Barron, A. D. Buckingham, Mol. Phys. 20, 1111 (1971); L. D. Barron, M. P. Bogaard, A. D. Buckingham, J. Am. Chem. Soc. 95, 603 (1973); W. Hug, S. Kint, G. F. Bailey, J. R. Scherer, ibid. 97, 5589 (1975); L. D. Barron, Tetrahedron 34, 607 (1978).
[74] See, e.g., E. H. Korte, S. Bualek, B. Schrader, Ber. Bunsenges. Phys. Chem. 78, 876 (1974); H. Stegemeyer, K.-J. Mainusch, Naturwissenschaften 58, 599 (1971).
[75] G. Snatzke, G. Eckhardt, Tetrahedron 24, 4543 (1968).
[76] G. Snatzke, Pure Appl. Chem., in press.

A Basis for Orbital Symmetry Rules

By Horia Metiu, John Ross, and George M. Whitesides[*]

The influence of molecular symmetry on reaction rates is examined with an approach in which reactions are viewed as electronic transitions between states of reactants and products (described, in turn, by quasiadiabatic potential surfaces). The molecular Hamiltonian is used to derive selection rules for these transitions. The *complete* Hamiltonian has no useful symmetry. Neglect of non-Born-Oppenheimer and spin-orbit terms (and of other angular momentum coupling terms) leads to an approximate Hamiltonian and to selection rules which form the basis for the Woodward-Hoffmann rules. This approach provides an alternative to the adiabatic potential surfaces, reaction coordinates, and transition state theory used in more familiar discussions of the Woodward-Hoffmann rules. Further, it provides a particularly clear method for discussing violations of these symmetry rules, and for differentiating concerted and nonconcerted reactions.

1. Introduction

The prediction of chemical reaction rates and rate constants is a difficult endeavor. Formal theories of reaction rates[1] are just beginning to be used successfully[2] (at times with great computational expense) for the simplest three-atom exchange reactions and are not presently applicable to more complex problems. The difficulty in analyzing the motion of many-atom systems can, however, be reduced substantially by considerations of symmetry. In molecular quantum mechanics, the classification of electron states of atoms and molecules according to symmetry is fundamental to the construction of correlation diagrams and optical selection rules. By considering symmetry, these rules can be constructed and applied without calculating details of the motion of the electrons and nuclei. Similarly, "symmetry rules" such as those proposed by *Wigner* and *Witmer*[3], *Shuler*[4], and *Woodward* and *Hoffmann*[5], and discussed by many other authors[6], have greatly clarified certain types of problems in kinetics, without requiring elaborate calculation. The Woodward-Hoffmann (W-H) rules for the prediction of relative rates of concerted reactions are based on considerations of the symmetry of the electronic wavefunctions of the chemical reactants and products. These wave functions seldom figure *explicitly* in applications of the W-H rules: because electronic wavefunctions calculated in the Hückel LCAO-MO approximation[7] reflect molecular symmetry in easily predictable ways, a knowledge of the molecular symmetry of the substance(s) of interest, and of the symmetry properties of the Hückel wavefunctions derived previously for these or related materials, normally is sufficient for an application of the W-H rules.

The Hückel wavefunctions, on which the application of the W-H rules usually depends, are calculated with an approximate Hamiltonian: any influence of nuclear motion on the electronic wavefunction is neglected (the Born-Oppenheimer approximation); angular momentum terms (molecular, electronic spin-orbit, and nuclear and electronic spin) are ignored; and electron-electron interactions are incorporated semi-empirically. The enormous predictive success of the W-H rules indicates that the neglected terms are normally unimportant for the success of *qualitative* arguments based on orbital symmetry. *Nonetheless, the complete molecular Hamiltonian does not have the symmetry required to provide a rigorous basis for the W-H rules*, and a more complete calculation, including Born-Oppenheimer terms and consideration of angular momentum may, in principle, lead to predictions different from those of the W-H rules.

The purpose of this article is to discuss a number of aspects of symmetry rules in chemical kinetics, particularly the W-H rules. We present a theoretical framework with which we:
- derive symmetry rules and their limits of applicability
- provide operational definitions of the concepts of concerted and nonconcerted reactions
- derive extensions of present symmetry rules.

[*] Prof. Dr. G. M. Whitesides, Prof. Dr. J. Ross
Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Mass. 02139 (USA)
Prof. Dr. H. Metiu
Department of Chemistry, University of California, Santa Barbara
Santa Barbara, California 93106 (USA)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0377 $ 02.50/0*

The utility of our analysis is tested for various applications. Further, we show that symmetry rules for reactions can be obtained as *selection rules* analogous to those used in optical spectroscopy.

Our interest is in the influence of symmetry on reaction rates and in the assumptions underlying the symmetry rules, not in the detailed calculation of rates for specific reactions. Recent work on photodissociation of polyatomic molecules[8] and dynamics of simple rearrangement reactions[2b] indicates, however, that the types of methods discussed here can be used to provide quantitative estimates of rates.

Our treatment of reaction rates clarifies the relationship between the relatively high symmetries assumed in applying these rules and the much lower symmetry actually characteristic of the complete molecular Hamiltonian. Two other worthwhile features emerge from this development. First, it is possible to derive relatively compact expressions which give the reaction rates in terms of the complete Hamiltonian (including nuclear and non-Born-Oppenheimer terms) and appropriate wave functions of reactants and products. This expression can be separated into a part having the symmetry assumed in the W-H rules (that is, the symmetry of the nuclear framework), and other parts that do not have this symmetry. The experimental observation that many reactions obey the W-H rules then makes it possible to identify terms in this rate expression that are normally *not* important in determining reaction rates. Thus, the observation that certain features of reaction rates are adequately described by terms having symmetries characteristic of only a part of the complete molecular Hamiltonian permits an estimation of the relative importance of the remaining parts in determining reaction rates. Second, by identifying explicitly the terms in the Hamiltonian that do not have the symmetry of the molecular framework, it is possible to suggest areas and circumstances in which the W-H rules might be expected to fail. Our discussion proceeds in four stages:

First, we describe the distinction between "adiabatic" and "quasiadiabatic" potential surfaces[*], and indicate the advantages of the latter in discussing the role of symmetry in the reaction rates. Briefly, *adiabatic* potential surfaces are those which organic chemists commonly use in discussing kinetics (Fig. 1). A continuous surface connects reactants and products, and the lowest energy path between the two is called the "reaction coordinate". The "activated complex" or "transition state" is considered as a discrete species at the position of highest energy along that path. A complete adiabatic surface is generated with a single electronic Hamiltonian: reactants, products, and intermediates are represented by eigenfunctions of this Hamiltonian calculated for different sets of nuclear coordinates. A reaction is the result of the motion of nuclei; since the adiabatic surface is continuous, reactants and products belong to the same electronic state. In the present work, a distinct *quasiadiabatic* potential surface is required for reactants and products; each is calculated using a procedure specifically designed to *eliminate* all of the interactions which provide the driving force for reaction. The wave functions used to represent these artificially non-reacting species are *not* eigenfunctions of the Hamiltonian for the complete system. A reaction is considered as an electronic transition between the quasiadiabatic surface (state) of the reactants and the quasiadiabatic surface of the product. The transition state may be viewed as the nuclear configuration at or near the crossing of these two surfaces. Although the quasiadiabatic picture of a reaction is not the one customarily used in physical organic chemistry, *Evans*[9] proposed and made innovative use of quasiadiabatic energy surfaces, as early as 1938, for a discussion of the electronic theory of reactions.

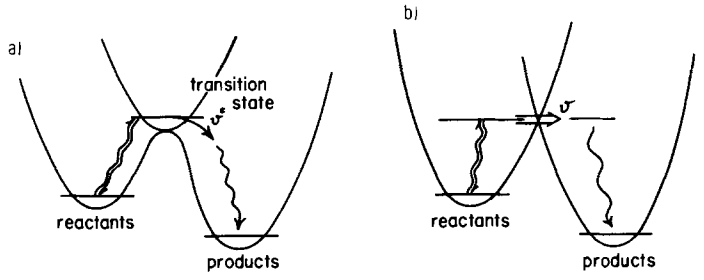


Fig. 1. A reaction in an adiabatic model (a) is represented by a smooth progression of nuclear positions within a *single* electronic state. All interactions present in the real physical system are, in principle, included in this representation. The highest energy species in this progression is called the transition state or activated complex, and, within the usual activated complex theory, is assumed to be in thermodynamic equilibrium with the ground state of the reactants. Its decomposition to products is the result of molecular motion along a vibrational coordinate having a negative force constant. A reaction in a quasiadiabatic model (b) is treated as a transition between electronic states of distinct species—"reactants" and "products".

[*] In this context, adiabatic and quasiadiabatic should be considered as arbitrary labels, with no obvious connection to the word adiabatic as used in classical thermodynamics.

Second, we state and develop an equation that describes the rate of a concerted reaction in terms of the quasiadiabatic wave functions for reactants and products, and the Hamiltonian of the reacting system. This equation permits the rate to be expressed in terms of contributions from several well-defined, although not necessarily easily calculated, quantities: overlap integrals of electronic wave functions; overlap integrals of nuclear wave functions; nuclear geometry at the intersection of the two quasiadiabatic potential surfaces; non-Born-Oppenheimer terms; and spin-orbit terms. Those terms which must be negligible for the reaction to follow orbital symmetry rules of the W-H type are easily identified.

Third, we study various contributions to the rate expression for reactions which are forbidden according to electronic symmetry rules of the W-H type. Examination of the vibronic and spin-orbit contributions to the rate shows that these also follow symmetry rules. These rules differ significantly from the W-H rules, however, and are neither generally nor easily applicable. These discussions are illustrated with the example of the closure of butadiene to cyclobutene.

Fourth, we discuss the concepts of concerted and nonconcerted reactions, and present useful (operational) definitions.

Our analysis emphasizes that many organic reactions classified according to the simplest electronic symmetry rules (W-H) as allowed or forbidden can in fact be categorized according to varying degrees of reactivity, and that reactions forbidden by these simplest rules may at times proceed at significant rates. Several representative reactions are classified in terms of "orders of forbiddenness". Identification of those terms in the complete rate equation that are not taken into account in the W-H treatment makes it possible to suggest reaction types in which violations of orbital symmetry rules might be expected.

2. Adiabatic and Quasiadiabatic Potential Surfaces

Most discussions of reaction kinetics based on transition state theory presuppose a single, continuous, potential surface connecting reactants and products. The points on this surface are calculated by assuming the nuclei to be stationary (the Born-Oppenheimer approximation) and solving the Schrödinger equation (1) to obtain electronic energies and wavefunctions for selected nuclear positions,

$$H_e(r, R_0)\Phi_i(r, R_0) = E_i(R_0)\Phi_i(r, R_0) \quad (1)$$

Here, H_e is the electronic Hamiltonian, r are the electronic coordinates, R_0 are the (fixed) nuclear coordinates, $\Phi_i(r, R_0)$ is the eigenfunction which describes a particular (i-th) electronic state (say the ground state, for thermal reactions) at the chosen values of R_0, and $E_i(R_0)$ is the associated electronic energy[*]. By varying the coordinates R_0 to correspond to the forming and breaking of bonds hypothesized for the reaction, we trace out a reaction coordinate. Many approximations have been introduced to make this procedure practical in the Hückel approximation; in particular, a limited number of atomic orbitals are used as the basis set, and two-electron terms and certain integrals are neglected.

For example, for the exchange of a hydrogen atom between dihydrogen and a hydrogen atom

$$H_A - H_B + H_C \rightarrow H_A + H_B - H_C$$

one can calculate the changes in energy accompanying the transfer of H_B from H_A to H_C by assuming a linear arrangement of three nuclei, choosing one distance, and minimizing the total energy of the system by varying the second distance. The results of such a calculation are summarized in Figure 2a. It is, of course, not generally useful to consider potential energies varying with a single distance for any purpose but schematic illustration; we shall do so here since a qualitative representation is all that is required. Surfaces generated in this way by the solution of Eq. (1) for the particular chosen system are called *adiabatic*. We emphasize that since a single Hamiltonian is used to calculate the energies and wavefunctions of nuclear configurations corresponding to what we call the reactants, products, and intermediates between the two, and since the resulting surface is continuous, all of these species are normally in the same electronic state: that is, they have the same electronic wave function.

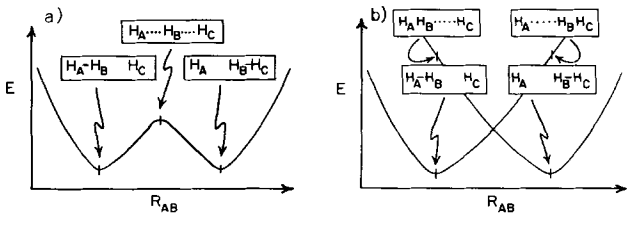


Fig. 2. Schematic adiabatic (a) and quasiadiabatic (b) potential surfaces for H_A—$H_B + H_C \rightarrow H_A + H_B$—$H_C$. For all curves, the distance between H_A and H_C, R_{AC}, is fixed, and R_{AB} is varied. In the left-hand curve for the quasiadiabatic surfaces, no interaction is allowed between H_B and H_C at any value of R_{AB}; for the right-hand curve, no interaction between H_A and H_B is allowed.

[*] Of course, this term also contains the Coulomb energy of the nuclear skeleton at rest.

Alternative theoretical methods for studying reaction rates are available, although they are not commonly used in physical-organic chemistry. The one employed throughout this paper involves calculations of two distinct potential surfaces, one for reactants and one for products. Reaction is considered to result from a transition between them. The procedure used to construct these so-called *quasiadiabatic* potential surfaces (and the corresponding electronic states) is based on calculating energies and wavefunctions for systems in which certain interactions actually present and crucial for the reaction to occur are intentionally omitted. This procedure is thus not based on finding electronic eigenfunctions for the chosen reacting system, and is thus very different in spirit from that used for adiabatic surfaces[10]. Typically, for the reaction of H_A—H_B with H_C, the calculation of a quasiadiabatic surface for the three-atom system that forms the reactants determines the energy of that configuration with explicit *exclusion* of bonding between H_C and H_A—H_B. The calculation of the quasiadiabatic surface of the products, that is the calculation for $H_A + H_B$—H_C, is done with explicit *exclusion* of bonding between H_A and H_B—H_C. The results of these calculations can be represented schematically by two intersecting potential energy curves (Fig. 2). The electronic quasiadiabatic wave functions are not eigenfunctions of the Hamiltonian of the complete system, because this Hamiltonian includes *all* the interactions present in the system. The quasiadiabatic wave functions explicitly exclude all *bonding* interactions between products and reactants.

Both adiabatic and quasiadiabatic representations have attractive features for describing chemical reactions. The former is more readily appreciated physically, and seems conceptually simple. Construction of an adiabatic energy surface involves assuming a position for the nuclei and then calculating the total electronic energy of the system at this position. This calculation is repeated for any nuclear positions that are considered relevant to the problem being considered. The resulting adiabatic energy surface thus (in principle) provides the correct energy of the system as a function of the nuclear positions. The continuous rearrangement of the nuclei from reactant to product configurations traces a path on this surface. The lowest energy path from reactants to products is frequently called the "reaction coordinate". The transition state is just the point of highest energy along this coordinate. In the activated complex theory, which is formulated with the adiabatic energy surface, the rate is determined by the curvature of the surface (that is, by the force constants) at the saddle point corresponding to the transition state. Adiabatic potential surfaces have the appeal of being "physically measurable", in the sense that they give the correct energy for the best approximation to this energy that can be calculated (with the particular procedure used) for any assumed set of nuclear positions. They have, however, a deficiency as the basis for discussing the influence of symmetry.

The reason for this will become clear as we proceed. At this point we only note that once the adiabatic energy surface is calculated the electronic wave function is eliminated from the problem. If we want to compute the rate of reaction numerically we have to solve the mechanical equations of motion (classical or quantum) with the adiabatic energy surface serving as potential energy. For instance, in Figure 3 we give a simple one-dimensional representation of this point,

where we show the adiabatic energy surface along the lowest path from reactants to products (usually called reaction coordinate). The total energy of the system is a constant and hence a straight line. The difference between the two lines is the kinetic energy of the nuclei, which changes as the reaction proceeds. The potential energy allows us to compute the forces exerted on the moving (reacting) nuclei, at any given nuclear configuration. Nowhere is the electronic symmetry of reactants and products obviously present in this type of treatment.

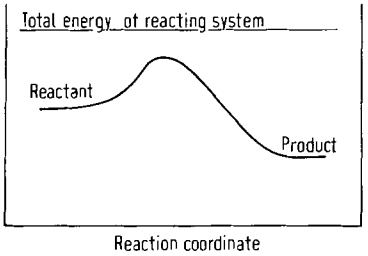


Fig. 3. Typical reaction coordinate. The level of the total energy of the reacting system, which is constant, is indicated by the horizontal line.

In the quasiadiabatic scheme the situation is conspicuously different. The reaction is considered to be a transition from the potential surface (*i. e.* the electronic state) of the reactants to the potential surface (*i. e.* the electronic state) of the products. We emphasize that the adiabatic and quasiadiabatic ways of describing reactions are equivalent and the choice of one of them depends on the problem to be solved. For a discussion of electronic symmetry it is more convenient to use a representation that displays the electronic degrees of freedom. The reader will discover, as he proceeds, that the language of the symmetry rules is that of the quasiadiabatic representation.

The quasiadiabatic potential surfaces do not necessarily give the correct energies, because the bonding interactions that are responsible for conversion of reactants to products are explicitly omitted in their calculation. For nuclear configurations which can be identified clearly as "products" or "reactants", quasiadiabatic potential surfaces give energies very close to those of adiabatic surfaces; for intermediate configurations, however, the two types or surfaces are very different. Although the idea of a reaction as a transition between two electronic states seems qualitatively more complex than that of a smooth progression along a reaction coordinate, the quasiadiabatic approach offers a great advantage for discussions of the influence of symmetry on rate. The reaction is considered as an electronic transition from a state of the reactant to a state of the product, and it is possible to calculate the rate using an expression of the form of Eq. (2)[6g].

$$k_{\text{reactant}\rightarrow\text{product}} \sim \langle\psi^{\text{product}}|\text{Operator}|\psi^{\text{reactant}}\rangle^2 \qquad (2)$$

$$\text{Intensity} = k_{\text{ground}\rightarrow\text{excited}} \sim \langle\psi^{\text{excited}}|O_{\text{dipole}}|\psi^{\text{ground}}\rangle^2 \qquad (3)$$

Once the symmetry of the appropriate operator and that of the wave functions ψ^{product} and ψ^{reactant} have been identified, then it is easily possible to establish whether the rate must be small *on the basis of symmetry* (it may, of course, be small, for reasons unrelated to symmetry). This type of procedure has abundant precedent in the development of optical selection rules (that is, in procedures for estimating the rules of spectroscopic transitions), where expressions of the same form are used [Eq. (3)]. The ability to classify reaction rates in terms of symmetries is of obvious pertinence to the W-H rules. This approach is also very convenient in dealing with "unusual" contributions to the kinetics, such as the dynamic effects arising from non-Born-Oppenheimer terms or spin-orbit coupling, which may cause violations of the W-H symmetry rules, much in the way in which they cause violations of the selection rules in spectroscopy. Such terms are not presently included in transition state theory.

To illustrate the construction of adiabatic and quasiadiabatic surfaces in an example directly relevant to pericyclic reactions, we consider the closure of butadiene to cyclobutene. For a qualitative discussion of an adiabatic potential energy surface for this transformation we consider only the interconversions of molecular orbitals formed from four atomic orbitals. Hückel-level calculation of the adiabatic potential surface would proceed with the solution of the secular determinant in the usual way for various nuclear coordinates corresponding to butadiene, cyclobutene, and plausible geometries intermediate between these extremes

$$\left|\begin{array}{cccc} \alpha_1-E & \beta_{12} & 0 & \beta_{14} \\ & \alpha_2-E & \beta_{23} & 0 \\ & & \alpha_3-E & \beta_{34} \\ & & & \alpha_4-E \end{array}\right| \begin{array}{l}\text{adiabatic} \\ = 0\end{array}$$

Changes in the magnitudes of the resonance ($\beta_{ij}=\langle i|H|j\rangle$) and Coulomb ($\alpha_i=\langle i|H|i\rangle$) integrals with geometry lead to changes in the energies of the molecular orbitals, and generate the associated adiabatic potential surfaces (Fig. 4a).

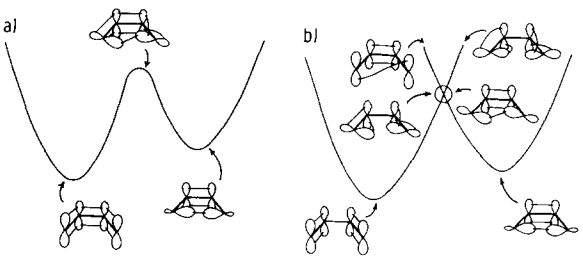


Fig. 4. Schematic adiabatic (a) and quasiadiabatic (b) potential surfaces describing the conrotatory interconversion of cyclobutene and butadiene. The lines connecting orbitals indicate those interactions included in the calculation. These interactions may, of course, range from large to zero (as shown by the magnitude of β_{12} in the adiabatic calculation).

Two different Hamiltonians are used for computing the quasiadiabatic states for butadiene and cyclobutene; neither is that used for the adiabatic calculation. For butadiene we take β_{23} and β_{14} to be zero, regardless of the nuclear configurations, to exclude from the quasiadiabatic electronic state of butadiene the bonding interactions characteristic of cyclobutene (Fig. 4). Similarly, the quasiadiabatic Hamiltonian for cyclobutene has β_{34} and β_{12} equal to zero to exclude the bonding interactions characteristic of butadiene.

$$\left|\begin{array}{cccc} \alpha_1-E & \beta_{12} & 0 & 0 \\ & \alpha_2-E & 0 & 0 \\ & & \alpha_3-E & \beta_{34} \\ & & & \alpha_4-E \end{array}\right| \begin{array}{l}\text{quasiadiabatic "butadiene"} \\ = 0\end{array}$$

$$\left|\begin{array}{cccc} \alpha_1-E & 0 & 0 & \beta_{14} \\ & \alpha_2-E & \beta_{23} & 0 \\ & & \alpha_3-E & 0 \\ & & & \alpha_4-E \end{array}\right| \begin{array}{l}\text{quasiadiabatic "cyclobutene"} \\ = 0\end{array}$$

This way of constructing the quasiadiabatic states gives the correct electronic symmetry of both butadiene and cyclobutene. Having imposed the conditions which characterize this pair of quasiadiabatic calculations, we can calculate potential surfaces relevant to the interconversion of butadiene and cyclobutene by varying appropriate parameters but the shape of these surfaces will depend on the parameters varied. Thus, calculations in which only the distance between C^1 and C^4 is allowed to vary will produce excited states of butadiene and cyclobutene which differ significantly in shape; calculations in which the torsional angles Φ around the C^1—C^2 and C^3—C^4 bonds are also allowed to vary produce structures that are more closely related geometrically. We shall discuss later, in more detail, the importance of this difference for the rate of the reaction[*].

3. The Transition Probability for Chemical Reactions

3.1. General Theory

A reaction can be treated as an electronic transition between two different electronic states corresponding to two different quasiadiabatic potential surfaces, one for reactants and one for products. The reactant system is taken to be in a given quasiadiabatic electronic state and in a given nuclear state (specified in terms of the rotation, vibration, and relative motion of reactants) corresponding to the given total energy of the reacting system. This energy may be determined by an equilibrium thermal distribution or by a non-equilibrium photoexcitation. *The state of the reactants, constructed as described to exclude the bonding interactions that characterize reaction, is not a stationary (time-independent) state of the complete Hamiltonian.* A stationary state description, based on the available quasiadiabatic wave functions, would require mixing of reactant and product states. Since the reactants are not in a stationary state, there is a time-dependent probability that they will undergo a transition to a state of the product. The rate of the transition between reactant and product states (as between all non-stationary states in quantum mechanics) is calculated in terms of an integral of the form $\langle\psi^{product}|\text{Operator}|\psi^{reactant}\rangle$ [Eq. (2)]; the practical problem is to define the appropriate operator for the reaction and to try to develop methods of estimating the magnitude of this integral without resorting to detailed computation.

It is helpful in describing the techniques used to calculate these transition probabilities from reactants to products (*i.e.* rates of reaction) to begin by describing an analogous and more familiar problem: *viz.* that of the electronic excitation of a molecule by the absorption of a photon[12]. The excitation is a transition between different electronic states (that is, between different adiabatic potential energy surfaces). The interaction of the dipole moment of the molecule and the electromagnetic field of the light provides the driving force for the transition: the dipole moment operator is the required operator. Two familiar assumptions are usually used in obtaining an expression for the transition probability: first, that the motion of the electrons is so much faster than that of the nuclei that only the nuclear positions influence the electronic wave functions and that the nuclear movements are not important (the Born-Oppenheimer approximation); second, that the electronic transition is sufficiently rapid that the nuclei are effectively motionless during the transition (the Franck-Condon approximation). The selection rules of optical spectroscopy follow from consideration of the symmetry properties of the initial state, the final state, and the dipole moment operator. We emphasize that these selection rules reflect approximations made concerning wave functions (Born Oppenheimer and Franck-Condon approximations, neglect of spin-orbit coupling, *etc.*) and the mechanism of interaction of light with the molecule (dipole moment approximation). If different assumptions are made, different selection rules may result. In general, the less drastic the assumptions, the weaker are the resulting selection rules.

Any given set of approximations yields a set of selection rules. If the system is not adequately described by these approximations, however, lines appear in experimental spectra which are not predicted on the basis of these selection rules. Such lines are sometimes called "forbidden". This adjective essentially implies that an improved analysis containing less drastic approximations is required to reconcile experiment and theory; that is, that the analysis should take into account more interactions in the initial and final state and more complicated (and usually smaller) interactions between light and the molecule. Thus in optical spectroscopy there exists a hierarchy of selection rules depending on the level of analysis.

We find a similar situation for chemical reactions. Symmetry rules such as the W-H rules can be derived as selection rules for the electronic transition from the quasiadiabatic electronic state of the reactants to that of the products. The essential difference between the W-H rules and the spectroscopic selection rules is the difference between the operator which causes the transition of interest: for spectroscopy it is, in the simplest case, the dipole moment operator, while for chemical reaction it is, again in the simplest case, an operator whose properties are outlined below. Since we are concerned here only with the development of symmetry rules for chemical reactions, it will be necessary to describe this operator only in sufficient detail to establish its symmetry properties and the symmetry properties of its constituent parts. Much of what follows will involve qualitative arguments, and mathematical development will be held to the minimum required to sketch the form of the important integrals. Detailed discussions of the basis for these arguments can be found elsewhere[6g, 13].

As the basis for our discussion of the influence of symmetry on reaction rates, we assume that for a reaction of interest, the appropriate quasiadiabatic potential surfaces and wavefunctions are available for reactants and products. We further assume the reaction to be concerted and mean thereby that only two quasiadiabatic surfaces are important for the transition from reactants to products (Fig. 1b). Although in most cases this definition corresponds closely to the one commonly used (a concerted reaction is one taking place in one step,

[*] Quasiadiabatic descriptions make it possible to consider most reactions as electronic transitions; this feature is convenient in the study of the role of the electronic symmetry on rates. There are, however, reactions ($CO_2 \rightarrow CO + O$ is one example) which actually include a transition from one electronic *adiabatic* surface to another (here spin angular momentum is not conserved) [11]. In such unusual cases the situation is reversed: the adiabatic states make it possible to consider the reaction as an electronic transition while the quasiadiabatic ones for this example would describe the reaction as a continuous evolution over a potential barrier located between reactants and products.

without intermediates) a detailed discussion of the relation between the two definitions will be deferred to a later section of this paper. The rate of the reaction—that is, the rate at which reactants are converted into products—is calculated from the probability of a transition from each state of the reactants (electronic and nuclear) to each state of the products. The probability of that transition is proportional to the square of a quantity T, called the transition matrix. The reaction rate constant is obtained by taking the average of $|T|^2$ over the thermal (Boltzmann) population of all states of the reactants. The transition matrix T can be written as the sum of three terms [Eq. (4)][13]:

$$T = T_1 + T_2 + T_3 \tag{4}$$

In this expression, T_1 is the term that gives rise to electronic orbital symmetry rules; T_2 contains contributions to the rate from non-Born-Oppenheimer terms; T_3 describes spin-orbit contributions.

The term T_1 is given by Eq. (5),

$$T_1 = \langle\langle \Phi_N^r(R) | \langle \psi_e^p(r,R) | O | \psi_e^r(r,R) \rangle | \Phi_N^r(R) \rangle\rangle \tag{5}$$

where the superscripts r, p refer to reactants and products respectively. This expression differs from those normally encountered in electronic theory of molecules in that it depends on both electronic ($\psi_e(r,R)$) and nuclear ($\Phi_N(R)$) wave functions. The integration over the electronic coordinates r is indicated by single brackets

$$\langle \psi_e^p(r,R) | O(r,R) | \psi_e^r(r,R) \rangle \equiv \int \psi_e^{p*}(r,R) | O(r,R) | \psi_e^r(r,R) \, dr \tag{6}$$

and the integration over the nuclear coordinates R by double brackets[14]:

$$\langle\langle \Phi_N^p(R) | O'(R) | \Phi_N^r(R) \rangle\rangle \equiv \int \phi_N^{p*}(R) | O'(R) | \Phi_N^r(R) \, dR \tag{7}$$

A detailed definition of the operator O requires complicated arguments, and is neither within the scope of this article nor required for an understanding of the influence of molecular symmetry on reaction rate. In what follows, we will simply assert without proof the results of development and simplification of the expression for T_1 given by Eq. (5), and for corresponding expressions for T_2 and T_3. The mechanics of this development is described elsewhere[6g, 13, 28]. Thus, the electronic part of Eq. (5) is given by

$$\langle \psi_e^p(r,R) | O(r,R) | \psi_e^r(r,R) \rangle = \langle \psi_e^p(r,R) | H_e(r,R) | \psi_e^r(r,R) \rangle \tag{8}$$

+ other (neglected) terms[*].

[*] The terms left unspecified originate from the fact that we have confined the model to only two electronic states, one for products and one for reactants, and disregarded the possible (but usually unlikely) contributions of electronically excited states; and from the fact that the electronic quasiadiabatic states of the reactants are not necessarily orthogonal to those of the products [13]. Terms due to lack of orthogonality have the same symmetry properties as the term written in Eq. (8) and hence may for simplicity be omitted. The operator $H_e(r,R)$ is the electronic Hamiltonian of the complete reacting system (including all interactions between all nuclei and electrons).

The second term in the transition matrix T is given by

$$T_2 = -\frac{\hbar^2}{2} \sum_i \frac{1}{M_i} \left\{ \left\langle\left\langle \Phi_N^p(R) \left| \left\langle \psi_e^p(r,R) \left| \frac{\partial}{\partial R_i} \right| \psi_e^r(r,R) \right\rangle \frac{\partial}{\partial R_i} \right| \Phi_N^r(R) \right\rangle\right\rangle \right.$$
$$\left. + \left\langle\left\langle \Phi_N^p(R) \left| \left\langle \psi_e^p(r,R) \left| \frac{\partial^2}{\partial R_i^2} \right| \psi_e^r(r,R) \right\rangle \right| \Phi_N^r(r,R) \right\rangle\right\rangle \right\} \tag{9}$$

Here M_i is the mass of the i-th nucleus and the summation extends over all the nuclei. Notice that both the operator $\partial^2/\partial R_i^2$ in Eq. (9) and the electronic Hamiltonian $H_e(r,T)$ in Eq. (8) are totally symmetric, which means that the terms $\partial^2\psi(r,R)/\partial R_i^2$ and $H_e(r,R)\psi(r,R)$ have the same symmetry as $\psi(r,R)$. The second term in Eq. (9), therefore, has the same symmetry properties as T_1. Due to this symmetry equivalence and to the fact that this term is generally much smaller than the first one in Eq. (9), we shall neglect it. The remaining first term in Eq. (9) represents the contribution to the transition probability (and hence to the rate) from any coupling of the motion of the nuclei to that of the electrons. Such terms, called non-Born-Oppenheimer terms, appear in an analogous way in spectroscopy[12].

There is a simple way of seeing the origin of the coupling term involving the operator $\partial/\partial R_i$ in the non-Born-Oppenheimer contribution T_2. In quantum chemistry the electronic wave functions and energies are calculated with an electronic Hamiltonian in which the nuclei are usually held fixed. In most cases, the electronic states thus calculated (Born-Oppenheimer states) are an excellent approximation. Within that approximation, the system is confined to a single electronic state and transitions between electronic states are not possible. The removal of the approximation of fixed nuclei must take into account the velocity (hence, kinetic energy) of the nuclear motion. The velocity of the nuclei is represented by an operator proportional to $\partial/\partial R_i$ which appears in T_2 and induces transitions between the Born-Oppenheimer states.

The third term in the transition matrix, T_3, describes contributions to the rate from spin-orbit interactions and is given by

$$T_3 = \langle\langle \Phi_N^p(R) | \langle \psi_e^p(r,R) | H_{SO} | \psi_e^r(r,R) \rangle | \Phi_N^r(R) \rangle\rangle \tag{10}$$

where H_{SO} is the spin-orbit Hamiltonian. This term could, in principle, be expanded to include contributions to the rate from other couplings of angular momentum terms. For instance, the various interactions between electronic spin, nuclear spin, and molecular motion that determine the rates of processes important in CIDNP experiments could be included here. Spin-orbit interactions may become important whenever electron spin and orbital angular momentum are coupled, characteristically in radicals having heavy atoms.

We shall show that electronic symmetry rules for reaction rates of the W-H type originate in the T_1 term and that for reactions classified as "symmetry forbidden" by the W-H rules T_1 is small. T_2 and T_3 may, however, be sufficiently large, compared to T_1, to make a symmetry forbidden reaction proceed rapidly. The success of W-H rules depends in part on the fact that contributions to the rate from T_2 and T_3 are normally negligibly small. Even if T_2 and T_3 are small, however, it is not necessarily the case that the relative magnitude of T_1 (and

hence of T) for two competitive processes can always be deduced solely from symmetry considerations.

3.2. Electronic Symmetry Rules of the Woodward-Hoffmann Type

In the remainder of this section we derive the conditions which lead to symmetry rules, and discuss certain conditions under which these rules fail.

We emphasize that the form of these rules depends on the level of approximation with which the system is described. In particular, the W-H rules emerge from the most simplified treatment, in which virtual transitions among excited electronic states of reactant and products, the non-Born-Oppenheimer terms, and spin-orbit coupling are ignored; the Franck-Condon approximation is used; and the electronic wave functions are generated by the Hückel method. Various other possible approximations are discussed in Section 4.

3.2.1. The Role of Nuclear Overlap

Using Eqs. (5) and (8) we can write T_1 as:

$$T_1 = \int \Phi_N^R(R)\Phi_N^r(R)dR\langle\psi_e^p|H_e|\psi_e^r\rangle \qquad (11)$$

The term $\langle\psi_e^p|H_e|\psi_e^r\rangle$ depends on the electronic wavefunctions and the electronic Hamiltonian and will be referred to as the electronic part of T_1; the product $\Phi_N^R(R)\Phi_N^r(R)$ depends on nuclear wave functions only and will be called the nuclear part of T_1. A similar classification can be made for T_2 and T_3, given by Eqs. (9) and (10). The W-H and other electronic symmetry rules originate from the electronic part of the transition matrix. The existence of such rules presupposes, however, certain properties for the nuclear part. These properties are discussed in this subsection.

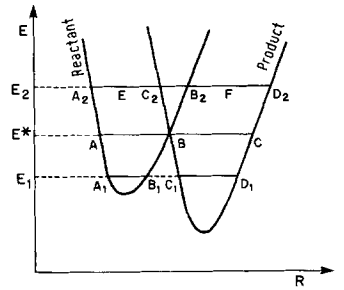


Fig. 5. Illustration of regions of substantial nuclear overlap for reactants and products. The heavy lines represent the quasiadiabatic energy surfaces of reactants and products. The light lines represent the nuclear configurations at which, for a given total energy of the reacting system, the nuclear wave functions (either one or both) are different from zero. For this qualitative discussion we neglect the small classically forbidden regions outside the wells of the heavy lines. At energy E_1, Φ_N^r is non-zero between A_1 and B_1 and Φ_N^R is non-zero between C_1 and D_1. The product $\Phi_N^r\Phi_N^R$ is therefore zero for all nuclear coordinates. At energy E_2, Φ_N^r is non-zero for nuclear configurations between A_2 and B_2, and Φ_N^R is non-zero for nuclear configurations between C_2 and D_2. Hence $\Phi_N^r\Phi_N^R$ is non-zero only between C_2 and B_2.

The functions $\Phi_N^R(R)$ and $\Phi_N^r(R)$ describe the nuclear positions and momenta[13]. The integral (11) for T_1 is non-zero only for those energies for which the two nuclear wavefunctions have an appreciable overlap (Fig. 5): that is, when the positions and momenta of the nuclei in the reactant and product configurations described by the chosen quasiadiabatic wavefunctions are similar. The nuclear overlap is zero at low energies, first becomes non-zero near the energy E^* at the crossing of the two quasiadiabatic surfaces, and then generally grows with the energy. We denote by $\Delta(E)$ the set of all nuclear configurations R for which, at a given total energy E, the product $\Phi_N^r(R)\Phi_N^R(R)$ is not zero. In the illustrative example presented in Figure 5, $\Delta(E_2)$ is the set of all nuclear configurations between C_2 and B_2. The integral (11) can be taken over $\Delta(E)$ only; no other nuclear configurations contribute to the integral T_1 since $\Phi_N^r(R)\Phi_N^R(R)$ is zero for R outside $\Delta(E)$,

$$T_1 = \int_{\Delta(E)} \Phi_N^R(R)\Phi_N^r(R)dR\langle\psi_e^p|H_e|\psi_e^r\rangle \qquad (12)$$

The immediate conclusion from this analysis is that the rate of reaction is zero if $\Delta(E)$ is zero, and that the energy of crossing, E^*, corresponds to the activation energy of transition state theory, since $\Delta(E) \neq 0$ for $E \geq E^*$ (Fig. 5). The physical picture which emerges from Eq. (12) is the following. If the energy is less than E^*, the nuclear overlap and the contribution to the rate from T_1 are zero. If the energy is greater than E^* the nuclear overlap is not zero and the reaction rate is therefore not restricted to zero by the nuclear wavefunctions. (We neglect discussions of tunneling, which do not alter the argument substantially.) If thermal or optical excitation increases the energy of reactants to E_2 (Fig. 5), the state of reactants will be $\psi_e^r(r,R)\Phi_N^r(R)$ and the nuclei will oscillate between A_2 and B_2 on the quasiadiabatic energy surface of reactants (corresponding to ψ_e^r). Since this state is not a stationary state of the total Hamiltonian, a transition may occur to the state of the products, described by the wavefunction $\psi_e^p(r,R)\Phi_N^R(R)$ (Fig. 5). In this state the nuclei will oscillate between C_2 and D_2 on the quasiadiabatic energy surface of the products. The probability of this transition is proportional to $|T_1|^2$. Loss of energy from the product at energy E_2 will produce a stable species with energy less than E^*, and complete the conversion of reactant to product.

This analysis of T_1 can be easily extended to T_2 and T_3 and indicates that regardless of the corresponding electronic parts of these terms, reaction occurs only if $\Delta(E) > 0$, and only at nuclear configurations contained in $\Delta(E)$. Since $\Delta(E)$ represents those nuclear configurations which are accessible from both reactant and product state we reach the following conclusions: regardless of how favorable the electronic conditions may happen to be, a reaction occurs only through conformations in which reactants and products have similar shapes. If the reacting molecules are excited specifically, so that the region of nuclear configurations $\Delta(E)$ available to both reactants and products is increased, the reaction will be faster. If the attainment of a common nuclear configuration for reactants and products is prevented by, say, a bulky group, then the reaction rate will be decreased.

These conclusions can be illustrated by a pertinent example provided by the reaction[15a]

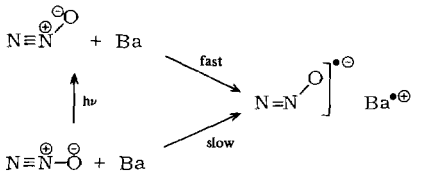
$$N_2O + Ba \rightarrow N_2 + BaO^*$$

BaO is produced in an electronically excited state and the rate of the reaction can be monitored, in a molecular beam

experiment, by measuring the light emission from BaO*. The mechanism is assumed to be

$$N_2O + Ba \rightarrow N_2O^{\bullet\ominus} + Ba^{\bullet\oplus} \rightarrow N_2 + BaO^*$$

where both the charge transfer and the molecular rearrangement occur in a single collision. Since N_2O is linear and $N_2O^{\bullet\ominus}$ is bent, then according to the above discussion the reaction rate should increase if the N_2O bending vibration ν_2 is excited. Experiments show indeed a substantial increase of the rate with excitation of this vibration. Similar arguments



underlie the theory of electron-transfer reactions developed by *Marcus*[15b].

3.2.2. The Role of Electronic Symmetry; Franck-Condon Approximation

After clarifying qualitatively the role of the nuclear part in the transition matrix, let us analyze the role of the electronic term in T_1

$$F_1(R) \equiv \langle \psi_e^p | H_e | \psi_e^r \rangle = \int \psi_e^p(r,R) H_e(r,R) \psi_e^r(r,R) dr$$

Through Eq. (11), the values of $F_1(R)$ for all nuclear coordinates in $\Delta(E)$ influence the rate. Suppose, however, that the major contribution to T_1 comes from nuclear configurations in a small range of nuclear coordinates around R_0 so that we can reasonably assume that the electronic term $F_1(R)$ may be evaluated with sufficient accuracy by taking into consideration only the region around R_0. (This assumption is equivalent to the Franck-Condon approximation.) We further assume that the nuclear configuration R_0 has some useful symmetry. Since the electronic Hamiltonian is totally symmetric, the electronic wave functions of reactants and products have the same symmetry properties as the nuclei (that is they belong to the irreducible representations of the group generated by R_0). If the electronic wave function of reactants has a different symmetry than that of the products (that is, if reactants and products belong to different representations) we call the reaction symmetry forbidden. All other reactions are symmetry allowed. To avoid confusion, we should emphasize that the precise meaning of such a statement depends upon the electronic functions ψ_e^r and ψ_e^p chosen to describe the system; Hückel wave functions would lead to slightly different conclusions than SCF ones. We discuss this issue in detail later.

Let us now return to Eq. (11) for T_1 and see under what conditions symmetry forbidden reactions are slow. For some symmetrical nuclear configuration R_0 for which reactants and products have different electronic symmetry we have for the electronic integral

$$F_1(R_0) \equiv \langle \psi_e^p(r,R_0) | H_e(r,R_0) | \psi_e^r(r,R_0) \rangle = 0 \qquad (13)$$

The expression $F_1(R)$ contributes to the rate T_1 [Eq. (11)] not only through its value at R_0, however, but also through its value at all nuclear configurations R contained in $\Delta(E)$. By continuity, if $\langle \psi_e^p | H_e | \psi_e^r \rangle$ is zero at R_0 it will be very small close to R_0. If $\Delta(E)$ is just such a small neighborhood of R_0 (that is, if the Franck-Condon approximation holds), then we can predict from the fact that ψ_e^r and ψ_e^p have different symmetries that T_1 is very small. If $\Delta(E)$ is large, however, we cannot make such a statement since nuclear configurations R which are inside $\Delta(E)$ but far from R_0 may result in a substantial value for T_1.

We can summarize this discussion with the following symmetry rule: a symmetry forbidden reaction will have a very small rate if T_2 and T_3 are negligible, and $\Delta(E)$ is small (corresponding closely to the Franck-Condon approximation made in spectroscopy). Of course, in order to be able to speak of a symmetry forbidden reaction in the first place, $\Delta(E)$ must contain a symmetrical nuclear configuration. For reactions which occur through nonsymmetric nuclear configurations there are no symmetry restrictions. We note also that the various approximations needed to derive the symmetry rules break the coupling of the total angular momentum[6g]. Hence symmetry rules are obtained if the components of the total angular momentum (electron spin, electronic orbital, nuclear, *etc.*) are conserved separately.

The general electronic symmetry rules derived contain as a particular case the Woodward-Hoffmann rules. The success of the latter, in dealing with many examples, indicates that the conditions of validity established are satisfied in most cases. There are, however, situations when these conditions are not satisfied. One example has been already presented: excitation of the bending mode of N_2O increases both $\Delta(E)$ and $\Phi_N^r \Phi_N^r$ and leads to an increase in the rate of the reaction

$$Ba + N_2O \rightarrow BaO^* + N_2$$

although the *electronic part* of T *has remained unchanged.*

We must emphasize that the symmetry of the electronic wave functions can tell us, under the circumstances specified above, whether a symmetry forbidden reaction is very slow. If, however, the reaction is allowed by symmetry (*i.e.*, if ψ_e^r and ψ_e^p have the same symmetry), it is not necessarily true that $\langle \psi_e^r | H_e | \psi_e^p \rangle$, and the rate, are large. Poor overlap may cause $\langle \psi_e^r | H_e | \psi_e^p \rangle$ to be small.

3.3. Violations of Electronic Symmetry Rules

We have seen that electronic symmetry rules are valid if we neglect coupling of electronic spin (T_3 small), make the Born-Oppenheimer approximation (T_2 small), and a Franck-Condon approximation [see Eqs. (11), (12) and accompanying discussion]. When any one of these conditions is not satisfied, then the electronic symmetry rules are violated and "forbidden reactions" may have large rates. Here we analyze these violations for the purpose of clarifying their origin and finding ways of increasing the rate of symmetry forbidden reactions.

3.3.1. Violations Caused by the Interaction of Electronic and Nuclear Motion (Vibronic Violations)

Let us analyze a symmetry-forbidden reaction for which the spin-orbit coupling contribution to the rate is unimportant ($T_3 \approx 0$). If we assume that $\Delta(E)$ is small, then the term T_1

will be practically zero. Under these conditions the rate is given by $T \approx T_2$; if T_2 is very small the forbidden reaction is slow. If T_2 is large the "forbidden" reaction is fast, in violation of the predictions of electronic symmetry rules.

The term T_2, given by Eq. (9) has a structure which is very similar to that of T_1, and it is useful again to speak of a nuclear contribution $\langle\langle \Phi_N^p | \partial \Phi_N^r / \partial R_i \rangle\rangle$ and an electronic contribution $\langle \psi_e^p | \partial \psi_e^r / \partial R_i \rangle$. As in the case of T_1, it is possible to make some qualitative predictions about the behavior of these terms. The contribution from the nuclear part can be increased by exciting those nuclear motions that make more nuclear configurations accessible to both reactants and products. The magnitude of the electronic term has not been calculated for quasiadiabatic states. It is, however, generally considered to be small for adiabatic states and is probably also small for quasiadiabatic ones. Its small magnitude does not preclude it from playing an important role in *large molecules* where the number of nuclear states is enormous and the contribution of a small electronic term is summed over all the nuclear states involved; the compounded effect may be significant. In fact, this term is known to cause fast radiationless transitions in large molecules[16]. In solids, which we may consider to be large molecules with periodic symmetry, these electronic integrals are responsible for important effects like superconductivity[17], exciton migration[18], electrical resistance[19], *etc.*

In the case of T_1 the magnitude of the electronic contribution depends on the symmetry of the electronic functions. The magnitude of the electronic part of T_2 is not determined by symmetry except for special situations. To justify this assertion, we use the fact that for small displacements around some symmetrical configuration, R_0, the symmetry coordinates Q_i and the nuclear positions R_i are linear combinations of each other[20]:

$$Q_j = \sum_i A_{ji} R_i$$

Here A_{ji} are numerical coefficients. Hence

$$\left\langle \psi_e^p \left| \frac{\partial}{\partial R_i} \right| \psi_e^r \right\rangle = \sum_j \left\langle \psi_e^p \left| \frac{\partial}{\partial Q_j} \psi_e^r \right\rangle \frac{\partial Q_j}{\partial R_i} = \sum_j A_{ji} \left\langle \psi_e^p \left| \frac{\partial \psi_e^r}{\partial Q_j} \right\rangle \right.$$

At a symmetric nuclear configuration R_0, the terms $\psi_e^p(r, R_0)$, $\psi_e^r(r, R_0)$, and Q_i have a definite symmetry[20, 21], and some, *but not all*, of the integrals $\langle \psi_e^p | \partial \psi_e^r / \partial Q_j \rangle$ are zero (by symmetry). Hence

$$\left\langle \psi_e^p \left| \frac{\partial}{\partial R_i} \right| \psi_e^r \right\rangle = \sum_j A_{ji} \left\langle \psi_e^p \left| \frac{\partial \psi_e^r}{\partial Q_j} \right\rangle \right.$$

where now the summation eliminates those Q_i for which symmetry annihilates the corresponding integral. Since the summation on the right of this equation is not constrained to be zero by symmetry, we cannot predict the magnitude of T_2 from consideration of symmetry. *Only in the special case in which one symmetry coordinate is adequate to describe the reaction can T_2 be estimated from symmetry.* For example, in a reaction of the type $A + BA \rightarrow AB + A$ this reaction coordinate may be $A \rightarrow \leftarrow B - A \rightarrow$, which indeed tends to break the molecule in the desired way. Let us assume that the displacements $A \leftarrow B \rightarrow A$ and $\begin{array}{c} \uparrow \\ A - B - A \\ \downarrow \quad \downarrow \end{array}$ are not capable of promoting the reaction, since they are not likely to create nuclear configurations that are accessible to the product. Hence we should consider that only $\langle \psi_e^r | \partial \psi_e^p / \partial Q_1 \rangle$, in which Q_1 denotes the symmetry coordinate $A \rightarrow \leftarrow B \rightarrow A$, contributes to T_2 in Eq. (9). If the reaction is symmetry forbidden and ψ_e^r and ψ_e^p have different symmetry, $\langle \psi_e^r | \partial \psi_e^p / \partial Q_1 \rangle$ need not be zero. In fact, Q_1 and therefore $\partial / \partial Q_1$ are of symmetry $\sum_u^+$. Assume, for example, that the electronic states are of symmetry $\sum_g^+$ and $\sum_u^+$. The integral $\langle \sum_g^+ | \partial / \partial Q_1 | \sum_u^+ \rangle$, which appears in T_2, need not be zero since Q_1 is of symmetry $\sum_u^+$, and the derivative $\partial / \partial Q_1 \sum_u^+$ is totally symmetric. In this illustrative example the electronic symmetry, through $\langle \psi_e^p | H_e | \psi_e^r \rangle$, causes T_1 to be very small while there is no indication that the term T_2, with electronic part $\langle \psi_e^p | \partial \psi_e^r / \partial Q_1 \rangle$, has to be small. If in this example the reaction is symmetry allowed, and the electronic states have the same symmetry, say $\sum_g^+$, the electronic contribution to T_2 is $\langle \sum_g^+ | \sum_u^+ | \sum_g^+ \rangle$ and it is zero. In this case T_2 must be negligible, for symmetry reasons, while T_1 is not. The argument is qualitative: it clearly is not possible to estimate the magnitude of T_2 relative to T_1 using these considerations. Nonetheless, the argument establishes a link between molecular symmetry and T_2 that corresponds to different "rules" than those of T_1 (which are essentially of Woodward-Hoffmann type) and is potentially useful in simple reactions in suggesting types of vibrational motions that might contribute to increasing the rate of those reactions which are forbidden according to electronic symmetry rules.

3.3.2. Interaction between Electron Spin and Electron Orbital Motion

Let us now analyze a symmetry forbidden reaction for which T_1 and T_2 are both zero, so that the rate depends on T_3 only. If T_3 is large the symmetry forbidden reaction is fast and we have what is called a spin-orbit violation of symmetry rules. It is usually assumed that the spin-orbit coupling is small and a negligible part of the Hamiltonian, as far as the rate of chemical reactions is concerned. This assumption is not necessarily correct. Assume that the reactant electronic wavefunction ψ_e^r is a singlet and the product ψ_e^p is a triplet. In this situation the electronic parts of T_2 and T_3, *i.e.*, $\langle \psi_e^p | H_e | \psi_e^r \rangle$ and $\langle \psi_e^p | \partial \psi_e^r / \partial R_i \rangle$, are zero, due to the orthogonality of the spin part of the wavefunction. The only surviving term in T is T_3. Hence

$$T = T_3 = \int_{\Delta(E)} \Phi_N^r(R) \Phi_N^p(R) \mathrm{d}R \langle \psi_e^p | H_{SO} | \psi_e^r \rangle \qquad (13a)$$

The rate of the reactions between singlet and triplet states is determined by T_3 (spin-orbit coupling) only. Since the spin-orbit coupling Hamiltonian H_{SO} is *not* totally symmetric[22], T_3 does not have to be small when the reaction is forbidden according to electronic symmetry rules (ψ_e^r and ψ_e^p have different symmetries). As an example consider the reaction[11]

$$CO_2(^1\sum_g^+) \rightarrow CO(^1\sum^+) + O(^3P)$$

Schematic energy surfaces are presented in Figure 6. The reactant state is singlet and the product state is triplet. Therefore T (=T_3) is given by Eq. (13a). The spin-orbit coupling term can be estimated from spectroscopic measurements to be about 50 cm^{-1}. The nuclear wavefunction can be computed for a simple model. The resulting rate coefficient agrees well with the measured one[11], indicating that the spin-orbit coupling is indeed the necessary interaction for this reaction.

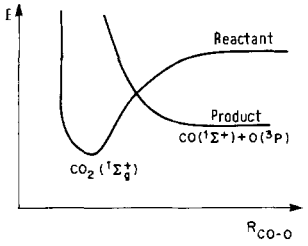


Fig. 6. Schematic energy surfaces for the reaction $CO_2(^1\Sigma_g^+) \rightarrow CO(^1\Sigma^+) + O(^3P)$.

The spin-orbit coupling may be enhanced in the presence of heavy atoms and inclusion of heavy atoms in reactants should increase the probability that they will take part in symmetry forbidden reactions.

3.3.3. The Role of Nuclear Motion. Violation of Electronic Symmetry Rules Due to Dynamics

We have already stressed the importance of the properties of the nuclear wave functions. If $\Delta(E)$ [see Eq. (12)] is very large and the nuclear overlap is very large, predictions of the magnitude of T_1, based on electronic symmetry alone, become doubtful. The difficulties in computing the nuclear wave functions make it impractical to propose any general calculational approaches to predicting violations of symmetry rules due to dynamics. Qualitatively, however, such violations occur when it is possible for the reactants to "look" like the product or *vice versa:* that is, for instance, when readily accessible vibrational states of the reactant(s) produce nuclear positions that closely resemble those of accessible vibrational states of the product(s). This results in an increase of the nuclear overlap, and in an increase in T_1 [Eq. (11)]. This qualitative consideration suggests that a plausible approach to increasing the rate of a symmetry forbidden reaction is to increase the vibrational energy of the reactant, most simply (but inefficiently) by heating, but also possibly by selective laser excitation of particular vibrational modes. A particularly pertinent example is provided by the reaction of H_2 and I_2. This reaction proceeding through a C_{2v} trapezoidal configuration is symmetry forbidden[23] (Fig. 7). Classical mechanical calculations[24] of reactive collisions indicate that as long as I_2 is in the vibrational ground state the reaction does not occur through a trapezoidal nuclear configuration, in agreement with the prediction of the W-H symmetry rules. If I_2 is, however, vibrationally excited, half of the reactive trajectories go through the trapezoidal configurations, contrary to the predictions of W-H rules.

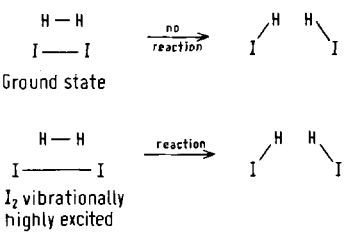


Fig. 7. Possible violation of the symmetry rules; a forbidden reaction is made possible by vibrational excitation.

4. Hierarchy of Symmetry Rules: *cis*-Butadiene—Cyclobutene Conversion

4.1. Molecular Orbital Description of Electronic Wave Functions

In the discussion of the previous Section we derived electronic symmetry rules without specifying any particular procedure for generating electronic wave functions. We shall now schematically illustrate the computation of the electronic part of T_1 for a specific example (butadiene → cyclobutene) and state the electronic symmetry rules in terms of the symmetry properties of Hückel *molecular orbitals* (as opposed to the symmetries of the *total electronic wave functions* used in the discussions of the previous section). We neglect here any contributions to the rate from T_2 and T_3. The reliability of the predictions resulting from these procedures depends on the quality of the electronic wave functions: different predictions might emerge, for example, from consideration of Hückel and SCF wave functions[13]. In such instances, it is worthwhile to understand the origin of the discrepancy and the ways of determining the correct prediction.

We begin our analysis by evaluating the relative magnitudes of the electronic part of T_1 [Eq. (13)] for four cases—thermal and photochemical conrotatory and disrotatory ring closures—and compare the procedure with that used in a W-H analysis. The W-H rules predict that the conrotatory pathway is thermally allowed and photochemically forbidden, and that the disrotatory pathway is thermally forbidden and photochemically allowed.

4.1.1. Thermal Reactions

The classification of the Hückel molecular orbitals for butadiene and cyclobutene orbitals by symmetry is too familiar to require discussion, but is summarized in Figure 8 for reference. One typical wavefunction for ground-state butadiene

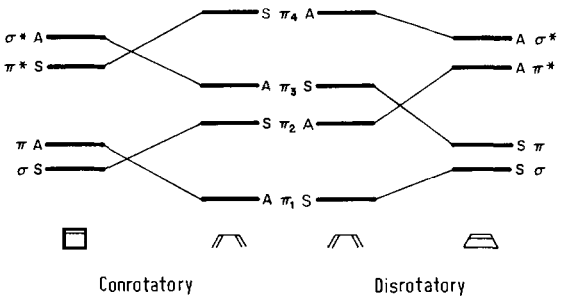


Fig. 8. Correlation diagram for Hückel molecular orbitals used for quasi-adiabatic description of conrotatory and disrotatory ring closure of butadiene.

is Eq. (14): In this expression, $\pi_1(1)$ indicates that the π_1 orbital contains an electron arbitrarily labeled 1. Eq. (14)

neglects the fact that it is not permissible to label electrons: equally valid distributions of electrons would be those given by Eqs. (15a) and (15b). The correctly antisymmetrized wave function for butadiene is therefore given by the appropriate Slater determinant [Eq. (16)].

$$\psi_r' = \pi_1(1)\pi_1(2)\pi_2(3)\pi_2(4)\Phi_N^r(R) \tag{14}$$

$$\psi_r'' = \pi_1(3)\pi_1(4)\pi_2(1)\pi_2(2)\Phi_N^r(R) \tag{15a}$$

$$\psi_r''' = \pi_1(3)\pi_1(1)\pi_2(4)\pi_2(2)\Phi_N^r(R) \tag{15b}$$

$$\psi^r = \frac{1}{\sqrt{4!}} \begin{vmatrix} \pi_1(1)\ \pi_1(2)\ \pi_1(3)\ \pi_1(4) \\ \pi_1(1)\ \pi_1(2)\ \pi_1(3)\ \pi_1(4) \\ \pi_2(1)\ \pi_2(2)\ \pi_2(3)\ \pi_2(4) \\ \pi_2(1)\ \pi_2(2)\ \pi_2(3)\ \pi_2(4) \end{vmatrix} \Phi_N^r(R)$$

$$\equiv \det\{\pi_1(1)\pi_1(2)\pi_2(3)\pi_2(4)\}\,\Phi_N^r(R) \tag{16}$$

Similar equations can be written for cyclobutene. Thus, using a one-electron Hamiltonian, Eq. (17), we can express Eq. (12) explicitly, for the reaction of interest, as Eq. (18):

$$H_e(r,R) = \sum_{i=1,4} H_i(r,R) \tag{17}$$

$$T_1 = \int_{\Delta(E)} \Phi_N^s(R)\Phi_N^r(R)\,dR\,\langle \det\{\sigma(1)\sigma(2)\pi(3)\pi(4)\} \left| \sum_{i=1,4} H_i(r,R) \right| \det\{\pi_1(1)\pi_1(2)\pi_2(3)\pi_2(4)\}\rangle \tag{18}$$

This expression for T_1, fully expanded, contains an inconveniently large number of terms. Fortunately it is unnecessary to evaluate all of these terms explicitly. Since we are interested initially only in the influence of molecular symmetry on T_1, we need only estimate the largest terms in this expression. To find these largest terms, consider two typical terms, for a thermal, conrotatory process as given in Eqs. (19) and (20); for convenience, these terms are also presented in a simplified form in which only the symmetry[*] of the appropriate molecular orbital is indicated.

$$\langle\sigma(1)|H_1|\pi_1(1)\rangle\langle\sigma(2)|\pi_1(2)\rangle\langle\pi(3)|\pi_2(3)\rangle\langle\pi(4)|\pi_2(4)\rangle = \\ = \langle S|H|A\rangle\langle S|A\rangle\langle A|S\rangle\langle A|S\rangle \tag{19}$$

$$\langle\sigma(1)|\pi_2(1)\rangle\langle\sigma(2)|H_2|\pi_2(2)\rangle\langle\pi(3)|\pi_1(3)\rangle\langle\pi(4)|\pi_1(4)\rangle = \\ = \langle S|S\rangle\langle S|H|S\rangle\langle A|A\rangle\langle A|A\rangle \tag{20}$$

Evaluation of these products of integrals requires remembering that $\langle S|H|A\rangle = \langle A|H|S\rangle = \langle A|S\rangle = \langle S|A\rangle = 0$: thus, on the basis of symmetry considerations above, all four terms in Eq. (19) are zero (at the chosen fixed, symmetrical nuclear configuration which serves to classify the MOs according to symmetry) and none of the four in Eq. (20) need be zero.

In general, for a system with n electrons: Expansion of the expression analogous to (18) affords a large number of terms [analogous to (19) and (20)], each being the product of n integrals of type $\langle\phi^p(i)|\phi^r(i)\rangle$ and (once per term) of type $\langle\phi^p(i)|H_i|\phi^r(i)\rangle$. *One* such integral is to be assigned to *each* of the n electrons in *each* term. ϕ^r is a singly or doubly occupied reactant orbital in the given reactant configuration, ϕ^p is a singly or doubly occupied product orbital in the given product configuration; all possible permutations of the orbitals occur in the various terms on assignment of these reactant and product orbitals to the electron i. However, each individual term reflects the given reactant and product configuration: a reactant orbital which is doubly occupied in the reactant will appear *twice* in the n integrals of each term, a singly occupied one *once*, and an unoccupied one *not at all*; the same applies to the product orbitals. The largest, *i.e.* dominant, terms obtained on expansion are those in which most of the n integrals $\langle\phi^r(i)|\phi^p(i)\rangle$ and $\langle\phi^r(i)|H_i|\phi^p(i)\rangle$ are characterized by the orbital ϕ^r and the orbital ϕ^p having the same symmetry; hence, it immediately follows that one of the dominant terms is obtained by making maximum possible use in its integrals $\langle\phi^p(i)|\phi^r(i)\rangle$ and $\langle\phi^p(i)|H_i|\phi^r(i)\rangle$ of those reactant orbitals ϕ^r and product orbitals ϕ^p which correlate with one another in the W-H orbital correlation diagram for the two reactant and product configurations under discussion! In what follows, we discuss only these largest terms which are easily determined by inspection of a W-H orbital correlation diagram. The number of integrals in a possible dominant term which are equal to zero for symmetry reasons is, of course, equal to the number of electrons which have to change orbitals in an orbital correlation diagram (formally, say at an orbital crossover point) in order that a given reactant configuration be transformed into a given product configuration along the correlation diagram.

For a thermal disrotatory ring closure, inspection of the correlation diagram (Fig. 8) immediately yields the following representative dominant term:

$$\langle\pi_1(1)|H_1|\sigma(1)\rangle\langle\pi_1(2)|\sigma(2)\rangle\langle\pi_2(3)|\pi(3)\rangle\langle\pi_2(4)|\pi(4)\rangle = \\ = \langle S|H|S\rangle\langle S|S\rangle\langle A|S\rangle\langle A|S\rangle \tag{21}$$

Since this ring closure (*i.e.* transition from the reactant configuration $\pi_1^2\pi_2^2$ to the product configuration $\sigma^2\pi^2$) involves changeover of two electrons from the π_2 orbital into the π orbital, two integrals in term (21) must be equal to zero for symmetry reasons, as is confirmed by inspection of this term.

The expressions in Eqs. (20) and (21), which represent the electronic part of T_1 for thermal conrotatory and disrotatory ring closure respectively, are qualitatively different: two of the terms in Eq. (21) are zero by symmetry; none is zero in Eq. (20). Since the magnitude of T_1 is related to the rate, the relative magnitudes of these expressions estimate the relative contributions to the rate attributable to molecular symmetry. Since Eqs. (20)—(21) represent the electronic part of T_1, they determine the rate through integrals over the nuclear coordinates [see Eq. (11)]; for the thermal disrotatory ring closure, for example, the appropriate integral is:

$$T_1(E) = \int_{\Delta(E)} \Phi_N^s \Phi_N^r \{\langle S|H|S\rangle\langle S|S\rangle\langle A|S\rangle\langle A|S\rangle\}\,dR$$

The terms $\langle A|S\rangle$ are zero for a symmetric nuclear configuration inside $\Delta(E)$. Since $\Delta(E)$ is assumed small, the values of $\langle A|S\rangle$ for all nuclear coordinates inside $\Delta(E)$ are very small: we designate the contribution of each of those small terms to T_1 by ε, and classify the size of T_1 by the number of the terms of magnitude ε which appear in the integral. Thus, T_1 for the thermal disrotatory reaction is of order ε^2, since two small terms appear in T_1. The same argument indicates that the magnitude of T_1 for the thermal conrotatory

[*] S stands for symmetric and A for antisymmetric.

ring closures, whose electronic part is given by Eq. (18), is of order $\varepsilon^0 = 1$. (In Section 4.1.2, which is concerned with the photochemical reaction, we show that T_1 for conrotatory and disrotatory photochemical ring closure is of order ε.) Then, since $|T_1|^2$ is the quantity related to rate, it is possible to classify the different types of conversions of butadiene to cyclobutene in terms of their "degree of forbiddenness", which is the exponent of ε in T_1. On grounds of symmetry alone, the quantity ε is a small number compared to integrals like $\langle S|S\rangle$ or $\langle A|A\rangle$; the greater the exponent of ε the smaller will be the value of $|T_1|^2$ due to the electronic integral. Qualitatively, there will be as many terms of magnitude ε in $T_1(E)$ as there are electrons that cross, in going from reactants to products, between orbitals of different symmetry.

This treatment thus differs from the standard W-H treatment in permitting "degrees of forbiddenness" rather than restricting reactions to the two categories of "symmetry allowed" and "symmetry forbidden". One should however be aware of the qualitative nature of this argument. Though each "symmetry forbidden" matrix element $\langle S|A\rangle$ or $\langle S|H|A\rangle$, contributes with a very small term ε, it is possible that different reaction pathways give ε's of different magnitude. If this difference of magnitude is large, though both ε are very small, our classification according to the powers of ε is not useful. Also, terms like $\langle S|S\rangle$ or $\langle A|A\rangle$ which need not be small by symmetry may be small for other reasons. Our classification based on powers of ε implicitly assumes that $\langle A|S\rangle \ll \langle S|S\rangle$ or $\langle A|A\rangle$. A test of these conditions for the case at hand is necessary before accepting this classification.

4.1.2. Photochemical Reactions

Since photochemical disrotatory and conrotatory ring closure have been the subject of numerous discussions and calculations[25], which sometimes seem to indicate the inadequacy of W-H rules in describing these reactions, we shall analyze such reactions in detail from the point of view of the present paper. Past discussions of these matters involved the details of the adiabatic energy surfaces and we find it useful to explore, for this particular example, the connection to our quasiadiabatic description. We shall use here quasiadiabatic wavefunctions which give a reasonable description of the two electronic states in the region of nuclear configuration in which the reactant resembles the product. For this purpose we modify the method described in Section 2 and choose the wavefunctions for the disrotatory, photochemical reaction to be:

$$S_1 = a_1 \det\{\pi_1 \pi_1 \pi_2 \pi_2\} + b_1 \det\{\sigma \sigma \pi^* \pi^*\} \quad (22)$$

$$A_1 = a_2 \det\{\pi_1 \pi_1 \pi_2 \pi_3\} + b_2 \det\{\sigma \sigma \pi^* \pi\} \quad (23)$$

$$S_2 = a_3 \det\{\pi_1 \pi_1 \pi_3 \pi_3\} + b_3 \det\{\sigma \sigma \pi \pi\} \quad (24)$$

Here, for example, S_1 corresponds to the ground state of butadiene when $a_1 = 1$ and $b_1 = 0$. The molecular orbitals used to form the determinants are those summarized in Figure 8. The second determinant in this expression serves to characterize the system in a state (for example, at high energy) which resembles cyclobutene sufficiently that MOs derived from butadiene no longer provide an adequate description: in these intermediate states, both a_1 and b_1 are non-zero. Variations in a_1 and b_1 provide a method of describing the system at any point in-between ground-state butadiene and cyclobutene in the corresponding doubly excited configuration. Equations (23) and (24) provide analogous descriptions of states which correspond at one extreme ($a = 1$, $b = 0$) to singly-excited and doubly-excited configurations of butadiene.

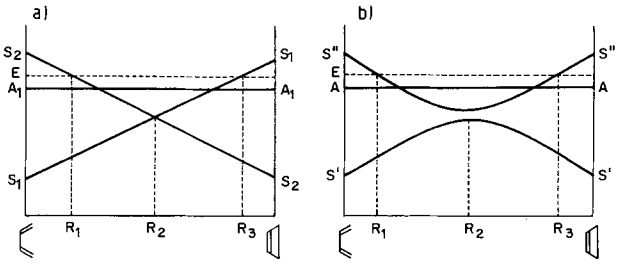


Fig. 9. Schematic quasiadiabatic (a) energy surfaces for the photochemical disrotatory electrocyclic reaction of butadiene to cyclobutane and corresponding adiabatic surfaces (b).

In Figures 9a and 9b we represent schematically the corresponding quasiadiabatic and adiabatic surfaces. The adiabatic surfaces resemble the results of van der Lugt and Oosterhoff[25].

The mechanism of reaction in the quasiadiabatic representation is as follows. Since only A_1 carries oscillator strength, the reaction starts with the molecule excited to A_1, at some energy E (see Fig. 9a). Because the energy surface of A_1 is fairly flat, as can be seen from the schematic correlation diagram Figure 9a or from the Lugt and Oosterhoff calculation, the molecule undergoes large amplitude oscillations along the reaction coordinate. For nuclear positions located at the right of R_1 (Fig. 9a) the electronic transition $A_1 \rightarrow S_2$ which generates vibrationally excited products becomes possible. In direct competition with this process, for nuclear configurations to the left of R_3, the transition $A_1 \rightarrow S_1$ is possible: this transition generates vibrationally excited reactants. If we assume that vibronic and spin-orbit contributions are small, then the rates of these transitions are determined by T_1. For the case $A_1 \rightarrow S_2$

$$T_1 = \int_{\Delta(E)} \Phi_N^P \Phi_N^R \langle A_1|H_e|S_2\rangle \, dR$$

Let us analyze the electronic part $\langle A_1|H_e|S_2\rangle$ from the point of view of the symmetry of the molecular orbitals. We see that A_1 is composed of two determinants [Eq. (23)] and inspection of Figure 8 indicates that both determinants have the same symmetry. The same is true for the determinants used in S_2. Hence all the terms in $\langle A_1|H_e|S_2\rangle$ have the same symmetry properties as:

$$\alpha \equiv \langle \det\{\pi_1 \pi_1 \pi_2 \pi_3\}|H_e|\det\{\sigma \sigma \pi \pi\}\rangle$$

If we repeat the analysis of Section 4.1.1, we find that the largest terms in α are represented by

$$\langle \pi_1|H_e|\sigma\rangle\langle \pi_1|\sigma\rangle\langle \pi_2|\pi\rangle\langle \pi_3|\pi\rangle = \langle S|S|S\rangle\langle S|S\rangle\langle A|S\rangle\langle S|S\rangle \sim \varepsilon^1$$

Thus the photochemical disrotatory ring closure is of order of forbiddenness one. By contrast, our previous analysis indicated that T_1 for the thermal disrotatory ring closure is of order ε^2 and this reaction is of order of forbiddenness two.

Hence, a disrotatory ring closure is predicted to take place more readily by a photochemical than by a thermal path.

There is no contradiction between this description of the reaction and that resulting from the adiabatic representation[25]: the latter however hides the role of symmetry. The quasiadiabatic process $A_1 \rightarrow S_2$ (see Fig. 9a) becomes in the adiabatic picture (Fig. 9b) $A \rightarrow S''$ (at configurations to the right of R_1) followed by $S'' \rightarrow S'$, at configurations around R_2. These transitions are due to non-Born-Oppenheimer coupling (between the *adiabatic states*) which may be quite important at R_2 since the electronic gap between S' and A is small. This adiabatic description of the reaction may seem different from that provided by the correlation diagrams and this apparent discrepancy has created some confusion. The adiabatic description is however equivalent to the quasiadiabatic one, which in turn is equivalent to the one provided by the correlation diagrams.

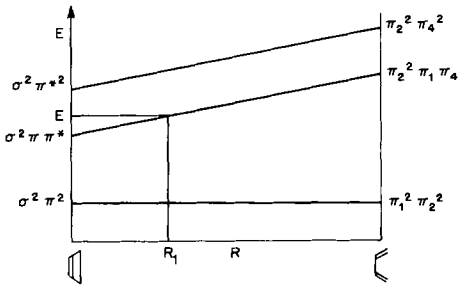


Fig. 10. Quasiadiabatic states for the conrotatory photochemical opening of cyclobutene to give butadiene.

The quasiadiabatic states for the conrotatory ring opening are presented in Figure 10. Since reactant and product states do not cross there is no possibility of an electronic transition which will lead to excited products.

We have ignored in the analysis kinetic factors that may become important in photochemical reactions, like radiative or radiationless de-excitation of the reactant state.

The discussion in this section serves to illustrate the electronic symmetry rules at the simplest level possible, when a Hückel description is used for the electronic wave function. Such rules are valid when $\Delta(E)$ is very small and the non-Born-Oppenheimer and spin orbit coupling are negligible. Under these circumstances we derive all the conclusions obtained from the original W-H rules. The rules derived here give more details about the reaction, indicating the possible existence of degrees of forbiddenness, and point out the important role that the overlap of the molecular orbitals plays in the electronic part of T_1, and hence in the rate.

4.2. Hierarchy of Symmetry Rules

We have emphasized at various places in this paper the fact that the predictions made by using the electronic symmetry rules depend on the degree of information that we have about the quasiadiabatic electronic wave functions. We illustrate this point now with the example of the ring closure reaction of butadiene. We represent the wave functions of both reactant and product, schematically, by indicating the symmetry of the molecular orbitals used to construct them. For the thermal disrotatory ring closure the reactant wave function is represented (Section 4.1.1) by SSAA, and that of the product by SSSS. As we have already discussed, when we know the symmetry of *each molecular orbital*, we can predict for this reaction an order of forbiddenness of two. Now let us assume that we want to use the electronic symmetry rules to predict the rate, but we know only the symmetry of *the wave functions* of the reactants and products (from spectroscopic measurements, for example) and know nothing about the symmetry of the molecular orbitals from which the wave function is built. For the disrotatory thermal ring closure the wave functions of reactants and products are both symmetric (the SSAA behaves upon reflection in the symmetry plane like SSSS since AA does not change sign). Therefore based on this information alone, using electronic symmetry rules, we see that the reaction is allowed; to be precise, this means that we cannot use electronic symmetry to state that the reaction is slow. Obviously the two predictions are different and the one based on the knowledge of the symmetry of the MOs is more useful. Different degrees of information need not lead to different conclusions. For example, in the case of reactions which can be represented as transitions from SSSA to SSSS or SAAA to SSSS, the symmetry of the electronic wave function of the reactants is different from that of the products and if we do not know the symmetry of the MOs we predict that both reactions are forbidden. The same prediction is made if the symmetry of the MOs is known and used, but in this case we gain the additional information that the first reaction (SSSA→SSSS) has an order of forbiddenness one while the second (SAAA→SSSS) has an order of forbiddenness three.

These examples illustrate how additional knowledge of the symmetry of MOs provides us with additional information which can change our ability to predict the outcome of the reaction. Thus a hierarchy of rules is possible, according to the details of knowledge of the symmetry of the wave function. This point has been made by *Silver*[6h] in a discussion based on a different approach.

4.3. The Role of the Electronic Interactions

In the previous subsection we have seen how the use of Hückel MO theory, which gives information about the symmetry of MOs, aids in learning more details about the rate of reaction. Hückel theory has, however, the disadvantage that it ignores to a large extent the interaction between electrons. In this section we discuss the effect that inclusion of electronic interactions, at the level of Hartree-Fock theory, has upon the predictions of reaction rates based on electronic symmetry.

It is very simple to take account of this interaction in the present approach in the electronic Hamiltonian H_e, which appears in the electronic part of T_1. If we write $H_e = H_e^{(1)} + H_e^{(12)}$, for the one- and two-electron parts ($H_e^{(12)}$ are the coulomb interactions between electrons), the two-electron operator contributes to T_1 terms of the form $\langle \psi_e^g | H_e^{(12)} | \psi_e^r \rangle$. For the thermal disrotatory reaction, for example, $\psi_e^r = \det\{SSAA\}$ and $\psi_e^g = \det\{SSSS\}$ and a representative two-electron term in $\langle \det\{SSSS\} | H_e^{(12)} | \det\{SSAA\} \rangle$ is $\langle SS|H_e^{(12)}|AA\rangle\langle S|S\rangle\langle S|S\rangle$. The one-electron contribution is, as already discussed, $\langle A|S\rangle\langle A|S\rangle\langle S|H_e^{(1)}|S\rangle\langle S|S\rangle$. The two-electron term has an order of forbiddenness zero, since SS

has the same symmetry as AA; the one-electron term has an order of forbiddenness two. In this particular case, the symmetry thus does not require that T_1 be small, although the one-electron contribution to T_1 is, in fact, very small. If the two-electron term is important (in other words, if the Hückel approximation is very poor) we will observe violations of the W-H rules. The success of W-H rules indicates that the joint contribution of all two-electron terms to T_1 is generally small. One should, however, keep them in mind as potential sources of violation of the rules. Notice also that for a reaction which can be described as SSSA→SSSS, and which has an order of forbiddenness one, the two-electron terms behave like the one-electron ones. Indeed both $\langle SA|H_e^{(12)}|SS\rangle$ and $\langle S|H_e^{(1)}|A\rangle$ are of order ε. Therefore the electronic interactions may change the predictions of the symmetry rules, based on one-electron terms, only in the case or reactions with order of forbiddenness two.

4.4. Role of Orbital Overlap

The principle of maximum bonding, which states that the reaction pathway is likely to be along the pathway of maximum MO overlap, is intimately connected to the symmetry rules by the present approach. In fact, in our approach the symmetry of molecular orbitals is used to determine whether the overlap between the MOs of the quasiadiabatic wave function of reactant and products is small. Poor overlap makes T_1 very small and leads to the same effect as selection rules based on the symmetry of the electronic wave function. Since the overlap between two MOs may be zero even if the symmetry does not require it to be so, it is useful to analyze the overlap whenever possible. For example let us compare again the disrotatory photochemical reaction with the disrotatory thermal reaction.

Figure 8 shows that the leading term in the electronic part of T_1 for the disrotatory photochemical reaction is

$$\langle\pi_1|H_e|\sigma\rangle\langle\pi_1|\sigma\rangle\langle\pi_2|\pi\rangle\langle\pi_3|\pi\rangle=\langle S|S|S\rangle\langle S|S\rangle\langle A|S\rangle\langle S|S\rangle$$

while that for the disrotatory thermal reaction is

$$\langle\pi_1|H_e|\sigma\rangle\langle\pi_1|\sigma\rangle\langle\pi_2|\pi\rangle\langle\pi_2|\pi\rangle=\langle S|S|S\rangle\langle S|S\rangle\langle A|S\rangle\langle A|S\rangle$$

The only difference is the replacement of $\langle\pi_3|\pi\rangle=\langle S|S\rangle$ in the expression for the photochemical reaction by $\langle\pi_2|\pi\rangle=\langle A|S\rangle$ to obtain the thermal one. Since $\langle A|S\rangle$ must be very small by symmetry and $\langle S|S\rangle=\langle\pi_3|\pi\rangle$ does not have to be, the symmetry rules predict that the thermal reaction is the slower of the two. This prediction will be inaccurate if the overlap of $\langle S|S\rangle=\langle\pi_3|\pi\rangle$ is very poor so that this term is in fact as small as $\langle\pi_2|\pi\rangle$. In this simple case, however, the overlap is large and the conclusion derived by using symmetry alone correct. In general, in comparing the photochemical (one electron excitation) with the thermal reaction, on pathways of the same symmetry (*e.g.*, both disrotatory), one has to compare the overlaps ⟨HOMO reactant|HOMO product⟩ and ⟨LUMO reactant|HOMO product⟩. If the latter is larger, then the photochemical reaction is faster.

The principle of maximum overlap has a broader validity than the electronic symmetry rules. The latter may be viewed as a particular case of the former in which the symmetry of the MOs is used to establish the existence of a very poor overlap. The principle of maximum overlap has the same limitations as the electronic symmetry rules in that both neglect possible coupling of electron spin, and both require the Born-Oppenheimer and Franck-Condon approximation. Thus both are restricted to consideration of electronic motion only; the neglect of nuclear motion limits the predictive value of these analyses of chemical kinetics.

5. Concerted and Nonconcerted Reactions

A definition of "concerted" and "nonconcerted" reactions is an integral part of any examination of symmetry rules for reaction rates, because these rules are usually applied to concerted reactions[26]. The traditional view is that a concerted reaction is one in which there is no intermediate. All bonds that break or form during the reaction do so simultaneously. A nonconcerted reaction is one in which there is an intermediate. These are useful qualitative notions. The discussions of the preceeding sections provide a framework with which to give operational definitions of both concerted and nonconcerted reactions.

We define a concerted reaction as one which consists of a *single* electronic transition from the quasiadiabatic state of reactants to that of the products. A nonconcerted reaction is one in which at least *two uncorrelated electronic transitions* are needed to complete the reaction. The most common situation which may give rise to a nonconcerted process is one in which three quasiadiabatic electronic states are required to describe the conversion of reactants to products (Fig. 11b). One describes the reactants, one the products and the third one (denoted I in Fig. 11b) is called the intermediate. The two electronic transitions required to make the reaction nonconcerted are, in this case, the transition from the state of reactants to that of the intermediate and a second transition from the intermediate state to that of the products. In this section we discuss nonconcertedness as it appears in reactive processes that may be characterized by three electronic states only. The need to consider more electronic states may arise but the discussion of such a situation is a straightforward generalization of the three-state case.

The points to be discussed here qualitatively are: 1) Since we define a nonconcerted reaction as one which requires two electronic transitions to complete the reaction, we must explain why the electronic symmetry rules break down for nonconcerted reactions and what the new symmetry rules are, if any. 2) How can one establish by a simple calculation whether a reaction is nonconcerted? 3) What is the connection between the present definition of nonconcertedness and the ones existing in the literature?

To answer the first question, let us consider the case presented in Fig. 11b. For energy E_t (the energy at R_1) the direct transition reactant→product by a single electronic transition is not possible since the overlap of the nuclear wave functions is extremely small. It is, however, possible to have a transition reactant→intermediate since the nuclear overlap is fairly substantial around the nuclear configuration R_1, cor-

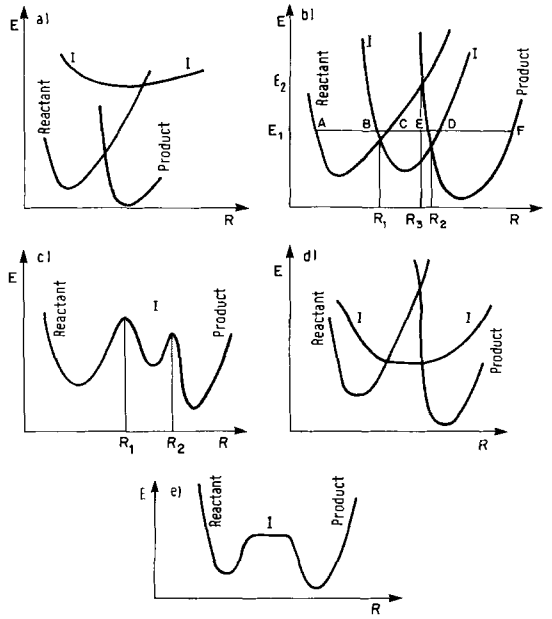


Fig. 11. a) A reaction for which the third electronic state (intermediate) (I) is too high to be accessible. The state I is not populated and the reaction is concerted. b) The third quasiadiabatic electronic state is low enough and the transitions R→I and I→P are energetically possible. At energy E_1 the reaction is nonconcerted. At energies around E_2 the reaction is both concerted and nonconcerted (see text for details). c) Adiabatic energy surface corresponding to the case of Fig. 11b. d) A flat intermediate quasiadiabatic energy surface which may be expected in the case of a diradical. e) The flat barrier on the adiabatic energy surface corresponding to Fig. 11d.

responding to the crossing of the energy surfaces of reactant and intermediate (Fig. 11b). Once the system is in the electronic state I the nuclei undergo oscillatory motion with the amplitude BD. Within a period of oscillation (10^{-13} s) the nuclei visit the region ED, in which the nuclear wave function in the state I overlaps well with that in the state P. A transition from I to P becomes possible and when this happens the reaction is completed. One can show that the electronic part of the transition probability for two uncorrelated transitions, corresponding to the part T_1 for concerted reactions, is of the type[13, 28]:

$$\langle\psi_e^P|H_e|\psi_e^I\rangle_{R_2}\langle\psi_e^I|H_e|\psi_e^R\rangle_{R_1} \tag{25}$$

where the subscripts R_1 and R_2 indicate that only the nuclear configurations located around R_1 and R_2 need to be considered. The derivation of the electronic symmetry rules for concerted reactions has been based on the fact that the electronic part of the transition matrix has the form $\langle\psi_e^P|H_e|\psi_e^I\rangle_{R_1}$ and the electronic states of *reactants and products* appear in the same matrix element. Integrals of this form do not occur in descriptions of the electronic part of a nonconcerted reaction, given by Eq. (25), and therefore the simple electronic symmetry rules which apply to concerted reactions do not apply. Other rules are, however, possible[28]. We can regard the two terms of Eq. (25) as electronic parts of two independent concerted reactions, one represented by R→I and the other by I→P. Hence symmetry rules apply for each of these terms separately. If, for example, R_1 is very close to a symmetric nuclear configuration R_1^0, and the wave functions ψ_e^R and ψ_e^I have different symmetry (they belong to different irreducible representations of the group generated by R_1^0), the reaction R→I is forbidden. Its rate, and correspondingly the rate of the nonconcerted reaction will be slow. The same argument applies separately to the "step" I→P, at nuclear configurations R_2. More details may be found in Ref.[28].

Concerning the second question: After clarifying how the involvement of a third state can make the reaction nonconcerted, let us indicate very briefly how one can test whether a given process is concerted or not. One should start by listing the chemical structures that are likely candidates for an intermediate. Then quasiadiabatic states should be constructed for each intermediate, at the level of simple Hückel theory. For example, in the case of butadiene ring closure one may think of a diradical with unpaired electrons at C^1 and C^4. A quasiadiabatic state for the diradical can be constructed by using a $2p_z$ orbital on each of the carbons labeled 2 and 3 and two localized orbitals for the single electrons on C^1 and C^4[29]. The electronic energy surface may be located with respect to the reactants and products as shown in Figure 11a. In this case the reaction is concerted. If the results are as shown in Figure 11b then at energies $E \approx E_1$ the reaction is nonconcerted. If the energy is raised (thermally or through laser induced vibrational excitation) close to E_2 the concerted reaction R→P starts competing with the nonconcerted one. This possibility of simultaneous coexistence of concerted and nonconcerted pathways has been inferred from experimental data[30].

Regarding the third question: Previous definitions of nonconcertedness[26a-d, 27] can be all derived from the present one. The adiabatic surface corresponding to the nonconcerted reaction (Fig. 11b) is shown in Figure 11c. We see that the presence of the intermediate state in Figure 11b creates a well in the adiabatic state of Figure 11c located between reactants and products. One of the early definitions of nonconcertedness required such a well (for a discussion of this see Ref. [27b]). There is, however, a possibility that the intermediate state may have a flat or a sloped shape between the points of intersection with the reactant and product surfaces. Computations show that a flat surface is very likely, for example, in the case of diradical intermediates[27a, 29]. Such a situation can be seen in Figure 11d which represents a nonconcerted reaction. The corresponding adiabatic surface is flat (Fig. 11e) and does not have a well. The possibility that a flat barrier, or an adiabatic surface, can be associated with nonconcertedness has been proposed in the literature[27a]. Finally, our description of a nonconcerted process fully agrees with and substantiates, in an obvious way, the one proposed by *Doering* and *Sachdev*[27c] which involves in the intermediate a set of vibrational states.

Thus, this formalism for reaction rates incorporates naturally inferences drawn from experimental studies concerning the characteristics required for a reaction to be nonconcerted. It does not answer explicitly[28] the question of the minimum lifetime required for the definable existence of an intermediate, but instead indicates that this question is not a useful one, since there is a smooth continuum of possible processes ranging from concerted to nonconcerted.

This work was supported in part by the National Science Foundation and the Energy Research and Development Administration.

Received: May 18, 1978 [A 271 IE]
German version: Angew. Chem. 91, 363 (1979)

[1] For a review see for example: *T. F. George, J. Ross*, Annu. Rev. Phys. Chem. *24*, 263 (1973); *J. C. Light*, Adv. Chem. Phys. *19*, 1 (1971); *R. D. Levine* in: M. T. P. International Review of Science, Theoretical Chemistry. Butterworths, Oxford 1971.

[2] *A. B. Elkowitz, R. E. Wyatt*, J. Chem. Phys. *62*, 2504 (1975); *A. Kuppermann, G. Schatz, ibid. 62*, 2502 (1975); *R. B. Walker, J. C. Light, A. Altenberger-Siczek, ibid. 64*, 1166 (1976); *G. C. Schatz, John Ross, ibid. 66*, 1021, 1037, 2943 (1977).

[3] *E. Wigner, E. E. Witmer*, J. Phys. *51*, 859 (1928).

[4] *K. Shuler*, J. Chem. Phys. *21*, 624 (1953).

[5] *R. B. Woodward, R. Hoffmann:* Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969); Die Erhaltung der Orbitalsymmetrie. Verlag Chemie, Weinheim 1970; The Conservation of Orbital Symmetry. Academic Press, New York; Verlag Chemie, Weinheim 1970; *R. E. Lehr, A. P. Marchand:* Orbital Symmetry. Academic Press, New York 1972; *T. A. Nguyen:* Les Regles de Woodward-Hoffmann. Ediscience, Paris 1970; Die Woodward-Hoffmann-Regeln und ihre Anwendung. Verlag Chemie, Weinheim 1972; *J. Michl*, Top. Curr. Chem. *46*, 1 (1974).

[6] There is an extensive literature on this subject. We select a few papers to represent various approaches: a) Perturbation Theory: *K. Fukui*, Bull. Chem. Soc. Jpn. *39*, 498 (1966); *K. Fukui, H. Fujimoto, ibid. 41*, 1989 (1968); b) Aromaticity: *M. G. Evans*, Trans. Faraday Soc. *35*, 824 (1939); *M. J. S. Dewar*, Tetrahedron Suppl. *8*, 75 (1966); Angew. Chem. *83*, 859 (1971); Angew. Chem. Int. Ed. Engl. *10*, 761 (1971). c) Möbius-Hückel Approach: *H. E. Zimmerman*, J. Am. Chem. Soc. *88*, 1564 (1966); *S. Masamune, N. Darby*, Acc. Chem. Res. *4*, 272 (1971); d) Nodal properties of wave functions: *C. Trindle*, J. Am. Chem. Soc. *92*, 3251 (1970); e) Properties of activated complex and reaction coordinate: *R. F. W. Bader*, Can. J. Chem. *40*, 1164 (1962); *J. W. McIver, Jr., R. E. Stanton*, J. Am. Chem. Soc. *94*, 8620 (1972); *J. W. McIver, Jr.*, Acc. Chem. Res. *7*, 72 (1974); *R. Pearson, ibid. 4*, 152 (1971); *H. Metiu, J. Ross, R. Silbey, T. F. George*, J. Chem. Phys. *61*, 3200 (1974); f) Properties of force constants: *L. Salem*, J. Am. Chem. Soc. *90*, 543 (1968); *L. Salem, J. S. Wright, ibid. 91*, 5947 (1969); *L. Salem*, Chem. Phys. Lett. *3*, 99 (1969); *L. S. Bartell*, J. Chem. Educ. *45*, 754 (1968); g) Collision theory: *T. F. George, J. Ross*, J. Chem. Phys. *55*, 3851 (1971); h) Other methods: *W. A. Goodard III, T. H. Dunning, Jr., W. J. Hunt, P. J. Hay*, Acc. Chem. Res. *6*, 368 (1973); *B. H. Mahan*, J. Chem. Phys. *55*, 1015 (1971); *N. Epiotis*, J. Am. Chem. Soc. *94*, 1924, 1935, 1941, 1946 (1972); *95*, 1191 (1973); *D. N. Silver, ibid. 96*, 5959 (1974).

[7] *H. E. Zimmerman:* Quantum Mechanics for Organic Chemist, Academic Press, New York 1975.

[8] *Y. B. Band, K. F. Freed*, Chem. Phys. Lett. *28*, 328 (1974); J. Chem. Phys. *63*, 3382, 4479 (1975).

[9] *M. G. Evans, M. Polanyi*, Trans. Faraday Soc. *34*, 11 (1938); see also *M. J. S. Dewar* in Orbital Symmetry Papers. A. C. S., Washington, D. C., 1974, p. 16.

[10] A discussion of quasiadiabatic states from the point of view of collision theory may be found in *T. F. O'Malley*, Adv. At. Mol. Phys. *7*, 223 (1971); *S. Mukamel, J. Ross*, J. Chem. Phys. *66*, 3759 (1977).

[11] *H. Gebelein, J. Jortner*, Theor. Chim. Acta *25*, 143 (1972).

[12] *I. N. Levine:* Quantum Chemistry. Allyn and Bacon, Boston 1970; *I. N. Levine:* Molecular Spectroscopy. Wiley, New York 1975.

[13] *H. Metiu*, Ph. D. Thesis, M. I. T. 1974.

[14] Since the purpose of this paper is limited to an analysis of symmetry rules of the W-H type which require some details of the electronic states, we can ignore all but some qualitative properties of the nuclear wavefunctions. These functions satisfy very complicated equations which will not be given here. In lowest order approximation, however, the nuclear wave function of reactants, for example, is equal to the wave function of the nuclei moving under the influence of the quasiadiabatic electronic energy of the reactants. Higher order calculations must of course include the fact that the state of products is also present.

[15] a) *D. J. Wren, M. M. Menzinger*, J. Chem. Phys. *63*, 4557 (1975); b) *R. A. Marcus*, Discuss. Faraday Soc. *29*, 21 (1960); J. Chem. Phys. *44*, 679 (1965); Annu. Rev. Phys. Chem. *15*, 155 (1964); *P. P. Schmidt*, Specialist Periodical Reports in Electrochemistry, Vol. 5, The Chemical Society, London 1975, p. 21 ff.

[16] *K. Freed*, Top. Appl. Phys., in press.

[17] *J. R. Schrieffer:* Theory of Superconductivity. Benjamin, New York 1971.

[18] *R. S. Knox:* Theory of Excitons, Supplement 5, Solid State Phys. (1963).

[19] *J. M. Ziman:* Electrons and Phonons. Oxford University Press, Oxford 1972.

[20] *E. B. Wilson, Jr., J. C. Decius, P. C. Cross:* Molecular Vibrations (McGraw-Hill, New York 1955).

[21] *D. S. Schonland:* Molecular Symmetry. Van Nostrand, Princeton, New Jersey, 1965.

[22] *R. M. Hochstrasser:* Molecular Aspects of Symmetry. Benjamin, New York 1966. Symmetry rules for T_3 are available.

[23] a) *R. Hoffmann*, J. Chem. Phys. *49*, 3739 (1968). b) Various studies of the potential energy surface do not agree in assigning a larger barrier to the reaction pathway through a trapezoidal configuration. A correlation diagram analysis (see [23a]) would indicate that the pathway which has a trapezoidal nuclear configuration has a higher activation energy. Various computations of this energy do not all agree with this statement and with each other: *L. C. Cusachs, M. Krieger, C. W. McCurdy*, J. Chem. Phys. *49*, 3740 (1968); *L. M. Raff, L. Stivers, R. N. Porter, D. L. Thompson, L. B. Sims, ibid. 52*, 3449 (1970); *F. L. Minn, A. B. Hanratty, ibid. 53*, 2543 (1970); Theor. Chim. Acta *19*, 390 (1970).

[24] *J. M. Henry, R. L. Jaffe, J. B. Anderson*, Chem. Phys. Lett. *20*, 138 (1973) and unpublished work. There is some controversy regarding the computational method involved: *R. N. Porter, D. L. Thompson, L. M. Raff, J. M. White*, J. Chem. Phys. *62*, 2429 (1975); *J. B. Anderson, ibid. 62*, 2446 (1975).

[25] *R. C. Dougherty*, J. Am. Chem. Soc. *93*, 7187 (1971); *W. T. A. M. van der Lugt, L. J. Oosterhoff*, Chem. Commun. *1968*, 1235; J. Am. Chem. Soc. *91*, 6042 (1969). See also *J. Michl*'s paper in Ref. [5].

[26] a) *J. E. Baldwin, A. H. Andrist, R. K. Pinschmidt, Jr.*, Acc. Chem. Res. *5*, 402 (1972); b) *S. H. Bauer*, J. Am. Chem. Soc. *91*, 3688 (1969); c) *J. A. Berson*, Acc. Chem. Res. *5*, 406 (1972); d) *J. P. Low*, J. Chem. Educ. *51*, 785 (1974); e) for the application of orbital symmetry considerations to nonconcerted reactions, see Ref. [26a, c].

[27] a) *R. Hoffmann, S. Swaminathan, B. G. Odell, R. Gleiter*, J. Am. Chem. Soc. *92*, 7091 (1970); b) *A. H. Andrist*, J. Org. Chem. *37*, 1772 (1972); c) *W. Doering, K. Sachdev*, J. Am. Chem. Soc. *96*, 1168 (1974).

[28] *H. Metiu, J. Ross, T. F. George*, Chem. Phys. *11*, 259 (1975).

[29] A detailed discussion of diradical wave functions may be found in *L. Salem, C. Rowlinson*, Angew. Chem. *84*, 86 (1972); Angew. Chem. Int. Ed. Engl. *11*, 92 (1972).

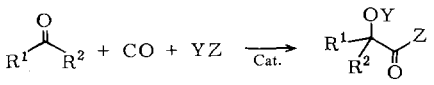
[30] *J. E. Baldwin, A. H. Andrist*, Chem. Commun. *1970*, 1561.

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.

Catalytic Conversion of Aldehydes into Higher α-Siloxy Aldehydes by Hydrosilane and Carbon Monoxide[**]

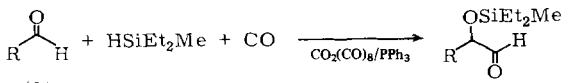
By *Shinji Murai, Toshikazu Kato, Noboru Sonoda, Yoshio Seki,* and *Kazuaki Kawamoto*[*]

Among the reactions belonging to the hardly explored realm of carbon monoxide chemistry, carbonylation at the carbonyl carbon of an aldehyde or a ketone [eq. (a)] is one of the most interesting.



(a)

Only a few ambiguous examples of reactions of type (a) have been reported: catalytic conversion of formaldehyde with CO and H_2 into α-hydroxyacetaldehyde in moist solvents[1] and that of acetaldehyde with CO and H_2O into α-hydroxypropionic acid[2]. These reactions, however, most likely proceed indirectly *via* hydrated aldehydes or poly(oxymethylenes)[3]. This paper describes a definite example of the catalytic reaction (a).

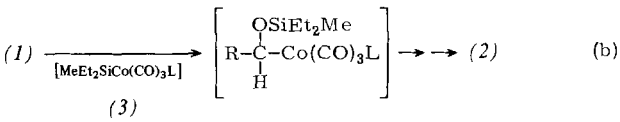


(1) *(2)*

(a), R = n-C_3H_7
(b), R = n-C_6H_{13}
(c), R = c-C_6H_{11}

The reaction of heptanal with $MeEt_2SiH$ (molar ratio 3:1) and CO (50 kg/cm²) in the presence of $Co_2(CO)_8$ and PPh_3 gave α-[diethyl(methyl)siloxy]octanal *(2b)* in 50% yield[4]. Similar results were obtained with butanal *(1a)* and cyclohexanecarboxaldehyde *(1c)*[4] (yields 49 and 54%, respectively). The use of an excess of the starting aldehyde is essential, since 1,2-bis(siloxy)alkenes are otherwise formed[5].—The reaction products, α-siloxyaldehydes *(2)* are useful intermediates in organic synthesis that are otherwise difficult to prepare.

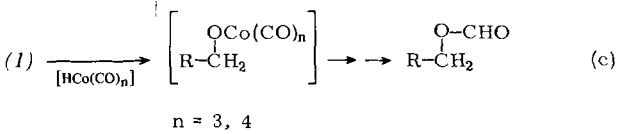
We suggest that the active catalyst is a silylcobalt complex *(3)*, L = CO or PPh_3, and the key intermediate is α-siloxyalkylcobalt compound *(4)* [eq. (b)]. The high affinity of the silyl group for the oxygen function may force bond formation between carbon and cobalt [eq. (b)]; this contrasts with the reaction of aldehydes *(1)* under oxo conditions (H_2 and CO) to give formates [eq. (c)], with $HCo(CO)_n$ as active catalyst[6].



(3)

(4), L = CO, PPh_3

(b)



n = 3, 4

(c)

The insertion of carbon monoxide into α-siloxyalkylmanganese has very recently been reported[7]. Reactions involving α-oxyalkyl-metal compounds such as this and *(4)* are important in relation to the mechanism of the Fischer-Tropsch reaction[8] and Union Carbide's ethylene glycol synthesis[9].

Experimental

Synthesis of *(2b)*: A solution of *(1b)* (4.2 ml, 30 mmol) diethyl(methyl)silane (1.02 g, 10 mmol), $Co_2(CO)_8$ (0.136 g, 0.4 mmol), and PPh_3 (0.104 g, 0.4 mmol) in benzene (20 ml) was placed in a 100-ml stainless steel autoclave. The autoclave was flushed with N_2 (50 kg/cm²) and CO (50 kg/cm²), then charged with CO (50 kg/cm²) and immersed in an oil bath preheated to 100°C and held at this temperature with stirring for 20 h. Analysis of the reaction mixture by GLC [Silicon OV-1, 5%, on Uniport KS, 3 m, 140°C, n-tetradecane as internal standard] showed it to contain *(2b)* in 50% yield. An analytical sample was obtained by distillation (b.p. 122–132°C/10 torr) and preparative GLC [Silicon OV-1, 170°C][4].

Received: January 24, 1979 [Z 193 IE]
German version: Angew. Chem. *91*, 421 (1979)

CAS Registry numbers:
(1a), 123-72-8; *(1b)*, 111-71-7; *(1c)*, 2043-61-0; *(2a)*, 69881-71-6; *(2b)*, 69881-72-7; *(2c)*, 69881-73-8; *(3)*, L = CO, 69897-17-2; *(3)*, L = PPh_3, 69897-18-3; $HCo(CO)_3$, 60105-25-1; $HCo(CO)_4$, 16842-03-8; $HSiEt_2Me$, 760-32-7; CO, 630-08-0

[*] Prof. Dr. S. Murai [+], T. Kato, Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)
Dr. Y. Seki, Prof. Dr. K. Kawamoto
Faculty of Economics, Kagawa University
Takamatsu, Kagawa 760 (Japan)
[+] Author to whom correspondence should be addressed.

[**] Transition Metal Reactions of Silanes. Part 6.—Part 5: [5].

[1] *T. Yukawa, H. Wakamatsu*, Brit. Pat. 1408857 (1974).
[2] *S. K. Bhattacharyya, S. K. Palit, A. D. Das*, Ind. Eng. Chem. Prod. Res. Dev. *9*, 92 (1970). These results could not be reproduced. *T. Yukawa*, personal communication.
[3] For examples of such reactions see: *F. Piancenti, M. Bianchi* in *I. Wender, P. Pino*: Organic Syntheses via Metal Carbonyls. Vol. 2, Wiley, New York 1977, p. 1.
[4] IR (without solvent) *(2a)*, 1737 cm⁻¹ (C=O); *(2b)*, 1740; *(2c)*, 1735. ¹H-NMR (in CCl_4, δ, CHO): *(2a)*, 9.44 (d, J = 2 Hz); *(2b)*, 9.45 (d, J = 2 Hz); *(2c)*, 9.46 (d, J = 2 Hz).
[5] *Y. Seki, S. Murai, N. Sonoda*, Angew. Chem. *90*, 139 (1978); Angew. Chem. Int. Ed. Engl. *17*, 199 (1978).

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0393 $ 02.50/0*

[6] *L. Marko*, Proc. Chem. Soc. *1962*, 67; *L. Marko, P. Szabo*, Chem. Tech. (Berlin) *13*, 482 (1961); Chem. Abstr. *56*, 7102 (1962); *M. Polievka, E. J. Mistrik*, Chem. Zvesti *26*, 149 (1972); Chem. Abstr. *77*, 113388 (1972). See also [3], pp. 12 and 84.
[7] *J. A. Gladysz, J. C. Selover, C. E. Strouse*, J. Am. Chem. Soc. *100*, 6766 (1978).
[8] *G. Henrici-Olivé, S. Olivé*, Angew. Chem. *88*, 144 (1976): Angew. Chem. Int. Ed. Engl. *15*, 136 (1976).
[9] *R. L. Pruett*, Ann. N. Y. Acad. Sci. *295*, 239 (1977).

Synthesis of Thymosin α_1, a Polypeptide of the Thymus[**]

By *Christian Birr* and *Ulrich Stollenwerk*[*]

The regulation of the immune defense mechanism of the body by polypeptides of the thymus gland is presently being studied with increasing interest.

It has been demonstrated by injection of cell-free protein extracts from calf thymus in genetically athymic mice (or after thymectomy) that immunologial deficiency diseases such as increased susceptibility to infection, higher probability of tumor formation, accelerated aging and diminished rejection of skin grafts could be suppressed with varying degrees of success[1].

With the aid of a purified "protein fraction no. 5" from calf thymus it could also be demonstrated that the differentiation of immature thymus-dependent immune defense cells (T-cells, T-lymphocytes) could be stimulated to form mature immune-competent T-lymphocytes[2]. This "protein fraction no. 5" was named "thymosin" and is administered in several clinical tests against different types of cancer[3]. Separation of thymosin by electrofocusing yielded an acidic polypeptide, thymosin α_1 (pI = 4.2)[4a]. The sequence of thymosin α_1 has been determined, but an announced description of its synthesis (*Wang et al.*, 1977) has not, as yet, been published[4b].

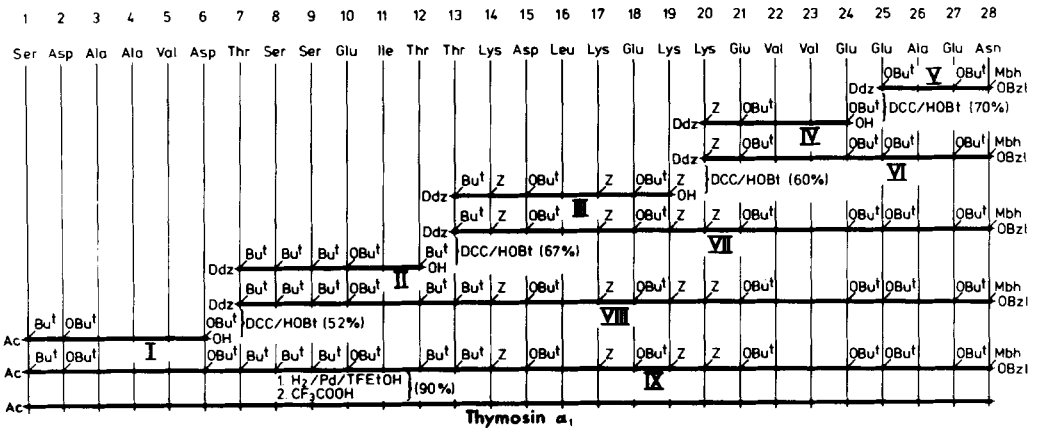
In the following we briefly outline a method for the synthesis of the sequence given for thymosin α_1[4] (scheme 1). Alternative routes and biological data will be published elsewhere[5].

The peptide was built-up by fragment condensation with dicyclohexylcarbodiimide/1-hydroxybenzotriazole (DCC/HOBt)[6] from 5 segments: I (1—6), II (7—12), III (13—19), IV (20—24) and V (25—28). All segments were synthesized fully protected by stepwise N-terminal sequence elongation. The syntheses were carried out in solution using an excess of the mixed anhydrides of the Ddz-amino acids prepared from isobutyloxycarbonyl chloride/*N*-methylmorpholine[7]. This resulted in the benzyl esters of segment I (67%) and V (39%), and the methyl esters of II (20%), III (31%) and IV (56%), respectively (overall yields in brackets). After alkaline saponification in aqueous dioxane, condensation of segment IV in dimethylformamide with V (after Ddz-deprotection with 1% trifluoroacetic acid/dichloromethane (v/v)) for 24 h afforded fragment VI in 70% yield.

Segment III, after saponification in aqueous tetrahydrofuran/methanol, was coupled with VI in dimethylformamide for 6 h, giving fragment VII in 60% yield. After Ddz-deprotection (as in V), VII was N-terminally elongated in 18 h at 0°C and 10 h at *ca.* 20°C with segment II (saponified in dioxane/H_2O 8:2 (v/v)) to give VIII in 67% yield.

Before the final condensation, the benzyl ester group was cleaved from the N-terminal acetyl segment I by hydrogenation (Pd/C) in 2-propanol/acetic acid. The free acid of I was coupled in the final condensation with VIII in *N*-methylpyrrolidone/dimethylformamide 2:1 (v/v) for 24 h, thus affording the completely protected end-product IX in 52% yield. IX was chromatographically purified on Sephadex LH 20 in 2,2,2-trifluoroethanol. Amino acid analysis (theor. values in brackets; 6 N HCl/110°C/24 h): Asp 4.11 (4); Thr 2.64 (3); Ser 2.38 (3); Glu 6.80 (6); Lys 4.59 (4); Ile 1.13 (1); Leu 1.23 (1); Ala 2.51 (3); Val 2.41 (3).

In three final reactions IX was liberated from all of its protecting groups: For cleavage of the benzyloxycarbonyl protecting groups and the C-terminal benzyl ester, the polypeptide IX was hydrogenated with Pd/C in 2,2,2-trifluoroethanol (96% yield). The resulting product was treated with trifluoroacetic acid/dichloromethane 1:1 (v/v) in the presence of 10% anisole for 30 min to cleave mainly the *tert*-butyl esters. After removal of volatile components *in vacuo* at room temperature, the residual polypeptide/anisole was treated with pure trifluoroacetic acid for the final cleavage of *tert*-butyl and 4,4'-dimethoxybenzhydryl protective groups (120 min, *ca.* 20°C). Precipitation and subsequent washing with ether yielded synthetic thymosin α_1, which was chromatographed on Biogel P-6 for purification and characterization. For this purpose the column



Scheme 1: Synthesis of thymosin α_1 by condensation of the fragments I—VIII. Double amounts of the N-terminal fragments were employed; yields are based on the C-terminal component. Protective groups: Ac: acetyl; Bu^t: *tert*-butyl; Bzl: benzyl; Ddz: 3,5-dimethoxy-α,α-dimethyl-benzyloxycarbonyl; Mbh: 4,4'-dimethoxybenzhydryl; Z: benzyloxycarbonyl.

[*] Priv.-Doz. Dr. Ch. Birr, Dipl.-Chem. U. Stollenwerk
Max-Planck-Institut für Medizinische Forschung
Abteilung Naturstoff-Chemie
Jahnstr. 29, D-6900 Heidelberg 1 (Germany)

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

(0.6 × 240 cm) was first calibrated by chromatography of oxidized insulin B chain (M.W. 3495) in 1% acetic acid (containing 10% trifluoroethanol) to determine the retention volume. Subsequently, the synthetic thymosin α_1 was chromatographed

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* 0570-0833/79/0505-0394 $ 02.50/0

and eluted in the proper volume according to its molecular weight (3107) (yield 90%, based on IX). Amino acid analysis (theor. values in bracket; 6 N HCl/110°C/24, 48, 96 h): Asp 4.11 (4); Thr 2.86 (3); Ser 2.70 (3); Glu 5.89 (6); Lys 3.98 (4); Ile 0.97 (1); Leu 1.00 (1); Ala 3.05 (3); Val 2.97 (3). Thin-layer chromatogram (silica gel MERCK 60 F-254; 0.25 mm): $R_f = 0.16$ (*n*-butanol/pyridine/glacial acetic acid/water 5:5:1:4 (v/v)), homogeneous. $[\alpha]_\lambda^{25}$: −96° (579 nm), −201.7° (435 nm), −242.5° (408 nm), −338.5° (365 nm), −587° (313 nm); $c = 0.083$ in water. The synthetic thymosin α_1 is biologically active in the stimulation of lymphocytes. in the E-rosettes test and in the mitogen assay. The data will be presented elsewhere[5].

Received: February 26, 1979 [Z 196 IE]
German version: Angew. Chem. *92*, 422 (1979)

CAS Registry numbers:
I, 69943-29-9; I, benzyl ester, 69943-30-2; II, 69943-31-3; II, methyl ester, 69943-32-4; III, 69943-33-5; III, methyl ester, 69943-34-6; IV, 69961-09-7; IV, methyl ester, 69943-35-7; V, benzyl ester, 69943-36-8; VI, 69961-08-6; VII, 69943-37-9; VIII, 70024-11-2; IX, 70024-10-1; thymosin α_1, 62304-98-7

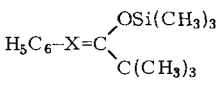
[1] *D. W. van Bekkum*: The Biological Activity of Thymic Hormones. Kooyker Scientific Publ., Rotterdam 1975; *J.-F. Bach, C. Carnaud*, Prog. Allergy *21*, 342 (1976).
[2] *J. A. Hooper, M. C. McDaniel, G. B. Thurman, G. H. Cohen, R. S. Schulof, A. L. Goldstein*, Ann. N. Y. Acad. Sci. *249*, 125 (1975).
[3] *L. A. Schafer, J. U. Gutterman, E. M. Hersh, G. M. Mavligit, A. L. Goldstein*, Prog. Cancer Res. Therapy *2*, 329 (1977).
[4] a) *A. L. Goldstein, T. L. K. Low, M. McAdoo, J. McClure, G. B. Thurman, J. Rossio, C.-Y. Lai, D. Chang, S.-S. Wang, C. Harvey, A. H. Ramel, J. Meienhofer*, Proc. Natl. Acad. Sci. USA *74*, 725 (1977); b) Note added in proof: *S. S. Wang, I. D. Kulesha, D. P. Winter*, J. Am. Chem. Soc. *101*, 253 (1979), describe a synthesis of thymosin α_1, in which the end product was obtained from a final deprotection reaction with HF in 92% yield.
[5] *Ch. Birr, U. Stollenwerk, O. Brodner, H.-G. Manke*, 6th Am. Pept. Symp., Washington, June 1979.
[6] *W. König, R. Geiger*, Chem. Ber. *103*, 788 (1970).
[7] *Ch. Birr, M. Nassal, R. Pipkorn*, Int. J. Pept. Protein Res. *13*, 287 (1979).

Mesityl(diphenylmethylene)arsane[**]

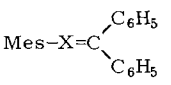
By *Theo C. Klebach, Hans van Dongen*, and *Friedrich Bickelhaupt*[*]

Dedicated to Professor Egbert Havinga on the occasion of his 70th birthday

Consistent with the empirical "double bond rule" and theoretical arguments, the tendency to form the pπ-hybridized state with coordination number 2 in Group 5 is still less pronounced with arsenic than with phosphorus. Relatively few compounds with two-coordinate arsenic are known, and they are less stable than those of phosphorus[1]. The requisite stabilization in the arsamethinecyanines[2] and in arsabenzene[3] and its derivatives is primarily due to delocalization. The only known stable compound with apparently localized As=C bonding is phenyl[2,2-dimethyl-1-(trimethylsiloxy)propylidene]arsane *(1a)*[4]; however, the extent to which the oxygen atom influences this bonding is still unclear.



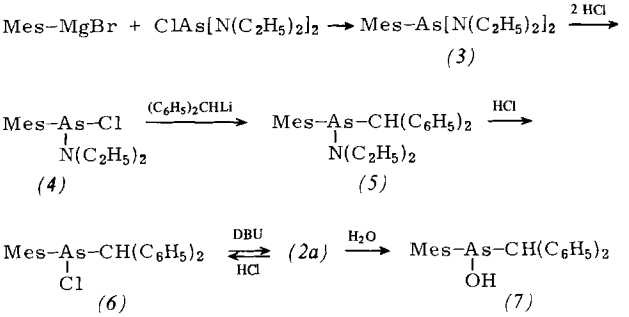
(1a), X = As
(1b), X = P



(2a), X = As
(2b), X = P
(2c), X = N



It therefore seemed worthwhile investigating whether a compound with a localized As=C bond substituted by carbon only is thermally stable. We have now been able to synthesize mesityl(diphenylmethylene)arsane *(2a)*, after it had been shown with the corresponding phosphorus compound *(2b)* that the mesityl group is suitable for steric shielding of the reactive P=C bond[5].



Reaction of mesitylmagnesium bromide with chlorobis(diethylamino)arsane in tetrahydrofuran (THF) afforded a solution of *(3)*, which was directly treated with two equivalents of HCl in THF at −40°C to give *(4)* [yield 40% based on chlorobis(diethylamino)arsane; b. p. 85—89°C/10^{-3} torr]. Reaction of *(4)* in THF with diphenylmethyllithium (20% excess) yielded *(5)*, which on passage of gaseous HCl reacted further to give *(6)* [yield *ca.* 50% based on *(4)*; m. p. 58—62°C after chromatographic purification on Al_2O_3 (Brockmann, Act. 2—3, toluene/chloroform 9:1) and sublimation (140°C/10^{-3} torr)]. Elimination of HCl from *(6)* with diazabicycloundecene (DBU) in THF (25°C, 3 h) proceeded almost quantitatively; after filtration from DBU-HCl, evaporation of the solution and extraction with cyclohexane afforded *(2a)* as a bright yellow viscous oil, which is stable at room temperature in the absence of air. Pure *(2a)* could hitherto be obtained only in a sealed high-vacuum system.

The spectral data of *(2a)* [Table 1; MS: $m/e = 360.0867$ (M^+, 15%), calc. 360.0859] confirm the assigned structure. Characteristic is the ^{13}C-NMR signal for the carbon of the As=C bond, which by its position at very low field reflects the hybridization of the carbon ($sp^2\pi$) and the effect of the neighboring arsenic[6]. As in the case of *(1a)* and *(1b)*[7], this signal lies at lower field in the arsenic compound *(2a)* than in the phosphorus compound *(2b)*. The UV maximum of *(2a)*, which is assigned to a n→π* transition[8], is shifted, as expected, to longer wavelength than that of *(2b)*.

As in *(2b)*, the steric hindrance to polymerization is apparently the most important factor determining the stability in *(2a)*. Attempts to synthesize phenyl(diphenylmethylene)ar-

Table 1. Spectral data of *(2a)* and *(2b)*.

	^{1}H-NMR [a]	^{13}C-NMR [a]	UV [b]
(2a)	7.80—7.00 (m, 10H, C_6H_5)	212.1 (As=C)	346 (3.52)
	6.63 (s, 2H, Mes-H)	140—125 (Aryl-C)	
	2.23 (s, 6H, *o*-CH_3)	22.8 (*o*-CH_3)	
	2.19 (s, 3H, *p*-CH_3)	20.6 (*p*-CH_3)	
(2b)	7.60—6.75 (m, 10H, C_6H_5)	193.37 (P=C)	254 (3.20)
[5]	6.69 (s, 2H, Mes-H)	144.9—125.5 (Aryl-C)	268 (3.01)
	2.27 (s, 6H, *o*-CH_3)	22.67; 22.06 (*o*,*o*'-CH_3)	324 (2.84)
	2.19 (s, 3H, *p*-CH_3)	20.96 (*p*-CH_3)	

[a] $CDCl_3$, δ-values. [b] THF, λ in nm (log ε).

[*] Prof. Dr. Bickelhaupt, Drs. Th. C. Klebach, H. van Dongen
Scheikundig Laboratorium der Vrije Universiteit
De Lairessestraat 174, Amsterdam-Z. (Netherlands)

[**] We thank Drs. *D. Schipper* for the ^{13}C-NMR spectra and Dr. *R. J. M. Weustink* for carrying out the experiments with phenyl(diphenylmethylene)arsane.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0395 $ 02.50/0*

sane afforded only polymeric material, even though the coplanarity, and thus the configuration of the aromatic rings is expected to be more favorable than in *(2a)*.—The X-ray structure analysis[9] of the nitrogen analogue *(2c)*[5] showed that the planes of the mesityl groups and *syn*-phenyl groups form a relatively large angle (73° and 60°, respectively) with the plane of the N=C bond.

From investigations carried out so far, the chemical behavior of *(2a)* would appear to resemble that of *(2b)*[5], but *(2a)* is certainly more reactive. In THF, *(2a)* adds HCl to give *(6)*, with arsenic expectedly functioning as the more positive partner of the As=C bond. However, whereas the addition of methanol to *(2b)* does not take place without base-catalysis and *(2b)* is stable under nitrogen, *(2a)* even adds traces of water under these conditions to give *(7)*. This reaction apparently proceeds more rapidly than atmospheric oxidation.

Received: January 25, 1979 [Z 199 IE]
German version: Angew. Chem. *91*, 423 (1979)

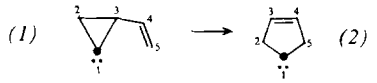
CAS Registry numbers:
(2a), 69961-41-7; *(3)*, 69943-40-4; *(4)*, 69943-41-5; *(5)*, 69961-42-8; *(6)*, 69943-42-6; *(7)*, 69943-43-7; Mes-Br, 576-83-0; $ClAs[N(C_2H_5)_2]_2$, 1734-99-2

[1] *C. Jongsma, F. Bickelhaupt* in *T. Nozoe, R. Breslow, K. Hafner, S. Ito, I. Murata:* Topics in Nonbenzoid Aromatic Chemistry. Hirokawa Publishing Co., Tokyo 1977, Vol. II, p. 139.
[2] *G. Märkl, F. Lieb*, Tetrahedron Lett. *1967*, 3489.
[3] *A. J. Ashe, III*, J. Am. Chem. Soc. *93*, 3293 (1971).
[4] *G. Becker, G. Gutekunst*, Angew. Chem. *89*, 477 (1977); Angew. Chem. int. Ed. Engl. *16*, 463 (1977).
[5] *Th. C. Klebach, R. Lourens, F. Bickelhaupt*, J. Am. Chem. Soc. *100*, 4886 (1978).
[6] *W. Schäfer, A. Schweig, K. Dimroth, H. Kanter*, J. Am. Chem. Soc. *98*, 4410 (1976).
[7] *G. Becker*, Z. Anorg. Allg. Chem. *423*, 242 (1976).
[8] Hartree-Fock-Slater calculations according to the discrete variational method on simple models; we thank Prof. Dr. Ir. *P. Ros* and *F. Visser* for communication of unpublished results.
[9] We thank *G. Bokkers*, Dr. *J. Kroon*, and Dr. *A. L. Spek* for these unpublished results.

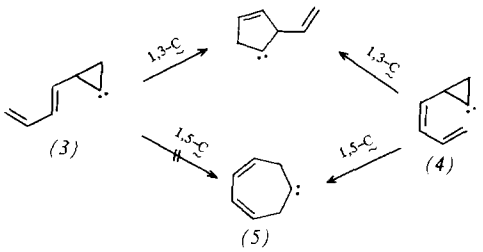
Carbene-Carbene Rearrangements of *cis*- and *trans*-2-(1,3-Butadienyl)cyclopropylidene[**]

By *Udo H. Brinker* and *Ilona Fleischhauer*[*]

Carbene-carbene rearrangements[1] in which the migrating divalent carbon retains its identity (Type II) are, with one exception[2], limited to the reorganizations of vinylcyclopropylidenes *(1)* into 3-cyclopentenylidenes *(2)*[3].

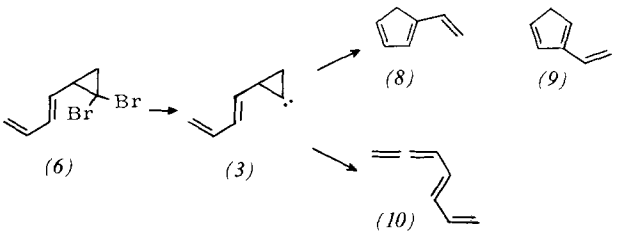


The formation of *(2)* is formally the result of a 1,3-shift of the C1—C3 bond in *(1)* to C5[1,2,4]. *(2)* gives 1,3-cyclopentadiene *via* a subsequent 1,2-hydrogen shift. Replacement of the vinyl group in *(1)* by a 1,3-butadiene unit affords the configurational isomers 2-(1,3-butadienyl)cyclopropylidenes *(3)* and *(4)*[5], which should be suitable as model compounds for the study of carbene-carbene rearrangements involving 1,3- and/or 1,5-carbon shifts. While the 1,3-shift can take place in *(3)* and *(4)*, only the *cis*-isomer *(4)* has the structural prerequisites for the 1,5-shift of the divalent carbon not yet observed.



We report here on the generation of *(3)* and *(4)* and their carbene-carbene rearrangements, which proceed with remarkable regiospecificity.

Addition of dibromocarbene to *trans*- and *cis*-1,3,5-hexatriene affords the two monoadducts[6] *(6)* and *(7)* in 42 and 37% yield, respectively. Reaction of *(6)* with methyllithium (molar ratio 1:1.5; ether, 0°C) gives the isomeric vinylcyclopentadienes[7] *(8)* and *(9)* in 52% yield and the previously



unknown 1,2,4,6-heptatetraene *(10)*[6] (see Table 1) in 48% yield. Consequently, in the *trans*-isomer the competing processes—carbene-carbene rearrangement with 1,3-carbon shift and cyclopropylidene-allene rearrangement[1]—take place, as expected, to a comparable extent.

Table 1. Physical data of compounds *(6)*, *(7)*, and *(10)*. The ^{1}H-NMR spectra were recorded at 60 MHz in CCl_4.

(6), ^{1}H-NMR: $\delta = 6.00$—6.70 (m, 2 olefinic H), 4.85—5.70 (m, 3 olefinic H), 1.40—2.55 (m, 3 cyclopropane H); UV (*n*-hexane): $\lambda_{max} = 229.5$ nm ($\varepsilon = 22400$)
(7), ^{1}H-NMR: $\delta = 6.00$—7.05 (m, 2 olefinic H), 4.95—5.50 (m, 3 olefinic H), 1.35—2.80 (m, 3 cyclopropane H); UV (*n*-hexane): $\lambda_{max} = 231$ nm ($\varepsilon = 18200$)
(10), ^{1}H-NMR: $\delta = 5.50$—6.65 (m, 4 olefinic H), 4.80—5.35 (m, 4 olefinic H); IR (CCl_4): $\nu = 1940\,cm^{-1}$ (C=C=C); UV (*n*-hexane): $\lambda_{max} = 250$ nm, sh ($\varepsilon = 30700$), 257 (39400), 268 (32800)

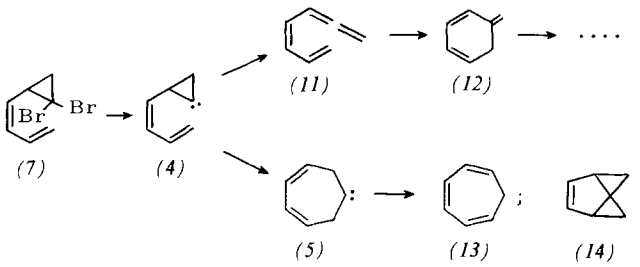
Surprisingly, no 1,3-shift, which should again afford the isomers *(8)* and *(9)*, is observed on reaction of the *cis*-isomer *(7)* under the same conditions. However, 1,3,5-cycloheptatriene *(13)* (17%) is formed as a major product, along with 5-methylene-1,3-cyclohexadiene *(12)* (14%), the arene derivatives toluene (10%), ethylbenzene (14%), and benzaldehyde (17%), as well as the diastereoisomeric *cis*- and *trans*-1-bromo-1-methyl-2-(1,3-butadienyl)cyclopropanes (21%) and 1-bromo-2-(1,3-butadienyl)cyclopropanes (7%). The last-mentioned products could be formed by methylation and protonation, respectively, of the organometallic intermediate formed on metalation.

The independent synthesis of *(12)*[8a] and studies on its reactive behavior under the conditions employed in the reaction of *(7)* confirmed that the aromatic compounds (toluene[8b], ethylbenzene, benzyl hydroperoxide → benzaldehyde[8c,d]) are secondary products of *(12)*. The formation of *(12)* can be initiated by cyclopropylidene-allene rearrange-

[*] Dr. U. H. Brinker, Dipl.-Chem. I. Fleischhauer
Abteilung für Chemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft. Presented in part at the EUCHEM Conference on Electron Deficient Intermediates, Geneva, October 9, 1978. *I. F.* gratefully acknowledges a study grant from the Studienstiftung des Deutschen Volkes. We are indebted to Prof. *W. Kirmse* for valuable discussions.

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0396 S 02.50/0



ment *(4)*→*(11)*. However, while the *trans*-1,2,4,6-heptatetraene *(10)* formed from *(6)* is stable under the reaction conditions, the *cis*-configurated allene *(11)* could be stabilized by electrocyclic ring closure to *(12)*. In the presence of tetracyanoethylene, *(12)* was trapped in the form of its known ene adduct[9].

For the formation of 1,3,5-cycloheptatriene *(13)* several alternative mechanisms have to be considered: insertion of the divalent carbon into the terminal vinylic C—H bond to give norcaradiene, which rapidly rearranges into the valence isomer *(13)*; to our knowledge, however, this insertion-type mechanism has hitherto not been reported for carbenoids. Intramolecular addition of the divalent carbon to the terminal double bond of *(4)* could afford tricyclo[4.1.0.0^{1,3}]hept-4-ene *(14)*, which either decomposes in a cheletropic retro-carbene addition to 3,5-cycloheptadienylidene *(5)* whereupon it forms stable *(13)*, or can undergo fragmentation and hydrogen shift to give cycloheptatriene *via* diradical intermediates; thermochemical estimates, however, show both processes to be endothermic. A plausible explanation for the formation of *(13)* is afforded by the novel carbene-carbene rearrangement with a 1,5-carbon shift in *(4)* to give 3,5-cycloheptadienylidene *(5)* followed by a 1,2-hydrogen shift.

(3) and *(4)* constitute the first pair of configurational isomers of carbenes which behave regiospecifically in carbene-carbene rearrangements.

Received: February 13, 1979 [Z 201 IE]
German version: Angew. Chem. *91*, 424 (1979)

CAS Registry numbers:
(3), 69961-19-9; *(4)*, 69961-20-2; *(5)*, 69961-21-3; *(6)*, 69961-22-4; *(7)*, 69961-23-5; *(8)*, 24460-02-4; *(9)*, 32379-33-2; *(10)*, 69961-24-6; *(11)*, 69961-25-7; *(12)*, 20679-59-8; *(13)*, 544-25-2; *(14)*, 69961-26-8; dibromocarbene, 4371-77-1; *trans*-1,3,5-hexatriene, 821-07-8; *cis*-1,3,5-hexatriene, 2612-46-6; toluene, 108-88-3; ethylbenzene, 100-41-4; *cis*-1-bromo-1-methyl-2-(1,3-butadienyl)cyclopropane, 69961-27-9; *trans*-1-bromo-1-methyl-2-(1,3-butadienyl)cyclopropane, 69961-28-0; *cis*-1-bromo-2-(1,3-butadienyl)cyclopropane, 69961-29-1; *trans*-1-bromo-2-(1,3-butadienyl)cyclopropane, 69961-30-4; benzaldehyde, 100-52-7

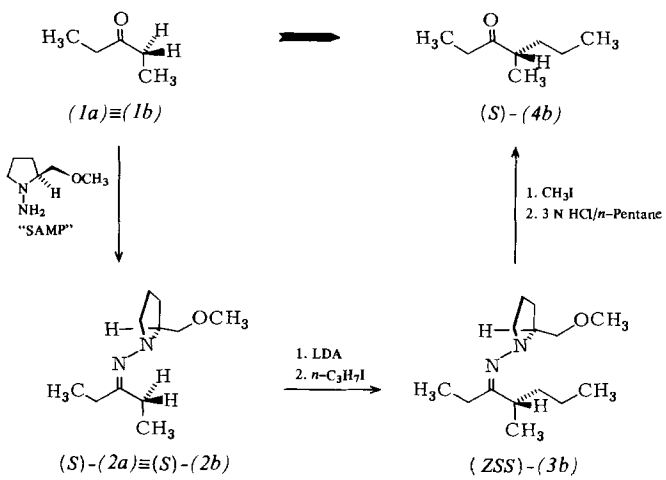
[1] *W. M. Jones, U. H. Brinker* in *A. P. Marchand, R. E. Lehr:* Pericyclic Reactions. Vol. I. Academic Press, New York 1977; *W. M. Jones*, Acc. Chem. Res. *10*, 353 (1977).
[2] *M. S. Baird, C. B. Reese*, J. Chem. Soc. Chem. Commun. *1972*, 523.
[3] *L. Skattebøl*, Tetrahedron *23*, 1107 (1967); *K. H. Holm, L. Skattebøl*, Tetrahedron Lett. *1977*, 2347; J. Am. Chem. Soc. *99*, 5480 (1977).
[4] *W. W. Schoeller, U. H. Brinker*, J. Am. Chem. Soc. *100*, 6012 (1978).
[5] *(3)* and *(4)* are carbenoids: for the behavior of carbenoids and carbenes in carbene-carbene rearrangements of type II, see *P. Warner, S.-C. Chang*, Tetrahedron Lett. *1978*, 3981.
[6] The new compounds (Table 1) gave correct elemental analyses.
[7] *J. M. E. Krekels, J. W. de Haan, H. Kloosterziel*, Tetrahedron Lett. *1970*, 2751; *R. Schröder, A. Striegler, G. Zimmermann, M. Mühlstädt*, Z. Chem. *11*, 149 (1971); Diene synthesis of *(8)* with *N*-phenylmaleimide affords a 1:1 adduct, whereas *(9)* after initial Diels-Alder reaction reacts further with the dienophile to give a 1:2 adduct.
[8] a) *W. A. Pryor, W. D. Graham, J. G. Green*, J. Org. Chem. *43*, 526 (1978); b) *W. J. Bailey, R. A. Baylouny, ibid. 27*, 3476 (1962); c) *C. Walling, S. A. Buckler*, J. Am. Chem. Soc. *77*, 6032 (1955); d) *W. A. Pryor, W. D. Graham*, J. Org. Chem. *43*, 770 (1978).
[9] *K. R. Kopecky, M.-P. Lau*, J. Org. Chem. *43*, 525 (1978); *D. Hasselmann, K. Loosen*, Angew. Chem. *90*, 641 (1978); Angew. Chem. Int. Ed. Engl. *17*, 606 (1978).

Asymmetric Synthesis of Ant Alarm Pheromones—α-Alkylation of Acyclic Ketones with almost Complete Asymmetric Induction[**]

By *Dieter Enders* and *Herbert Eichenauer*[*]

(+)-(*S*)-4-Methyl-3-heptanone (*S*)-*(4b)* has been identified as an alarm pheromone in four ant genera in the subfamily *Myrmicinae*[1a]. It is the principal alarm pheromone of the leaf-cutting ant *Atta texana*, being 400 times more active than its optical antipode[1c]. Thus it was shown for the first time that insects can distinguish between enantiomers[1b]. The synthesis of enantiomerically pure *(4b)* formerly required numerous steps and/or a time-consuming and uneconomical resolution[1c, 2]. A profitable route for the synthesis of acyclic ketones of high enantiomeric purity would be the asymmetric α-alkylation *(1)*→*(4)*. In contrast to the reactions with cyclic ketones and aldehydes, initial reactions of this type *via* metalated hydrazones of (*S*)-1-amino-2-methoxymethylpyrrolidine (SAMP)[3] gave only unsatisfactory optical yields[3a, 4].

Using a somewhat modified approach, we have now succeeded in alkylating acyclic ketones enantioselectively and with practically complete asymmetric induction. To this end, diethyl ketone *(1b)*, for example, is converted into the corresponding hydrazone (*S*)-*(2b)*, which is metalated with lithium diisopropylamide (LDA) in ether at 0 °C followed by treatment of the suspension of the lithium compound with *n*-propyl iodide at −110 °C. The resulting hydrazone (*ZSS*)-*(3b)* is subjected to acid cleavage *via* its *N*-methyl iodide in a two-phase system (3 N HCl/*n*-pentane). The optical purity of the product (*S*)-*(4b)* prepared by this three-step procedure (overall yield 60 %) consistently exceeded 99 % in several preparations.



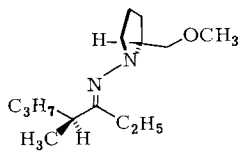
In order to confirm this exceptionally high degree of asymmetric induction, we have examined not only the rotation of the final product but also the diastereomeric purity of the hydrazone *(3b)*. For this purpose a 1:1 diastereomeric mixture of (*SS*)-*(3b)* and (*SR*)-*(3b)* (*E*:*Z*=70:30) (Fig. 1a)

[*] Dr. D. Enders, Dipl.-Chem. H. Eichenauer
Institut für Organische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Lahn-Giessen 1 (Germany)

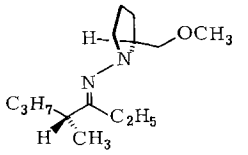
[**] This work was supported by the Deutsche Forschungsgemeinschaft.

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0397 $ 02.50/0

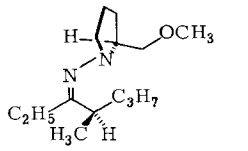
was prepared from racemic 4-methyl-3-heptanone *(4b)*[5] and SAMP, and the OCH_3 singlet region of the ^{1}H-NMR spectrum compared, after addition of the shift reagent Eu(fod)$_3$, with that of the hydrazone *(3b)* prepared from *(2b)* (Fig. 1b). Of the four possible diastereomers, alkylation *(2b)*→*(3b)* gives almost exclusively (*ZSS*)-*(3b)* which undergoes partial isomerization to the thermodynamically more stable (*ESS*)-*(3b)* in solution. No (*SR*)-*(3b)* could be found within the limit of detection (≥2%).



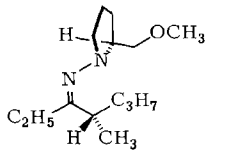
(*ESS*)-*(3b)*



(*ESR*)-*(3b)*



(*ZSR*)-*(3b)*



(*ZSS*)-*(3b)*

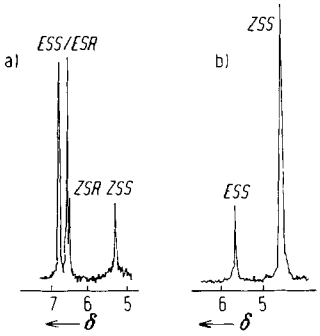


Fig. 1. 100-MHz ^{1}H-NMR spectra [$CDCl_3$, Eu(fod)$_3$] of the region of the OCH_3 singlets. a) 1:1 (*SS*)-*(3b)*/(*SR*)-*(3b)* diastereomeric mixture, E:Z≈70:30 [from racemic *(4b)*]. b) (*SS*)-*(3b)* from (*S*)-*(2b)*, E:Z≈20:80 (*ca.* 5:95 at the start of measurement). The high *Z* content reflects the Z_{CN} configuration of the lithium compound obtained from (*S*)-*(2b)* [6].

In a similar way, we have prepared several other acyclic ketones *(4)*, including another ant alarm pheromone [*(4a)*, *Manica*][7] in high enantiomeric purity (Table 1).

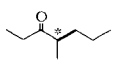
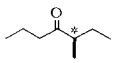
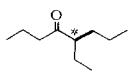
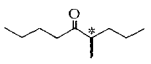
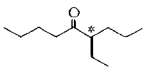
The extent of asymmetric induction varies considerably according to the solvent used. Thus the enantiomeric excess of *(4b)* was 99.5% in ether, 93% in dimethoxyethane, 85% in tetrahydrofuran, and 20% in tetrahydrofuran/hexamethylphosphoramide. The glass surface of the equipment was deactivated with chlorotrimethylsilane to avoid possible racemization during distillation of the ketones.

The asymmetric electrophilic substitutions *via* metalated SAMP-hydrazones described above demonstrate the extremely high stereoselectivity of the deprotonation of *(2)*[6] and of the alkylation to give *(3)*, as well as the absence of racemization on cleavage in the two-phase system hydrochloric acid/*n*-pentane. The absolute configuration of the ketones *(4)* is predictable with a considerable degree of certainty owing to the unique reaction mechanism[9].

Procedure

Synthesis of (*S*)-*(4b)*: Diethyl ketone *(1b)* (2.23 ml, 21 mmol) is added to SAMP (2.6 g, 20 mmol) with stirring at 20°C and the mixture is warmed to 60°C for 20 h. A solution of the crude product in CH_2Cl_2 is dried with Na_2SO_4, concentrated in a rotary evaporator, and distilled. (*S*)-*(2b)* (3.45 g, 87%) is obtained as a colorless oil of b.p. 47°C/0.05 torr, $[\alpha]_D^{20} = +297°$ (*c*=1, benzene). To a stirred solution of LDA [8.5 mmol, prepared from 1.57 N *n*-butyllithium solution (5.4 ml) and diisopropylamine (1.2 ml) in ether (40 ml) at 0°C] is added dropwise at 0°C (*S*)-*(2b)* (1.59 g, 8 mmol). After 10 h, the mixture is cooled to −110°C and *n*-propyl iodide (0.86 ml, 8.8 mmol) is added dropwise. Stirring is continued

Table 1. Chiral acyclic ketones *(4)* synthesized by enantioselective α-alkylation. The newly formed CC bonds are shown in bold print.

(4)	Alkylating agent	$[\alpha]_D^T$ (*c*, solvent) [a]	ee [%] (configuration) [b]	Chem. yield [%] [c]
(a) 	C_2H_5I	+ 30.2^{23} (3.7, Et_2O) + 32.18^{20} (2.5, Et_2O) [8] [d]	94 (*S*)	61
(b) 	*n*-C_3H_7I	+ 22.0^{22} (1.83, *n*-hexane) + 22.1^{25} (1.0, *n*-hexane) [1b]	99.5 (*S*)	60
(c) 	CH_3I	− 20.9^{22} (1.64, Et_2O) + 17.5^{20} (1.8, Et_2O) [8]	≥98 [e] (*R*)	55
(d) 	*n*-C_3H_7I	+ 1.11^{22} (1.98, Et_2O)	(*S*) [f]	50
(e) 	CH_3I	− 17.7^{22} (2.62, Et_2O) − 12.8^{25} (2.6, Et_2O) [4]	≥98 [e] (*R*)	54
(f) 	C_2H_5I	− 1.14^{22} (1.42, Et_2O)	(*R*) [f]	55

[a] Upper line: rotations of the distilled, spectroscopically (IR, NMR) and gas-chromatographically (10 m, OV 101, capillary column) pure ketones *(4)*. Lower line: highest values of rotations given in the literature (in degrees). [b] ee stands for enantiomeric excess. [c] Overall chemical yields by analogy with *(1)*→*(4)*. The yields can be improved by *ca.* 10—20% if 6 N HCl is used for the hydrolysis step *(3)*→*(4)*. [d] Rotation of neat substance $[\alpha]_D^{20} = +32.2$: *F. Nerdel, E. Henkel*, Chem. Ber. *86*, 1002 (1953). [e] Diastereomeric excess of the hydrazone *(3)* as determined by NMR spectroscopy. [f] Postulated configuration.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0398 $ 02.50/0*

for 1 h, the temperature is allowed to rise to 20 °C, and the product is worked up with CH_2Cl_2, dried over Na_2SO_4, and concentrated in a rotary evaporator. The crude product is treated with methyl iodide (1.9 ml, 30 mmol) and refluxed (60 °C) for 16 h. Excess methyl iodide is removed in a rotary evaporator and the residual oil stirred vigorously with 3 N HCl (40 ml)/*n*-pentane (200 ml) for 30 min. The organic phase is separated off, dried over Na_2SO_4, and carefully evaporated down. Molecular distillation over quartz wool [130—140 °C (oil-bath temperature)/110 torr] affords 0.71 g (69 %) of practically enantiomerically pure (*S*)-*(4b)*.

Received: January 29, 1979 [Z 194 IE]
German version: Angew. Chem. *91*, 425 (1979)

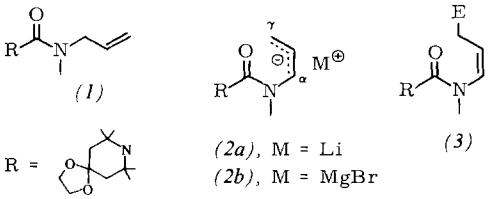
CAS Registry numbers:
(1b), 96-22-0; (*S*)-*(2b)*, 59983-36-7; (*ZSS*)-*(3b)*, 69943-24-4; (*ESS*)-*(3b)*, 69943-25-5; (*ZSR*)-*(3b)*, 69943-26-6; (*ESR*)-*(3b)*, 69943-27-7; (*S*)-*(4a)*, 20086-34-4; (*S*)-*(4b)*, 51532-30-0; (±)-*(4b)*, 70004-03-4; (*R*)-*(4c)*, 67462-47-9; (*S*)-*(4d)*, 69943-28-8; (*R*)-*(4e)*, 67410-09-7; (*R*)-*(4f)*, 69961-10-0; SAMP, 59983-39-0; C_2H_5I, 75-03-6; *n*-C_3H_7I, 107-08-4; CH_3I, 74-88-4

[1] a) *R. G. Riley, R. M. Silverstein, J. C. Moser*, J. Insect. Physiol. *20*, 1629 (1974); b) Science *183*, 760 (1974); c) *R. G. Riley, R. M. Silverstein*, Tetrahedron *30*, 1174 (1974).
[2] *K. Mori*, Tetrahedron *33*, 289 (1977).
[3] a) *D. Enders, H. Eichenauer*, Angew. Chem. *88*, 579 (1976); Angew. Chem. Int. Ed. Engl. *15*, 549 (1976); b) Tetrahedron Lett. *1977*, 191; c) Chem. Ber. *112* (1979), in press; d) *H. Eichenauer, E. Friedrich, W. Lutz, D. Enders*, Angew. Chem. *90*, 219 (1978); Angew. Chem. Int. Ed. Engl. *17*, 206 (1978).
[4] Concerning asymmetric alkylation of acyclic ketones, see also *A. I. Meyers, D. R. Williams*, J. Org. Chem. *43*, 3245 (1978); cf. also *M. Larcheveque, E. Ignatova, T. Cuvigny*, Tetrahedron Lett. *1978*, 3961.
[5] Synthesized by propylation of diethyl ketone *(1b)* using the hydrazone method: *E. J. Corey, D. Enders*, Chem. Ber. *111*, 1337, 1362 (1978).
[6] *H. Ahlbrecht, E. O. Düber, D. Enders, H. Eichenauer, P. Weuster*, Tetrahedron Lett. *1978*, 3691; *K. G. Davenport, H. Eichenauer, D. Enders, M. Newcomb, D. E. Bergbreiter*, J. Am. Chem. Soc. *101* (1979), in press.
[7] *H. M. Fales, M. S. Blum, R. M. Crewe, J. M. Brand*, J. Insect. Physiol. *18*, 1077 (1972).
[8] *D. Seebach, V. Ehrig, M. Teschner*, Justus Liebigs Ann. Chem. *1976*, 1357.
[9] Correct elemental analyses were obtained for all new compounds; the spectroscopic data (IR, NMR, MS) are in agreement with the structures given.

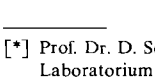
A Metalated Allylurea with Sterically Protected Carbonyl Group as Novel d^3-Reagent

By *Tillmann Hassel* and *Dieter Seebach*[*]

On reaction with *n*-butyllithium in tetrahydrofuran (THF) the urea *(1)* (b.p. 107 °C/0.001 torr)—which is readily accessible from 2,2,6,6-tetramethyl-4-piperidone ethylene acetal (TMPA), phosgene, and allylmethylamine[1]—undergoes metalation[2] to give *(2a)*. Like most heterosubstituted allyllithium derivatives[3], *(2a)* reacts with electrophiles at the positions α *and* γ to the hetero atom to give a mixture of



(1)

R = 

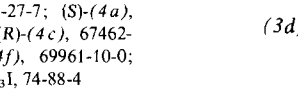
(2a), M = Li
(2b), M = MgBr

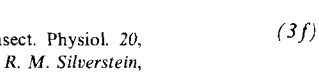
(3)

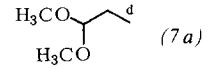
[*] Prof. Dr. D. Seebach
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Dipl.-Chem. T. Hassel
Institut für Organische Chemie der Universität Giessen
Heinrich-Buff-Ring 58, D-6300 Lahn-Giessen (Germany)

products. Normally, replacement of lithium by a less electropositive metal (Mg, Zn, Cd)[3,4] leads to increased α-reactivity. In contrast, the magnesium compound *(2b)* obtained from *(2a)* and $MgBr_2$·ether reacts with all hitherto employed electrophiles almost exclusively at the γ-position to give the *cis*-enamides *(3)* (cf. Table 1). Like other TMPA derivatives[1], these products solvolyze on acid-catalysis at room temperature: thus *(3b)*, *(3d)*, and *(3f)* in anhydrous methanol in the presence of a few drops of sulfuric acid form the acetals *(4)*[5], *(5)*[6], and *(6)* (b.p. 150 °C/17 torr), respectively [total yields from *(1)* with iodooctane, benzaldehyde, and cyclohexanone are 62, 60, and 75 %, resp.]. Hence, *(2b)* is demonstrated as being a d^3-reagent[7] [see the synthons *(7a)*—*(7c)*].

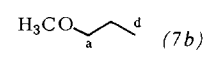
(3b) → $(H_3CO)_2CH{-}C_{10}H_{21}$ *(4)*

(3d) →  *(5)*

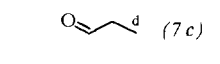
(3f) →  *(6)*



(7a)



(7b)



(7c)

Table 1. Products *(3a)*—*(3f)* from the magnesium compound *(2b)* and the electrophiles: iodomethane, iodooctane, propionaldehyde, benzaldehyde, 2-butanone, cyclohexanone, and benzophenone (yields of analytically pure chromatographed samples). All spectroscopic data are consistent with the given structures; the ^{1}H-NMR spectra show a *cis*-coupling of the vinyl-H atoms.

	Products	Yield	M.p. [°C]
(3)	E	[%]	
(3a)	CH_3	80	38
(3b)	*n*-C_8H_{17}	— [a]	oil
(3c)	$C_2H_5CH(OH)$	83	glass
(3d)	$C_6H_5CH(OH)$	85	63
(3e)	$C_2H_5C(OH)CH_3$	54	60
(3f)	$(CH_2)_5C(OH)$	87	82
(3g)	$(C_6H_5)_2C(OH)$	63	131

[a] This product also contains the α-isomer; it was transformed without separation into *(4)*.

Procedure

A stirred solution of *(1)* (1.48 g, 5 mmol) in 25 ml THF is treated with 5.5 mmol *n*-BuLi (1.5 M in hexane) at −80 °C. After 90 min an equivalent amount of $MgBr_2$·ether is added and the mixture warmed until the precipitate is completely dissolved. The solution is then cooled to the temperature of dry-ice. After addition of 5.5 mmol of the electrophile the mixture is allowed to warm overnight to room temperature and then worked up with ether/water. Analytically pure samples (see Table 1) are obtained by chromatography on silica gel (cyclohexane/ethyl acetate or pentane/ether). The crude *(3)* can be methanolyzed directly: a solution of *(3)* in 15—20 ml anhydrous methanol is treated with 10 drops of conc. H_2SO_4 and stirred for 8 h at room temperature. The mixture is then treated with solid anhydrous K_2CO_3 and stirring continued for a further 12—15 h. Extraction with pentane/water and subsequent chromatography (SiO_2, pentane/ether 4 : 1) furnishes the pure acetals, *e.g. (4)*—*(6)* [0.46 g (82 %) *(6)* from 1.29 g of pure *(3f)*].

Received: February 2, 1979 [Z 203 IE]
German version: Angew. Chem. *91*, 427 (1979)

CAS Registry numbers:
(1), 69961-43-9; *(2a)*, 69961-44-0; *(3a)*, 69961-45-1; γ-*(3b)*, 69961-46-2; α-*(3b)*, 69961-47-3; *(3c)*, 69961-48-4; *(3d)*, 69961-49-5; *(3e)*, 69961-50-8;

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0399 $ 02.50/0*

(3f), 69961-51-9; *(3g)*, 69961-52-0; *(4)*, 52517-67-6; *(5)*, 63298-04-4; *(6)*, 69961-53-1; iodomethane, 74-88-4; iodooctane, 629-27-6; propionaldehyde, 123-38-6; benzaldehyde, 100-52-7; 2-butanone, 78-93-3; cyclohexanone, 108-94-1; benzophenone, 119-61-9

[1] *T. Hassel, D. Seebach*, Helv. Chim. Acta *61*, 2237 (1978).

[2] The metalation can also be carried out at −80°C with lithium diisopropylamide (LDA), but on warming to 0°C reprotonation takes place, not to *(3)*, E = H, but to the *trans*-isomer [J_{trans} = 15 Hz]; cf. *A. N. Tischler, M. H. Tischler*, Tetrahedron Lett. *1978*, 3407.

[3] Reviews: *G. Courtois, L. Miginiac*, J. Organomet. Chem. *69*, 1 (1974); *D. Seebach, K.-H. Geiss*, J. Organomet. Chem. Library *1*, 1 (1976); *H. Ahlbrecht*, Chimia *1977*, 391.

[4] *D. Seebach, K.-H. Geiss, M. Pohmakotr*, Angew. Chem. *88*, 449 (1976); Angew. Chem. Int. Ed. Engl. *15*, 437 (1976); *S. F. Martin, M. T. Du Priest*, Tetrahedron Lett. *1977*, 3925; *P. W. K. Lau, T. H. Chan, ibid. 1978*, 2383.

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

[6] *K.-H. Geiss, D. Seebach, B. Seuring*, Chem. Ber. *110*, 1833 (1977).

[7] *D. Seebach*, Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).

Ligand Concentration-Control in the System Nickel(0)/Triphenylphosphane/Butadiene[**]

By *Frank Brille, Paul Heimbach, Joachim Kluth*, and *Hartmut Schenkluhn*[*]

In the cyclooligomerization of butadiene on nickel catalysts the degree of oligomerization and distribution of isomers can be controlled by addition of suitable phosphanes and phosphites[1]. The isolation of some intermediary complexes in the cyclotrimerization[2] and in the cyclodimerization[3] opens up the possibility of elucidating the elementary steps of the catalytic process. We have now attempted with the aid of ligand-concentration control maps to explain how the nature and number of the elementary steps are influenced *in situ* by addition of the controlling ligands.

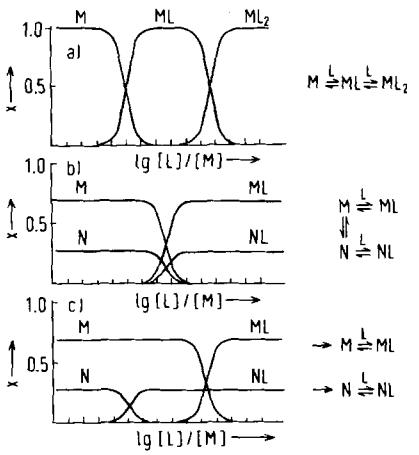


Fig. 1. Typical titration curves for (a) the stepwise twofold association of the ligand L to the metal complex M, (b) the association of L and two metal complexes M and N in equilibrium, and (c) the association of L to two metal complexes M and N not in equilibrium (kinetically separated).

[*] Prof. Dr. P. Heimbach [+], Ing. (grad.) F. Brille, Dipl.-Chem. J. Kluth, Dr. H. Schenkluhn [+]
Universität Essen – Gesamthochschule, Fachbereich 8 – Chemie, Organische Chemie I
Postfach 6843, D-4300 Essen 1 (Germany)
and Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim/Ruhr (Germany)

[**] Control of Metal-Catalyzed Reactions, Part 6. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft.—Part 5: *H. Bandmann, P. Heimbach, A. Roloff*, J. Chem. Soc. (S) *1977*, 261; (M) *1977*, 3055.

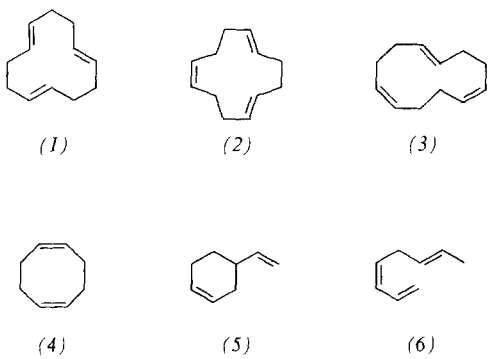
[+] Authors to whom correspondence should be addressed.

We have carried out the nickel-catalyzed cyclooligomerization of butadiene with different concentrations of the directing ligand and determined the changing product pattern gas-chromatographically. For the graphical representation the logarithm of the ligand/metal ratios ($lg[L]_0/[M]_0$) is plotted on the abscissa and the product distribution in mol-% on the ordinate.

Assuming that the product ratios are proportional to the concentration of the intermediary complexes and that switching-on and switching-off phenomena may be neglected, the product curves, in analogy to classical titration curves, afford information on the number of the intermediate products, their relation to one another, and their concentration in the steady state.

Figure 1 shows three frequently occurring association schemes and the corresponding titration curves.

Figure 2 is the ligand-concentration control map for the system nickel/triphenylphosphane/butadiene[4]. The six products *(1)*—*(6)*[5] are formed in varying amounts, depending on the $lg[L]_0/[Ni]_0$ ratio. At low $lg[L]_0/[Ni]_0$ ratios the cyclotrimers *(1)*—*(3)* predominate, at higher ratios the cyclodimers *(4)*—*(6)* [*(6)* is not shown in Fig. 2 since its amount



is too small; besides 1,*cis*-3,-*trans*-6-octatriene, 1,*trans*-3,*trans*-6-octatriene is also formed.

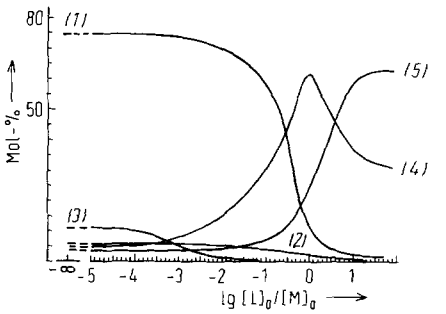


Fig. 2. Ligand-concentration control map for the catalytic system nickel/triphenylphosphane/butadiene; product distribution in mol-% referred to totally converted butadiene. T = 60°C, $[Ni]_0$ = 40 mmol/l, t = 15 h, $[Ni]_0$:[butadiene]$_0$ = 1:70, toluene as solvent.

The catalytic reactions were carried out on the 10-ml scale, and $lg[L]_0/[Ni]_0$ was determined gas-chromatographically *via* the ratio of two internal standards (tetralin/*n*-dodecane) (for experimental details, see [6]).

To obtain information on the control of the degree of oligomerization the distribution of the cyclotrimers and cyclodimers was plotted against $lg[L]_0/[Ni]_0$ on a partial control map (Fig. 3a). An almost typical titration curve is obtained[4]; the curve largely corresponds to a single ligand-association process (cf. Fig. 1a; for the partial control map of the trimers see [6]).

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979*

0570-0833/79/0505-0400 $ 02.50/0

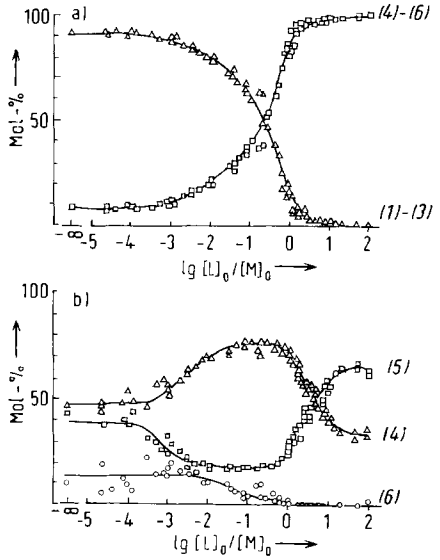


Fig. 3. Partial control maps (a) for the distribution of oligomers: product distribution in mol-% referred to converted butadiene; (b) the distribution of dimers: sum of dimers equals 100%.

Figure 3b shows the ratio of the dimers *(4)*—*(6)* as a function of $\lg[L]_0/[Ni]_0$. Several association processes are recognizable. The controlling first association of the ligand occurs at different ligand/metal ratios depending upon the product. Consequently, the respective intermediary complexes should be kinetically separated according to Figure 1c. It is interesting, moreover, that in the case of *(4)* and *(5)* there are two different association processes[7] (cf. Fig. 1a). Thus, for interpretation of this finding it is necessary to postulate multiple associations of the controlling ligand and several partially kinetically separated intermediary complexes for which the range of existence can be given[8].

In the case of homogeneous metal-catalyzed reactions the concentration-control maps can be used not only for the analysis of the mechanisms (minimum number of intermediary complexes and their coupling) but also for the following: 1) optimization of the catalyzed processes, 2) comparison of catalysts, 3) determination of the limiting conditions for separation of the thermodynamic and kinetic selectivity as prerequisite for recognition of property-specific control and thus *e.g.* separation of the steric and electronic influence of ligands[9].

Received: January 8, 1979 [Z 204a IE]
German version: Angew. Chem. *91*, 428 (1979)

CAS Registry numbers:
(1), 676-22-2; *(2)*, 706-31-0; *(3)*, 2765-29-9; *(4)*, 1552-12-1; *(5)*, 100-40-3; *(6)*, 22038-68-2; butadiene, 106-99-0; Ni, 7440-02-0

[1] a) *P. Heimbach*, Angew. Chem. *85*, 1035 (1973); Angew. Chem. Int. Ed. Engl. *12*, 975 (1973); b) *P. W. Jolly, G. Wilke:* The Organic Chemistry of Nickel. Vol. 2. Academic Press, New York 1975.

[2] *P. W. Jolly, G. Wilke:* The Organic Chemistry of Nickel. Vol. 1. Academic Press, New York 1974.

[3] *B. Barnett, B. Büssemeyer, P. Heimbach, P. W. Jolly, C. Krüger, I. Tkatchenko, G. Wilke*, Tetrahedron Lett. *1972*, 1457.

[4] It should be noted that Figure 1 considers the actual equilibrium concentration. In the ligand-concentration control maps (Fig. 2 and 3) the chosen reference to the external amounts of L and M (as well as for ligand-dependent inhibition- and activation phenomena) yields characteristic changes in the shape and position of the curves.

[5] The cyclodimer divinylcyclobutane [1a] which is also formed rearranges into *(4)* and *(5)* during the catalysis and no longer can be detected after the long reaction time chosen by us (complete conversion of butadiene).

[6] *F. Brille, J. Kluth, H. Schenkluhn*, J. Mol. Catal. *5*, 27 (1979).

[7] For ligands such as triphenyl phosphite and phenyldiphenoxyphosphane even a stepwise threefold association can be detected[8]. Interestingly, every subsequent ligand association leads to a reversal of the product ratio of *(4)* and *(5)*.

[8] *J. Kluth*, Dissertation, Universität Essen (GHS), planned for 1979.

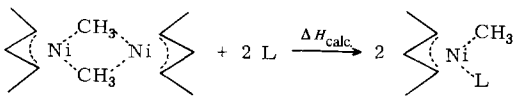
[9] *H. Schenkluhn, W. Scheidt, B. Weimann, M. Zähres*, Angew. Chem. *91*, 429 (1979); Angew. Chem. Int. Ed. Engl. *18*, 401 (1979).

Separation of Steric and Electronic Effects in the Reaction Enthalpies of Association of Phosphorus Ligands[**]

By *Hartmut Schenkluhn, Walter Scheidt, Bruno Weimann*, and *Manfred Zähres*[*]

In homogeneous transition-metal catalysis the addition of Lewis bases (*e.g.* phosphanes and phosphites) plays an important role, since the catalytic reactions can then be varied within wide limits. Hence, data for characterization of the metal-ligand bonding are of special interest for gaining an insight into the directing influence of such ligands.

Only very few quantitative results have so far been reported in this connection. An attempt has been made to describe the bonding character in rhodium(I) complexes by resolution into predominant covalent and electrostatic components[1].



(1) *(2)*

Table 1. Reaction enthalpies of association of phosphorus ligands to *(1)* (corrected for the heats of mixing of the ligands); experimental conditions: $T = 273$ K; *(1)*: 0.05 M in tetralin, L: addition of 1 M tetralin solution.

No.	Ligand L	χ_j [cm^{-1}]	Θ_j [°]	$\Delta H_{exp.}$ [a] [kJ/mol]	$\Delta H_{calc.}$ [kJ/mol]
1	$P(t\text{-}C_4H_9)(c\text{-}C_6H_{11})_2$	0.2	171	71	77
2	$P(C_6H_5)_3$ [b]	12.6	145	75	(112)
3	$P(t\text{-}C_4H_9)(i\text{-}C_3H_7)_2$	2.0	167	86	82
4	$P(i\text{-}C_3H_7)_3$	3.1	160	91	88
5	$P(C_6H_5)_2(C_2H_5)$ [b]	10.6	141	99	(111)
6	$P(n\text{-}C_3H_7)_3$	4.8	132	103	106
7	$P(n\text{-}C_4H_9)_3$	4.2	132	108	105
8	$P(C_6H_5)(C_2H_5)_2$	7.9	136	110	109
9	$P(C_6H_5CH_2)_3$ [b]	10.3	165	113	(97)
10	$P(C_6H_5)(CH_3)_2$	9.2	127	113	116
11	$P(C_2H_5)_3$	5.6	132	113	108
12	$P(C_6H_5(O{-}C_{10}H_{19})_2$ [c]	16.8	142	117	121
13	$P(CH_3)_3$	8.0	118	120	120
14	$P(O{-}C_{10}H_{19})_3$ [c]	18.9	140	121	125
15	$P(O\text{-}i\text{-}C_3H_7)_3$	18.9	130	131	131
16	$P(O\text{-}o\text{-}C_6H_4CH_3)_3$	28.0	141	134	140
17	$P(O\text{-}o\text{-}C_6H_4C_6H_5)_3$	28.9	152	140	135
18	$P(O{-}C_2H_5)_3$	20.2	110	142	144
19	$P(O{-}n\text{-}C_4H_9)_3$	19.5	112	143	142
20	$P(C_6H_5)(O{-}C_6H_5)_2$	23.7	134	144	136
21	$P(C_6H_5)_2(O{-}C_2H_5)$ [b]	15.5	133	147	(123)
22	$P(O{-}C_6H_5)_3$	29.2	128	148	149

[a] ±4 kJ/mol. [b] These ligands were not taken into account in the determination of the functional relationship. [c] $(OC_{10}H_{19})$ = O-menthyl.

[*] Dr. H. Schenkluhn [+], Ing. (grad.) M. Zähres
Universität Essen—Gesamthochschule, Fachbereich 8—Chemie
Postfach 6843, D-4300 Essen (Germany)
and Max-Planck-Institut für Kohlenforschung
D-4330 Mülheim/Ruhr (Germany)
Ing. (grad.) W. Scheidt, Dr. B. Weimann
Max-Planck-Institut für Kohlenforschung
D-4330 Mülheim/Ruhr (Germany)

[**] Organometallic Complex Compounds, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft. We thank Dr. *E. Koch*, Institut für Strahlenchemie im MPI für Kohlenforschung, for help with the construction of the DTA apparatus.—Part 3: *P. Heimbach, M. Molin*, J. Organomet. Chem. *49*, 483 (1973).—Part 2: *P. Heimbach, M. Molin, ibid. 49*, 477 (1973).—Part 3: *P. Heimbach*, Angew. Chem. *76*, 586 (1964); Angew. Chem. Int. Ed. Engl. *3*, 648 (1964).

[+] Author to whom correspondence should be addressed.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0401 $ 02.50/0*

A parametrization of the "electronic" and "steric" ligand influences has been described by *Tolman*[2]. Using this method the first examples for the dominance of steric ligand influences could be found in calorimetric investigations on platinum(II)[3a] and nickel(0) complexes[3b]. We have now established that these ligand parameters are suitable not only for the qualitative estimation but also for the quantitative determination of the "steric" and "electronic" ligand influences. This is illustrated here for the reaction enthalpy of the association of Lewis bases to di-μ-methylbis[1-methyl-1—3-η-(2-butenyl)]dinickel *(1)*[4] (Table 1).

A slightly modified calorimeter for differential thermal analyses in solution[5] was used for the determination of the enthalpy of reaction. The values were determined at 0°C in a 0.05 M solution of *(1)* in tetralin and the data thus obtained were corrected for the heat of mixing of the ligands, since ligand addition was carried out from 1 M solution.

A plot of the measured values z_j against the electronic ligand parameter χ_j and against the steric ligand parameter Θ_j gave no definite indication of a functional relationship. We therefore attempted a separation of the electronic and steric components by regression analysis.

There already is a good approximation for the polynomial

$$z(\chi_j, \Theta_j) = 172.0 + 1.65\,\chi_j - 0.56\,\Theta_j$$

since the quotient of the variance of fit ($S^2 = 18$) and the variance of the measured data ($\sigma^2 = 16$) is approximately unity[6]. In Figure 1[7] each ligand L (χ_j, Θ_j) is characterized

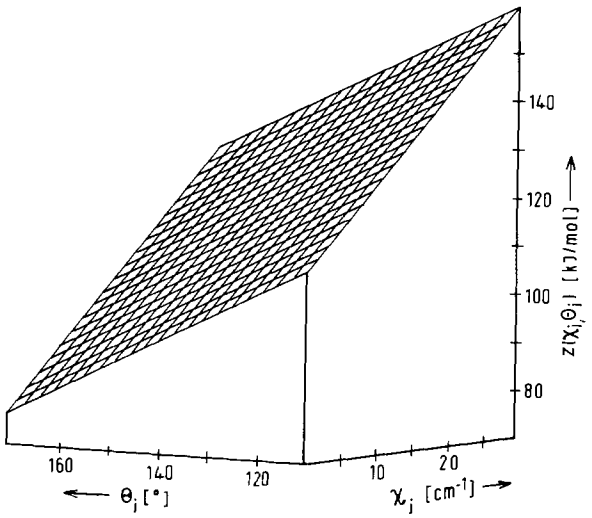


Fig. 1. Threedimensional representation of the reaction enthalpies of association of phosphorus ligands to the nickel complex *(1)* as a function of the electronic χ_j and steric Θ ligand parameters [2a].

by a point in the x,y-plane; the respective measured value z_j is given in the z-direction. An intersection vertical to the abscissa corresponds to the separated steric influence, while an intersection vertical to the ordinate corresponds to the separated electronic influence; surprisingly, in the former case there is a simple linear relationship for both parameters. Collectively, the calculated enthalpies of association span a range of 82 kJ/mol, of which 48 kJ/mol is ascribed to the electronic influence and 34 kJ/mol to the steric influence (electronic to steric ratio of 60 : 40). In the regression analysis the phosphorus ligands PPh_3, PPh_2OEt, PPh_2Et, and $P(benzyl)_3$ show the worst approximation. This would indicate that a description of the bonding character with the aid of the two chosen ligand parameters does not suffice in the case of overwhelmingly covalent bonding[8]. A still undefined "mesomeric effect" may have to be taken into consideration, corresponding to the parameterization of the substituent effects in organic chemistry.

Received: July 12, 1978 [Z 204b IE]
revised: February 23, 1979
German version: Angew. Chem. *91*, 429 (1979)

CAS Registry numbers:
(1), 68472-10-6; *(2)*, L = P(*t*-C_4H_9)(*c*-C_6H_{11})$_2$, 69991-16-8; *(2)*, L = P(C_6H_5)$_3$, 69991-17-9; *(2)*, L = P(*t*-C_4H_9)(*i*-C_3H_7)$_2$, 69991-18-0; *(2)*, L = P(*i*-C_3H_7)$_3$, 69991-19-1; *(2)*, L = P(C_6H_5)$_2$(C_2H_5), 69991-20-4; *(2)*, L = P(*n*-C_3H_7)$_3$, 69991-21-5; *(2)*, L = P(*n*-C_4H_9)$_3$, 69991-22-6; *(2)*, L = P(C_6H_5)(C_2H_5)$_2$, 70006-11-0; *(2)*, L = P($C_6H_5CH_2$)$_3$, 69991-23-7; *(2)*, L = P(C_6H_5)(CH_3)$_2$, 69991-24-8; *(2)*, L = P(C_2H_5)$_3$, 69991-25-9; *(2)*, L = P(C_6H_5)(O—$C_{10}H_{19}$)$_2$, 69991-26-0; *(2)*, L = P(CH_3)$_3$, 69991-27-1; *(2)*, L = P(O—$C_{10}H_{19}$)$_3$, 70006-00-7; *(2)*, L = P(O—*i*-C_3H_7)$_3$, 69991-28-2; *(2)*, L = P(O—*o*-$C_6H_4CH_3$)$_3$, 69991-29-3; *(2)*, L = P(O—*o*-$C_6H_4C_6H_5$)$_3$, 69991-30-6; *(2)*, L = P(O—C_2H_5)$_3$, 69991-31-7; *(2)*, L = P(O—*n*-C_4H_9)$_3$, 69991-32-8; *(2)*, L = P(C_6H_5)(O—C_6H_5)$_2$, 69991-33-9; *(2)*, L = P(C_6H_5)$_2$(O—C_2H_5), 69991-34-0; *(2)*, L = P(O—C_6H_5)$_3$, 69991-35-1

[1] *M. P. Li, R. S. Drago*, J. Am. Chem. Soc. *98*, 5129 (1976).
[2] a) The electronic parameter χ_j of ligand L_j is determined IR spectroscopically *via* the induced shift of the ν_{CO}(A1) band of the $L_jNi(CO)_3$ complex, with respect to the reference ligand tri(*tert*-butyl)phosphane with ν_{CO}(A1) = 2056.1 cm^{-1} [$\chi_j = \nu_{j,CO}$(A1) − 2056.1 cm^{-1}]. The steric parameter is obtained as conic angle Θ_j of the corresponding atomic space filling model; b) Review: *C. A. Tolman*, Chem. Rev. *77*, 313 (1977).
[3] a) *L. E. Manzer, C. A. Tolman*, J. Am. Chem. Soc. *97*, 1955 (1975); b) *C. A. Tolman, D. W. Reutter, W. C. Seidel*, J. Organomet. Chem. *117*, C 30 (1976).
[4] For the synthesis of *(1)* and *(2)* see *H. Schenkluhn*, Dissertation, Universität Bochum 1971.
[5] *E. Koch*, Chem.-Ing.-Tech. *37*, 1004 (1965).
[6] For the regression, the polynomial expression

$$z_{m,n}(\chi_j, \Theta_j) = \sum_{i=0}^{m} a_i \chi_j^i + \sum_{i=1}^{n} b_i \Theta_j^i$$

with the variance of fit

$$S^2_{m,n} = \frac{\sum_{j=1}^{m} (z_{m,n}(\chi_j, \Theta_j) - z_j)^2}{N - m - n - 1}$$

was chosen; m, n were optimized with the quotient $S^2_{m,n}/\sigma^2$ and a Chi^2 test (σ^2 = variance of measured value).
[7] This plot is related to *Tolman*'s "steric and electronic box" [2b].
[8] Similar observations were made in the analysis of a series of catalytic experiments on nickel ligand catalysts (*P. Heimbach, J. Kluth, H. Schenkluhn*, unpublished). The fact that we could, on the other hand, satisfactorily resolve *e. g.* the results on platinum(II) complexes [3a] into the electronic and steric ligand influence with incorporation of P(benzyl)$_3$ and P(phenyl)$_3$ is due to the extremely small electronic influence (20 % with respect to the total ligand property control, 26 ligands, polynomial degree m, n = 3, 3).

Regiospecific Synthesis of Disubstituted Benzene Derivatives[**]

By *Guy Félix, Jacques Dunoguès*, and *Raymond Calas*[*]

We have been able to extend application of the "organosilicon method"[1], which had previously been employed only in individual cases[2] for the regiospecific synthesis of benzene derivatives, to the synthesis of numerous disubstituted benzene derivatives. The method proposed by us is based on the stepwise exchange of the trimethylsilyl groups of the readily accessible[3] *o*-, *m*-, or *p*-bis(trimethylsilyl)benzenes *(1o)*, *(1m)*, and *(1p)*, respectively (see reaction scheme and Table 1).

[*] Prof. Dr. R. Calas, Dr. G. Félix, Dr. J. Dunoguès
Laboratoire de Chimie Organique et Laboratoire de Chimie des Composés Organiques du Silicium et de l'Etain associé au CNRS (n° 35)
Université de Bordeaux I
351, Cours de la Libération, F-33405 Talence Cédex (France)

[**] We wish to thank *Françoise Pisciotti* for her valuable experimental assistance.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* 0570-0833/79/0505-0402 $ 02.50/0

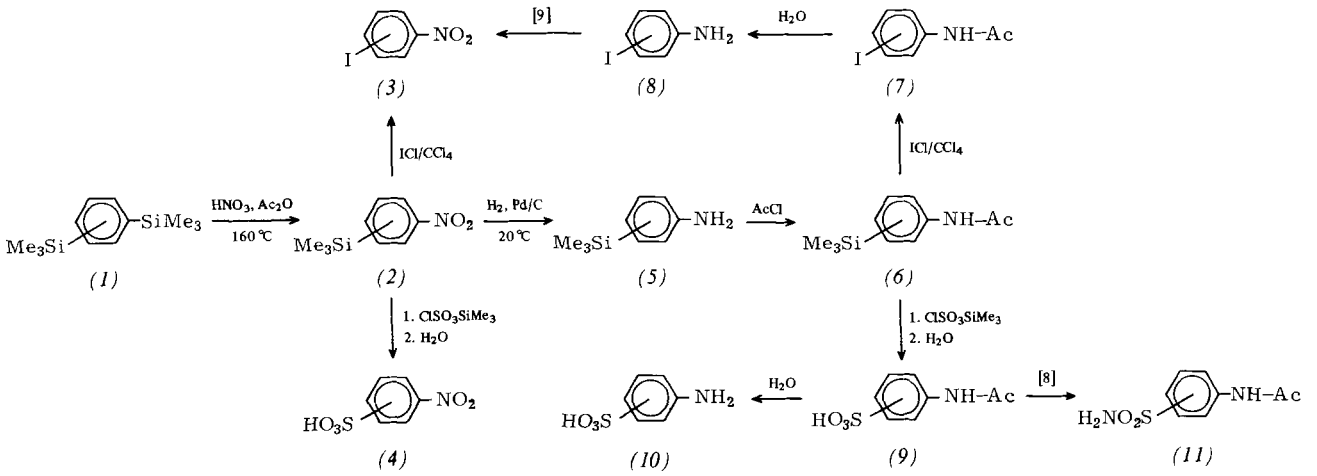


Table 1. Compounds synthesized.

Reaction	Yield [%]	M. p. [°C] [a] B. p. [°C/torr]
(1o) → (2o)	82	135—137/25
(1m) → (2m)	80	150—155/30
(1p) → (2p)	75	37
(8o) → (3o)	0	54
(2m) → (3m)	90	38
(2p) → (3p)	78	174
(2o) → (4o)	76	[b, c]
(2m) → (4m)	90	[b, c]
(2p) → (4p)	83	[b, c]
(2o) → (5o)	83	125—127/25
(2m) → (5m)	90	125/30
(2p) → (5p)	86	130—132/30
(5o) → (6o)	82	130
(5m) → (6m)	89	114—115
(5p) → (6p)	92	169—170
(6o) → (7o)	87	109
(6m) → (7m)	83	119
(6p) → (7p)	92	184
(7o) → (8o)	≈100	60—61
(7m) → (8m)	≈100	33
(7p) → (8p)	≈100	67—68
(6o) → (9o)	91	[c]
(6m) → (9m)	67	[c]
(6p) → (9p)	95	[c]
(9o) → (10o)	≈100	[c]
(9m) → (10m)	≈100	[c]
(9p) → (10p)	≈100	[c]
(9o) → (11o)	70	153
(9m) → (11m)	75	142
(9p) → (11p)	75	165—166

[a] From ethanol. [b] Hygroscopic crystals. [c] Sodium salts were recrystallized from ethanol.

The diverging influence of the first substituents on the orientation of the second substituents is circumvented.

All the nitro(trimethylsilyl)benzene derivatives *(2)*[4] as well as the amino- *(5)*[4a, 5a–e] and the acetylamino-derivatives *(6)*[5] are known. We have used the route proposed by *Deans* and *Eaborn*[4c] for the synthesis of *(2)* from *(1)*. *(2m)* and *(2p)* could be readily reduced to *(5m)* and *(5p)*, respectively[4a,c,d,f]; the reduction of *(2o)* to *(5o)* *via* this route was difficult (see Procedure).

In contrast, attempts by *Hashimoto*[5e] to carry out regiospecific reactions of disilylbenzene derivatives had proved unsuccessful. Thus the bromination and nitration of *(6m)* [prepared from *(1m)*] led respectively to the undesired compounds 3,4-$Br_2C_6H_3NHAc$ and 2-O_2N-5-Me_3Si—C_6H_3NHAc as major product under the conditions given by the author.

We have been able to replace the second trimethylsilyl group in *(2)* and *(6)* by iodine and by the sulfo group.

Although the compounds *(3)*, *(4)*, *(6)* and *(11)* are all well-known, their synthesis was previously very difficult in some cases because of the substituent effects in the second substitution. Thus, the direct sulfonation is not always satisfactory or convenient and iodination often requires the reaction sequence : nitration → reduction → diazotization → reaction with alkali-metal iodide.

Besides the high yields, the regiospecificity of this method makes it very attractive for the synthesis of *o*-disubstituted benzene derivatives [*(3o)* can be obtained by oxidation of *(8o)*][9]. For example, the hitherto difficultly accessible[6] *o*-aminobenzenesulfonic acid *(10o)* and its sulfonamide *(11o)* can now be obtained quite easily. The method has also proven convenient for the preparation of *m*-iodoaniline *(8m)*.

Procedure

The synthesis of *(1)* and the iodinations were carried out according to [2b], the synthesis of *(2)* according to [4c]. For the sulfonation a mixture of equimolar amounts of *(2)* and $ClSO_3SiMe$ in CCl_4 (25 ml per 50 mmol of reactants) was heated under reflux for 2 h; after hydrolysis with NaOH the sodium salt of *(4)* was isolated according to the procedure given in [2a].

Hydrogenations were carried out by stirring a solution of *(2)* (5 g) in benzene (50 ml) under hydrogen pressure (*ca.* 1 atm) in the presence of 100 mg Pd/C (10 % Pd) until hydrogen absorption had ceased. After filtration through SiO_2 and removal of solvent, *(5)* was isolated by distillation (cf. also [5e]).

For the acylation a solution of *(5)* (1.7 g, *ca.* 10 mmol) in pyridine (20 ml) was treated dropwise with 0.8 g (≈10 mmol) acetyl chloride and the mixture heated under reflux for 3 h. After cooling, ether (50 ml) was added and the mixture was washed several times with 100 ml of weakly acidic saturated aqueous NaCl solution and then with pure cold water. The ethereal layer was dried over $MgSO_4$ and, after removal of ether, the acetanilides *(6)* were recrystallized from ethanol.—*(6)* was sulfonated according to the procedure given in [2a].

The acetanilides *(7)* and *(9)* were hydrolyzed under the usual conditions[7] to *(8)* and *(10)*, respectively; for conversion into the sulfonamides *(11)* the sodium salts of *(9)* were treated with (i) PCl_5 and (ii) NH_3 (see [8]).

Received: December 28, 1978 [Z 198 IE]
German version: Angew. Chem. *91*, 430 (1979)

CAS Registry numbers:
(1o), 17151-09-6; *(1m)*, 2060-89-1; *(1p)*, 13183-70-5; *(2o)*, 15290-22-9; *(2m)*, 15290-24-1; *(2p)*, 4405-33-8; *(3o)*, 609-73-4; *(3m)*, 645-00-1; *(3p)*, 636-98-6; *(4o)*, 80-82-0; *(4m)*, 98-47-5; *(4p)*, 138-42-1; *(5o)*, 57792-17-3; *(5m)*, 15290-25-2; *(5p)*, 17889-23-5; *(6o)*, 18001-42-8; *(6m)*, 15290-26-3;

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0403 $ 02.50/0*

(6p), 17983-71-0; *(7o)*, 19591-17-4; *(7m)*, 19230-45-6; *(7p)*, 622-50-4; *(8o)*, 615-43-0; *(8m)*, 626-01-7; *(8p)*, 540-37-4; *(9o)*, 69943-38-0; *(9m)*, 54981-39-4; *(9p)*, 121-62-0; *(10o)*, 88-21-1; *(10m)*, 121-47-1; *(10p)*, 121-57-3; *(11o)*, 69943-39-1; *(11m)*, 23010-42-6; *(11p)*, 121-61-9; $ClSO_3SiMe_3$, 4353-77-9

[1] a) *T. Hashimoto*, Yakugaku Zasshi *87*, 528 (1967); b) *K. Dey, C. Eaborn, D. R. M. Walton*, Organomet. Chem. Synth. *1*, 151 (1971); c) For a review see: *C. Eaborn*, J. Organomet. Chem. *100*, 43 (1975).

[2] a) *P. Bourgeois, R. Calas*, J. Organomet. Chem. *84*, 16 (1975); b) *G. Félix, J. Dunoguès, F. Pisciotti, R. Calas*, Angew. Chem. *89*, 502 (1977); Angew. Chem. Int. Ed. Engl. *16*, 488 (1977).

[3] For the synthesis of *(1o)* see [2]; *(1m)* and *(1p)* can be obtained *via* organomagnesium compounds; see *C. Eaborn, R. W. Bott* in *A. G. McDiarmid:* The Bond to Carbon. Marcel Dekker, New York 1968, Vol. 1.

[4] a) *R. A. Benkeser, P. E. Brumfield*, J. Am. Chem. Soc. *73*, 4770 (1951); b) *J. L. Speier, ibid. 75*, 2930 (1953); c) *F. B. Deans, C. Eaborn*, J. Chem. Soc. *1957*, 498; d) *T. Hashimoto*, Yakugaku Zasshi *87*, 524 (1967); e) *C. Eaborn, D. R. M. Walton, D. J. Young*, J. Chem. Soc. *B1969*, 15; f) *C. Eaborn, P. M. Jackson, ibid. B1969*, 21.

[5] a) *R. A. Benkeser, P. E. Brumfield*, J. Am. Chem. Soc. *74*, 253 (1952); b) *L. Summers*, Iowa State Coll. J. Sci. *1952*, 292; c) *R. A. Benkeser, H. R. Krysiak*, J. Am. Chem. Soc. *75*, 2421 (1953); d) *Y. Sakata, T. Hashimoto*, Yakugaku Zasshi *79*, 875, 881 (1959); e) *T. Hashimoto, ibid. 80*, 730 (1960); f) *R. C. Neville*, J. Org. Chem. *24*, 870 (1959).

[6] See also *P. K. Maarsen, H. Cerfontain*, J. Chem. Soc. Perkin II *1976*, 1006; Org. Synth. Collect. Vol. *2*, 471 (1943).

[7] See, *e.g.*, Org. Synth. Collect. Vol. *3*, 661 (1955).

[8] Org. Synth. Collect. Vol. *1*, p. 84 (1941).

[9] See *R. L. Augustine:* Oxidation. Marcel Dekker, New York 1969, Vol. 1, pp. 251—2, and references cited therein.

Unsymmetrical Binuclear Complexes of Tungsten with Three OR Bridges, η^3-$C_7H_7(CO)_2W(OR)_3W(CO)_2$-$\eta^4$-$C_7H_8$ [**]

By *Wolfgang Schulze, Klaus Weidenhammer*, and *Manfred L. Ziegler*

On allowing η^7-$C_7H_7Mo(CO)_2Br$ to react with sodium alkoxides or phenoxides in the corresponding alcohols or CH_2Cl_2 we obtained species of the type η^7-$C_7H_7Mo(OR)_3$-$Mo(CO)_2$-η^3-C_7H_7 *(1)*[1]. Attempts to carry out this reaction with the analogous tungsten system η^7-$C_7H_7W(CO)_2I$ *(2)* surprisingly led to compounds of the type η^3-$C_7H_7(CO)_2W$-$(OR)_3W(CO)_2$-η^4-C_7H_8 *(3)* [R = CH_3 *(3a)*, C_2H_5 *(3b)*, C_3H_7 *(3c)*, C_6H_5 *(3d)*]. To our knowledge these compounds constitute the first triply OR-bridged binuclear complexes of tungsten; also unusual is the η^4-bonded cycloheptatriene ring, as was previously assumed merely in the case of $C_7H_8Fe(CO)_3$[2]. The compounds *(3)* were characterized by elemental analysis, IR, ^{1}H-NMR, and mass spectra, and in the case of *(3a)* also by X-ray analysis[3] (Fig. 1).

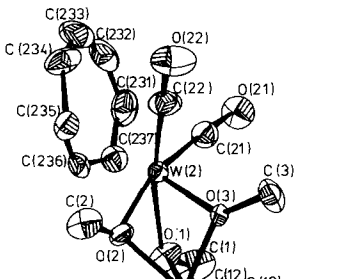


Fig. 1. Crystal structure of η^3-$C_7H_7(CO)_2W(OCH_3)_3W(CO)_2$-$\eta^4$-$C_7H_8$ *(3a)*; the thermal ellipsoids correspond to a probability of 50 %.

The compounds *(1)* and *(3)* are examples which neatly illustrate how the homologues molybdenum and tungsten solve electron problems of the same type in different ways. The odd number (nine) of electrons which are transferred to the two central atoms by the three bridge ligands is not balanced in the molybdenum system; the paramagnetic mixed valence compounds *(1)* are formed. In the tungsten system, on the other hand, a cycloheptatrienyl ligand is reduced to a cycloheptatriene ligand by uptake of a hydride ion. η^4-Bonding leads to formation of the diamagnetic complex *(3)*, in which the 18-electron rule applies for both tungsten atoms. As expected the CO bands of *(3)* are shifted to lower wave numbers as compared to those of *(2)*[4]. In the mass spectrum (Varian MAT CH7, temperature of ion-source 150 °C, ionization energy 70 eV, vaporization temperature 148 °C) the fragments $(M-CO)^+$, $(M-2CO)^+$ and $(M-3CO)^+$ appear with weak intensity only in the case of *(3b)*.

The ^{1}H-NMR spectra[5] reveal that the ring ligands, in contrast to those in *(2)*, are no longer η^7-bonded. Two of the signals for the methoxo protons in *(3a)* are comparable with those of similarly triply methoxo-bridged molybdenum compounds[6]; the position of the third signal ($\delta = 4.85$) indicates that this methoxo-group is situated in a different chemical environment. According to X-ray structure analysis, O(3) bridges the two W atoms in a sp^2 configuration.

In the synthesis of *(3a)* hydride transfer to the cycloheptatrienyl ligand is effected by the solvent methanol; on reaction of *(2)* with $NaOCD_3$ in CD_3OD under argon η^3-$C_7H_7(CO)_2W(OCD_3)_3W(CO)_2$-$\eta^4$-$C_7H_7D$ *(4a)* could be isolated. The positions and intensities of the ν_{CO} bands of *(4a)* are identical with those of *(3a)*[4].

Of the multiplets for the methylene protons of the cycloheptatriene ring of *(3a)*, only one still appears in the ^{1}H-NMR spectrum of *(4a)* at $\delta = 2.31$, corresponding to the >CHD group. The remaining signals of *(4a)* are identical to those of *(3a)*[5]; the signals of the methoxo groups are absent.

Received: January 12, 1979 [Z 207 IE]
German version: Angew. Chem. *91*, 432 (1979)

CAS Registry numbers:
(2), 12082-10-9; *(3a)*, 70006-04-1; *(3b)*, 70006-05-2; *(3c)*, 70006-06-3; *(3d)*, 70006-07-4; *(4a)*, 70046-76-3

[*] Dipl.-Chem. W. Schulze, Dr. K. Weidenhammer, and Prof. Dr. M. L. Ziegler
Anorganisch-Chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

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

[1] *D. Mohr, H. Wienand, M. L. Ziegler*, J. Organomet. Chem. *134*, 281 (1977).

[2] *A. Reckziegel, M. Bigorgne*, J. Organomet. Chem. *3*, 341 (1965).

[3] *(3a)* [from CH_2Cl_2/petroleum ether (60—70 °C) (1 : 2)] forms monoclinic crystals, space group C_{2h}^5-$P2_1/c$; $a = 1175.6(3)$, $b = 1174.6(3)$, $c = 1571.4(2)$ pm, $\beta = 91.52(2)°$; $Z = 4$. 5437 independent reflections other than zero were recorded with an automatic single-crystal diffractometer (Siemens AED); $R = 5.6$ %.

[4] ν_{CO} (CH_2Cl_2): *(3a)* 1990, 1920 (sh), 1830; *(3b)* 1985, 1915, 1900, 1830; *(3c)* 1985, 1920, 1900, 1830; *(3d)* 1995, 1930 (sh), 1840; *(4a)* 1990, 1920 (sh), 1830 cm^{-1}.

[5] ^{1}H-NMR (HFX-90, Brüker; $CDCl_3$, TMS): *(3a)*, $\delta = 4.13$ s (3), 4.20 s (3), 4.85 s (3) (OCH_3), 1.76 (1, (H_B), 2.31 (1 H_A in C_7H_8; $J_{AB} = 21$ Hz), 3.1–5.0 m (10), 5.1–5.5 m (2), 6.0 m (1) (unsatisfactory resolution, partially superposed multiplets of C_7H_7 and C_7H_8).

[6] *E. F. Ashworth, J. C. Green, M. L. H. Green, J. Knight, R. B. A. Pardy, N. J. Wainwright*, J. Chem. Soc. Dalton Trans. *18*, 1693 (1977).

© Verlag Chemie, GmbH, 6940 Weinheim, 1979

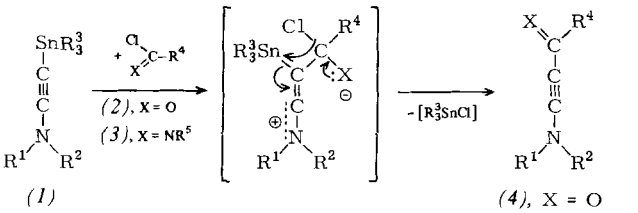
0570-0833/79/0505-0404 $ 02.50/0

β-Stannylated Ynamines as Aminoethynylation Reagents

By *Gerhard Himbert*[*]

(Stannylethynyl)amines *(1)* are readily accessible, can be purified by recrystallization (R^3 = Ph) or distillation (R^3 = Me, Bu), and can be stored for several weeks in a refrigerator without decomposition[1]. They add azides[1a], and react with heterocumulenes[2] and acetylenedicarboxylates[1b,c] by (aminoethynyl)metalation to give novel ynamines.

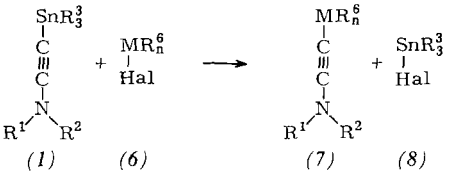
We have now found that the stannylated ynamines *(1)* react in a preparatively simple way with acyl chlorides *(2)* and imidoyl chlorides *(3)* to give the substituted ynamines *(4)* and *(5)* in good yields. The reaction mechanism can plausibly be explained in terms of an addition-elimination sequence.



(1) *(2)*, X = O; *(3)*, X = NR^5 → $-[R^3_3SnCl]$ → *(4)*, X = O; *(5)*, X = NR^5

So far only very few acylynamines *(4)* have been synthesized[3,4]. The salient features of the new method of synthesis are the freedom of choice of acyl components *(2)*, the ease of handling and isolation, and the high yields (cf. Table 1).

Reaction of *(1)* with *(2)* or *(3)* in ether or acetonitrile is complete within 1—3 h at room temperature; the new ynamines *(4)* and *(5)* are (in most cases) isolated by addition of petroleum ether, cooling, and rubbing. Carboxylic anhydrides can replace the acid chlorides; however, in most cases workup is inconvenienced by the sparing solubility of the stannylcarboxylates.



(1) *(6)* → *(7)* *(8)*

The (stannylethynyl)amines *(1)* undergo metathesis with the element halides *(6)*. The germanium derivative *(7a)* and arsenic derivative *(7b)* are cited here (Table 1) as examples.

The structures of *(4)*, *(5)*, and *(7)* are confirmed by the spectra (Table 1), the analytical data, and, in the case of *(7a)*[1a] and *(7b)*[5], by comparison of the IR data with those of authentic samples.

Experimental

Synthesis of (*E*)-5-(*N*-methylanilino)-1-phenyl-1-penten-4-yn-3-one *(4c)*: The mixture of *N*-methyl-*N*-(tributylstannylethynyl)aniline[1d] (4.2 g, 10 mmol) and cinnamoyl chloride (1.7 g, 10 mmol) in ether (30 ml) is stirred for 3 h at room temperature. After addition of 30 ml petroleum ether (40—70 °C) *(4c)* crystallizes within 10 min.

Synthesis of *N*-(diphenylarsinoethynyl)-*N*-methylaniline *(7b)*: The mixture of *N*-methyl-*N*-(tributylstannylethynyl)aniline (4.2 g, 10 mmol) and chloro(diphenyl)arsane (2.7 g,

Table 1. Preparative and spectroscopic data of compounds *(4)*, *(5)* and *(7)*.

	R^1	R^2	R^4	R^5	Yield [a] [%]	B.p. [°C/torr] M.p. [°C] (solvent)	IR (KBr) [cm^{-1}] [d] C≡C	*(4)*: C=O *(5)*: C=N	NMR ($CDCl_3$) [δ values] Charact. signals [f]
(4a)	Me	Ph	*i*Pr		60 [b]	125/0.15 [b] 43–44 (pet. ether)	2180, 2174 sh	1638	1.21 (d, 6H, $CHMe_2$), 2.64 (hept, 1H, $CHMe_2$), 3.33 (s, 3H, NMe)
(4b)	Me	Ph	CH(OAc)Ph		81	124—125 ($CHCl_3$/ether)	2184 sh, 2177 2158 sh	1740, 1654	2.19 (s, 3H, COMe), 3.31 (s, 3H, NMe), 6.13 (s, 1H, CH)
(4c)	Me	Ph	CH=CHPh(*E*)		54	138—139 (ether)	2180	1631	3.48 (s, 3H, NMe), δ_A = 6.80, δ_B = 7.72 (J_{AB} = 16 Hz)
(4d)	Et	Et	C_6H_4—NO_2(*p*)		57	87—89 (ether)	2160	1613, 1586	1.36 (t, 6H, $NCCH_3$), 3.31 (q, 4H, NCH_2)
(4e)	Ph	Ph	C_6H_4—CH_3(*p*)		53	110—111 (ether)	2188	1628, 1615	2.40 (s, 3H, Aryl *Me*)
(4f)	Me	Ph	CO_2Me		72	77—78 (ether)	2180, 2170	1727, 1643	3.50 (s, 3H, NMe), 3.93 (s, 3H, OMe)
(4g)	Me	Ph	C_6H_4—CO_2SnMe_3(*o*)		77	129—130 (dec.) (CH_2Cl_2/ether)	2180	1621	0.60 (s, 9H, $SnMe_3$), 3.46 (s, 3H, NMe)
(5a)	Me	Ph	Ph	Ph	42	140—141 (ether)	2200 sh, 2190	1557	3.23 (s, 3H, NMe)
(5b)	Me	Ph	Ph	NHPh	43	105—106 (ether)	2204	3315 [e]	3.52 (s, 3H, NMe); 8.52 (s, 1H, NH)
(5c)	Ph	Ph	Ph	NHTos	69	200—201 (ether)	2200	3260 [e]	2.38 (s, 3H, Aryl *Me*), 8.19 (s, 1H, NH)
(5d)	Et	Et	—N=C(Cl)—N=C(Cl)—		65	95—96 (ether)	2180	1568, 1515	1.32 (t, 6H, $NCCH_3$), 3.31 (q, 4H, NCH_2)
(7a) [c]	Me	Ph	MR^6_n = $GePh_3$		55	101—102 (pet. ether)	2160	—	3.32 (s, 3H, NMe)
(7b) [c]	Me	Ph	MR^6_n = $AsPh_2$		96	69—70 (pet. ether)	2152	—	3.27 (s, 3H, NMe)

[a] Yields (not optimized) based on 10 mmol starting material in 30 ml acetonitrile [in the case of *(5a)* and *(5b)*] and in 30 ml ether [in all remaining syntheses], using *(1)*, R^3 = Me [in the case of *(4a)*, *(4e)*, and *(4g)*] and *(1)*, R^3 = Bu [in all remaining reactions]. Phthalic anhydride is used for the synthesis of *(4g)*. [b] In the case of *(4a)*, on completion of reaction the mixture is treated with 100 ml ether and 3 g triethylamine, extracted with 3 × 50 ml water (removal of Me_3SnOH), the ethereal phase dried over $CaCl_2$, the solvent removed in a vacuum, the residue distilled in a Kugelrohr and the solidified distillate recrystallized from petroleum ether. [c] *(7a)* [1a] and *(7b)* [5] have already been prepared by reaction of the corresponding lithium acetylide with $BrGePh_3$ and $ClAsPh_2$, respectively. The same element halides are used in these new reactions. [d] Apparatus: Perkin Elmer IR spectrometer 394. [e] NH absorption. [f] Apparatus: Varian EM 390, TMS int., $^3J_{H,H}$ for ethyl and isopropyl protons = 7 Hz.

[*] Dr. G. Himbert
Fachbereich Chemie der Universität
Postfach 3049, D-6750 Kaiserslautern (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0405 $ 02.50/0*

10 mmol) in ether (40 ml) is stirred for 3 h at room temperature. After addition of 30 ml petroleum ether and cooling to −70 °C, crystallization of *(7b)* is initiated by rubbing.

Received: February 13, 1979 [Z 200 IE]
German version: Angew. Chem. *91*, 432 (1979)

CAS Registry numbers:
(1), R^1 = Me, R^2 = Ph, R^3 = Me, 67370-99-4; *(1)*, R^1 = Me, R^2 = Ph, R^3 = Bu, 69943-09-5; *(1)*, R^1 = Et, R^2 = Et, R^3 = Bu, 69943-10-8; *(1)*, R^1 = Ph, R^2 = Ph, R^3 = Me, 67857-50-5; *(2a)*, 79-30-1; *(2b)*, 1638-63-7; *(2c)*, 17082-09-6; *(2d)*, 122-04-3; *(2e)*, 874-60-2; *(2f)*, 5781-53-3; *(2g)*, 69943-11-9; *(3a)*, 4903-36-0; *(3b)*, 7598-88-1; *(3c)*, 31910-69-7; *(3d)*, 108-77-0; *(4a)*, 69943-12-0; *(4b)*, 69943-13-1; *(4c)*, 69943-14-2; *(4d)*, 69943-15-3; *(4e)*, 69943-16-4; *(4f)*, 69943-17-5; *(4g)*, 69943-18-6; *(5a)*, 69943-19-7; *(5b)*, 69943-20-0; *(5c)*, 69943-21-1; *(5d)*, 69943-22-2; *(6)*, $MR_n^6 = GePh_3$, 3005-32-1; *(6)*, $MR_n^6 = AsPh_2$, 712-48-1; *(7a)*, 58528-66-8; *(7b)*, 69943-23-3

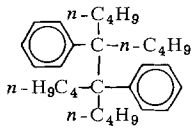
[1] *G. Himbert, D. Frank, M. Regitz*, Chem. Ber. *109*, 370 (1976); b) *G. Himbert*, J. Chem. Res. *1978*, (S) 102; (M) 1445; c) *ibid. 1979*, (S) 88; d) the tributylstannyl compounds *(1)* have been synthesized analogously to the trimethylstannyl derivatives *(1)*; unpublished.
[2] *G. Himbert, W. Schwickerath*, Tetrahedron Lett. *1978*, 1951.
[3] *U. Lienhard, H.-P. Fahrni, M. Neuenschwander*, Helv. Chim. Acta *61*, 1609 (1978), and references cited therein.
[4] a) *M. E. Kuehne, P. J. Sheeran*, J. Org. Chem. *33*, 4406 (1968); b) *G. Himbert, M. Regitz*, Synthesis *1972*, 571.
[5] *M. Regitz, D. Frank, G. Himbert*, unpublished results.

Discovery of an Exceptionally Long Unbridged Carbon-Carbon Bond[**]

By *Walter Littke* and *Ulrich Drück*[*]

Substituted ethane compounds show a greater or lesser degree of thermal lability, depending on the nature and size of the substituents[1]: anomalous bond lengths and angles can be expected for bulky molecules.

We have examined 5,6-dibutyl-5,6-diphenyldecane *(1)*. Well-formed single crystals could be grown from an ethanol



(1)

solution (conditions[2]); crystal data[3]: $a = 8.04_3$, $b = 10.06_2$, $c = 10.42_1$ Å; $\alpha = 75.36$, $\beta = 116.95$, $\gamma = 120.20°$; $V = 649.4$ Å^3; $Z = 1$; space group $P\bar{1}$; $\rho_{exp.} = 1.05$, $\rho_{calc.} = 1.04$ g cm^{-3}[4]. The unit cell was chosen such that it contains as many atoms of the same molecule as possible. The center of inversion lies at the center of the molecule and the unit cell, and the phenyl groups are thus arranged in the *anti* conformation.

The thermal vibrations of the atoms increase with increasing distance from the centroid of the molecule. The maximum elongation of the vibrational ellipsoids of the central C atoms 1 and 1′ occurs preferentially in the direction of the labile ethane bond; overall, however, the thermal effects on the molecule are much less pronounced ($0.0347 < U_{11} < 0.1361$ Å^2) than would be expected for a thermolabile compound. As shown by molecule packing studies, this is attributable to strong intra- and intermolecular van der Waals interactions between the H atoms. The ten C atoms 5 to 5′ of the decane chain shown vertical in Figures 1 and 2 lie almost exactly in a single plane; the greatest deviation from the least-squares plane is found for C2 (−0.071 Å) and C2′ (0.071 Å). The torsional angles of the phenyl groups are −86.14° and 86.14° (relative to bonds 1/10 and 1′/10′).

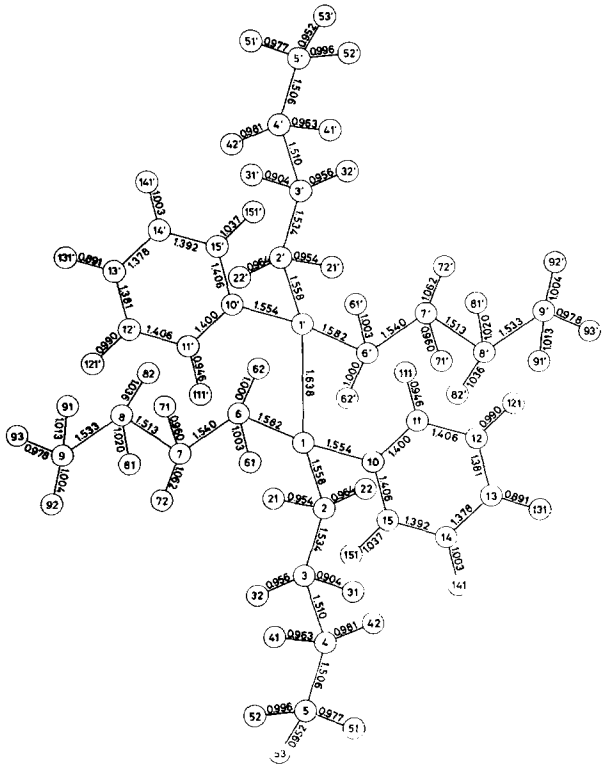


Fig. 1. Molecular geometry of *(1)*; bond lengths [Å].

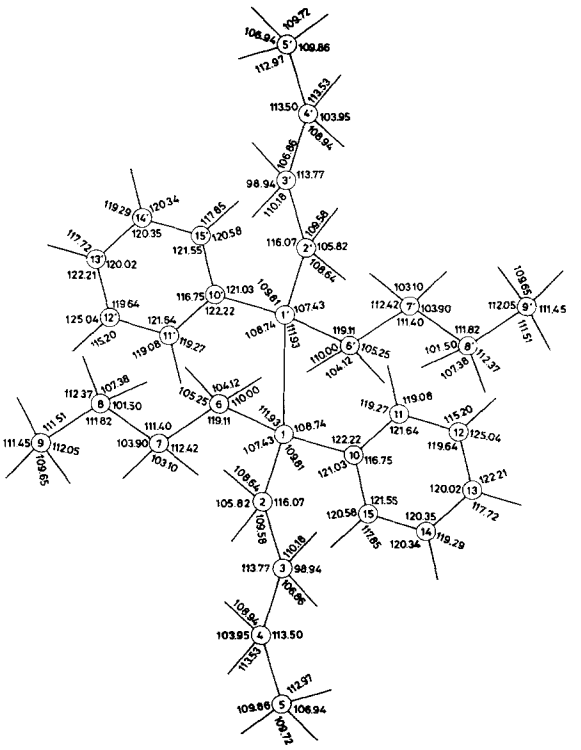


Fig. 2. Molecular geometry of *(1)*; angles [°].

[*] Dr. W. Littke [+], Dr. U. Drück
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)
[+] To whom correspondence should be addressed.

[**] This work was supported by the Deutsche Forschungsgemeinschaft. We wish to thank Prof. *C. Rüchardt* and Dr. *H.-D. Beckhaus*, Freiburg, for sufficient material to grow single crystals.

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0406 $ 02.50/0

The molecule exhibits numerous intramolecular H/H contacts; the H/H distances are up to 15% shorter than the

Table 1. Intramolecular H/H contacts arranged in order of increasing interpenetration. The distances of the symmetrically equivalent H/H contact pairs are not included.

H/H Contact pair	Contact distance [Å]	H/H Contact pair	Contact distance [Å]
42/53	2.391	21/32	2.289
21/72	2.387	131/141	2.286
141/151	2.384	62/82	2.272
81/93	2.378	62/111	2.254
71/62	2.357	22/151	2.105
41/52	2.349	32/72	2.100
32/41	2.335	22/62′	2.057
111/121	2.289	62/22′	2.057

expected van der Waals distance (2.40 Å). Extensive interpenetration of some of the H/H atom pairs (Table 1) leads to enormous strain within the molecule and thus to anomalous bond lengths and angles as well as thermal instability. The close double contact 22/62′ = 62/22′ (2.057 Å) is particularly remarkable. It lengthens the central C—C bond to 1.638(6) Å: this is the longest known unbridged C—C bond. The strain also extends to the bonds 1/2 and 1′/2′, albeit to a much lower degree.

Further anomalies visible in Figures 1 and 2 are due entirely to steric effects. Thus the lengthened distances 1/6 and 1/10 arise on the one hand from the H/H contact 62/111 (2.254 Å); on the other hand, the distance 1/6 undergoes further elongation due to the close H/H contact 32/72 (2.100 Å) and the C7—C6—C1 angle is widened to 119.11°—an unusually large value for an sp^3-hybridized C atom. The close H/H contact 22/151 (2.105 Å) not only increases the distance 1/10 but also effects a slight shift of C2 out of the plane of the decane chain. The slightly increased tetrahedral angle at C7 (111.40°) is attributable to the contact 62/82.

Attempts to calculate the exact length of the central C—C bond by the EFF method using force fields according to *Allinger*[6] and *Engler-Schleyer*[7] failed to give accurate results: the value converged to 1.60 Å[8]. This is due to the empirical nature of the method.

Received: January 9, 1979 [Z 205 IE]
German version: Angew. Chem. *91*, 434 (1979)

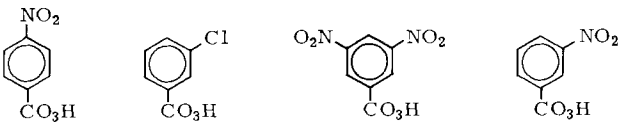
CAS Registry number:
(1), 69961-18-8

[1] *K. Ziegler, W. Deparade*, Justus Liebigs Ann. Chem. *567*, 123 (1950); *C. Rüchardt, H.-D. Beckhaus, G. Hellmann, S. Weiner, R. Winiker*, Angew. Chem. *89*, 913 (1977); Angew. Chem. Int. Ed. Engl. *16*, 875 (1977); *G. Hellmann, H.-D. Beckhaus, C. Rüchardt*, Chem. Ber., in press.
[2] *W. Littke*, Naturwissenschaften *61*, 684 (1974).
[3] *W. Littke, Th. Baumann, K. Berroth*, to be published.
[4] Automatic four-circle diffractometer ($Mo_{K\alpha}$ radiation), 2646 independent reflections of which 1284 were considered unobserved ($I < 2\sigma_I$); solution by direct methods [5]. All atomic sites could be localized by Fourier or difference Fourier syntheses; C atoms treated anisotropically and H atoms isotropically; $R = 5.7$ % (weighting schemes: *M. Martinez-Ripoll, F. H. Cano:* PESOS Computer program 1975, Madrid).
[5] *H. Ammon, C. Dickinson, R. V. Chastain, E. G. Boonstra, J. M. Stewart:* XRAY 70 System with SIGMA 2 incorporated. Computer Science Center, University of Maryland, College Park, Maryland.
[6] *M. L. Allinger, M. T. Tribble, M. A. Miller, H. D. Wertz*, J. Am. Chem. Soc. *93*, 1637 (1971).
[7] *E. M. Engler, J. D. Andose, P. v. R. Schleyer*, J. Am. Chem. Soc. *95*, 8005 (1973).
[8] *H.-D. Beckhaus*, personal communication.

Regio- and Stereospecific Hydroxylation of Alicyclic Hydrocarbons with Substituted Perbenzoic Acids

By *Walter Müller* and *Hans-Jörg Schneider*[*]

Selective oxidations of alkanes RH→ROH by peroxycarboxylic acids have so far claimed interest not only as reaction steps in syntheses[1] but also as models for reactions of monooxygenases[2]. Reaction of trifluoroperacetic acid with molecules containing secondary and tertiary C—H bonds leads to product mixtures[3] whose formation cannot be hindered



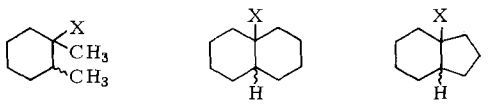
(1a) *(1b)* *(1c)* *(1d)*

even under mild conditions[4]. On the other hand, on reaction with substituted perbenzoic acids *(1a)*—*(1d)* of medium acidity, hydrocarbons [*e.g. (2)*—*(4)*, X=H] are converted directly with high regioselectivity and with retention of configuration into the monohydroxy compounds *(2)*—*(4)*, X=OH[5] (Table 1).

Table 1. Hydroxylation of the alicyclic hydrocarbons *cis-* and *trans-(2)* through *cis-* and *trans-(4)*, X=H, with *p*-nitroperbenzoic acid to the alcohols *cis-* and *trans-(2)* to *-(4)*, X=OH.

	(2)	*(3)*	*(4)*
trans-Compounds, X=H→X=OH			
Regiospecificity [a]	97	95	95
Stereospecificity [b]	97	100	95
cis-Compounds, X=H→X=OH			
Regiospecificity [a]	98	96	96
Stereospecificity [b]	98.5	99	100

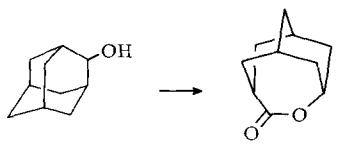
[a] $\sum$*sec*-alcohol + *tert*-alcohol = 100%. [b] Retention of configuration in %.



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

The rate of reaction increases with increasing acidity of the peracid; this and the deactivating effect of a hydroxy group already incorporated in the alkane underscores the electrophilic character of the substitution. Possible participation of a radical side reaction is revealed *e.g.* by the formation of chlorobenzene from *(1b)* and a concomitant proportional decrease in regio- and stereoselectivity; this side reaction can be largely inhibited by addition of iodine (*ca.* 1 mg/ml).

Under the reaction conditions secondary hydroxy groups are oxidized to ketones, and thence according to a Bayer-Villiger reaction; thus, *e.g.* the 4-oxa-4-homo-5-adamantanone *(6)* is formed from 2-adamantol *(5)*.



(5) *(6)*

[*] Prof. Dr. H.-J. Schneider, Dipl.-Chem. W. Müller
Fachrichtung Organische Chemie der Universität
D-6600 Saarbrücken 11 (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0407 $ 02.50/0*

Hydroxy groups can, however, be readily protected by acylation and then, like other electronegative substituents, serve to direct the reaction of alkanes containing several tertiary C—H bonds.

Procedure

Synthesis of *cis-(3)*, X=OH: A mixture of *cis-(3)*, X=H (20 g, 0.145 mol) and *(1a)* (20.3 g, 0.108 mol) (98 %, iodometric) in $CHCl_3$ (100 ml) is heated under reflux for 7 h; after further addition of *(1a)* (20.3 g, 0.108 mol) and $CHCl_3$ (30 ml), refluxing is continued for a further 16 h. The reaction mixture is then allowed to cool to room temperature, filtered, and the filter-cake washed with 350 ml ether. The resulting organic phase is washed with 1 N NaOH and H_2O, and dried over Na_2SO_4. The residue remaining after removal of solvent by distillation is found (gas-chromatographically) to contain 82 % *cis-(3)*, X=OH. Distillation in a saber side-arm flask (b.p. 120—135 °C/20 torr) furnishes 15.6 g (69 %) of *cis-(3)*, X=OH, which is contaminated with 5 % each of hydrocarbon and side-products.

Received: February 9, 1979 [Z 195 IE]
German version: Angew. Chem. *91*, 438 (1979)

CAS Registry numbers:
(1a), 943-39-5; *(1b)*, 937-14-4; *(1c)*, 66358-48-3; *(1d)*, 2453-41-0; *trans-(2)* (X=H), 6876-23-9; *cis-(2)* (X=H), 2207-01-4; *trans-(2)* (X=OH), 19879-12-0; *cis-(2)* (X=OH), 19879-11-9; *trans-(3)* (X=H), 493-02-7; *cis-(3)* (X=H), 493-01-6; *trans-(3)* (X=OH), 1654-87-1; *cis-(3)* (X=OH), 3574-58-1; *trans-(4)* (X=H), 3296-50-2; *cis-(4)* (X=H), 4551-51-3; *trans-(4)* (X=OH), 13366-91-1; *cis-(4)* (X=OH), 13366-92-2; *(5)*, 700-57-2; *(6)*, 21898-84-0

[1] Review: *G. A. Olah, D. G. Parker, N. Yoneda*, Angew. Chem. *90*, 962 (1978); Angew. Chem. Int. Ed. Engl. *17*, 909 (1978).
[2] *V. Ullrich*, Angew. Chem. *84*, 689 (1972); Angew. Chem. Int. Ed. Engl. *11*, 701 (1972).
[3] *N. C. Deno, N. Messer*, J. Chem. Soc. Chem. Commun. *1976*, 1051.
[4] *H.-J. Schneider, W. Kropf*, unpublished results.
[5] Similar results are obtained with α-haloperoxycarboxylic acids (*H.-J. Schneider, L. Wong*, unpublished work). The identity of the product was confirmed by ^{13}C-NMR spectroscopy.

Problem of the Structure of Carbodiphosphoranes, R_3PCPR_3: New Aspects

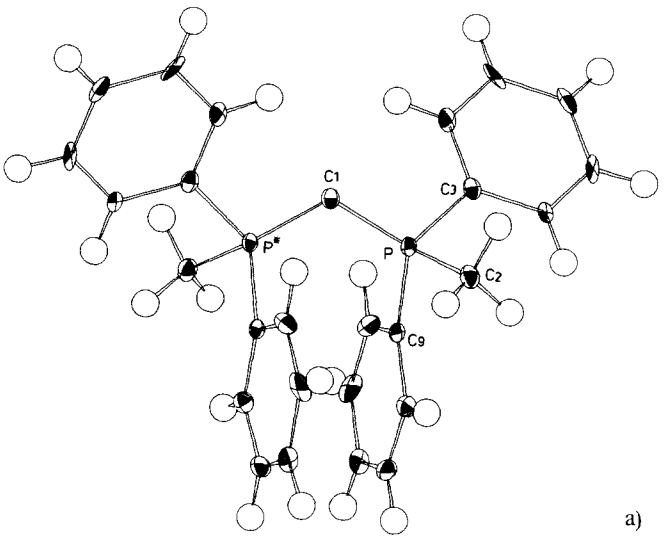
By *Hubert Schmidbaur, Georg Hasslberger, Ulrich Deschler, Ulrich Schubert, Charles Kappenstein*, and *Albin Frank*[*]

"Carbodiphosphoranes" R_3PCPR_3, which are formal derivatives of bis(phosphoranediyl)methane, have posed many a riddle since their discovery, some of which have hitherto remained unsolved. The longest known representative with R=C_6H_5 *(1)*[1] exhibits triboluminescence in one of its crystal forms, and its derivatives are photochromic[2a]. X-Ray structure analysis of the triboluminescent modification showed that the unit cell contains two different molecules with widely differing PCP bond angles of 130.1(6) and 143.8(6)°[3]. On the other hand, another modification of *(1)* shows only one kind of molecule with a PCP angle of 131.7(4)°[2b]. Electron diffraction experiments on the hexamethyl compound *(2)*[4] revealed a high degree of flexibility of the PCP angle in the gaseous state; an apparent angle of 148° is observed as a result of a shrinkage effect[5]. Since the triboluminescence has been correlated, *e.g.*, with angular deformation in the crystal[2], we looked for further interesting structural features.

$(C_6H_5)_3P{=}C{=}P(C_6H_5)_3$ *(1)* $(CH_3)_3P{=}C{=}P(CH_3)_3$ *(2)*

$CH_3(C_6H_5)_2P{=}C{=}P(C_6H_5)_2CH_3$ *(3)*

Surprisingly, we discovered that the crystals[6] of the deep yellow dimethyl(tetraphenyl) compound *(3)*[7a] contain molecules with an exceptionally small PCP angle of 121.8(3)°, deviating by only 1.8° from the ideal value for sp^2 hybridization of the central C atom (Fig. 1). This finding provides the first evidence that formula *(A)* is entirely appropriate for describing the bonding in carbodiphosphoranes. It is also in accord with the latest measurements of dipole moments in ylides[8]. The almost exclusively employed formulation *(B)* would rather suggest a stretched molecular skeleton.



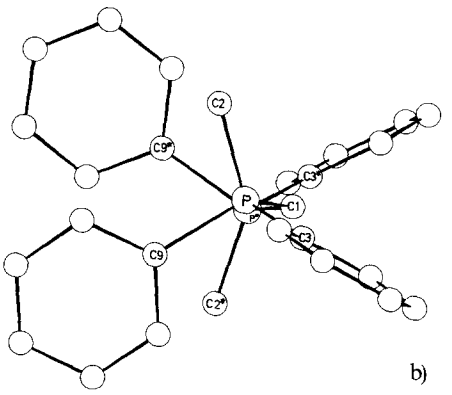


Figure 1. Molecular structure of $MePh_2PCPPh_2Me$ *(3)*: a) front view, b) side view.

Principal interatomic distances [pm] and bond angles [°]

C1—P	164.8(4)	P*—C1—P	121.8(3)
C2—P	182.1(6)	C1—P—C2	117.2(3)
C3—P	181.7(6)	C1—P—C3	110.9(3)
C9—P	183.3(6)	C1—P—C9	117.2(3)
		C2—P—C3	103.5(3)
		C2—P—C9	103.9(3)
		C3—P—C9	102.3(3)

[*] Prof. Dr. H. Schmidbaur, Dr. G. Haßlberger, U. Deschler, Dr. U. Schubert, Dr. C. Kappenstein [+], Dr. A. Frank
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)
[+] Present address: Université de Reims (France).

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0408 $ 02.50/0

The structure of *(3)* reveals yet another important detail: two of the C_6H_5 rings are arranged in parallel planes in such a way that the π-systems just fail to interpenetrate (Fig. 1). Their mutual separation of 328 pm is considerably shorter than the van der Waals separation of aromatic compounds (340 pm, cf. [7b]). Any further compression of the PCP bond in *(3)* or mutual twisting of the PC_4 tetrahedra must therefore lead to strong perturbation of the electronic states, and we suspect that this is the reason for the mechanically induced photoeffects. The few other known cases of triboluminescence of organometallic and organic compounds are similarly characterized by relatively large π-systems in a parallel arrangement[2c, 9]. It should be noted that the triboluminescence of such "molecular" examples could not yet be interpreted unequivocally—apart from an indication of strong piezoelectric charging[2c, 9].



(A) *(B)*

Moreover, crystallization experiments on *(1)* in benzene gave a new modification, the diffraction data of which are compatible with a *cubic* structure[10]. This result again shows that the packing of *(1)* in the crystal lattice is possible in a variety of ways and that the molecular geometry of carbodiphosphoranes can readily adapt to a given situation without incurring large energy losses. The angular flexibility deduced from slight energy differences between *(A)* and *(B)* has parallels in the isoelectronic cations $R_3PNPR_3^{\oplus}$, which were also found to have widely varying bond angles between 134.6 and 180°[11]. Concerning the relative energy levels of the two isosteric series, mention should be made of a recent theoretical publication[12]; the predictions of the influence of electron-donating substituents contradict our structural findings [*(1)*/*(3)*]. On the basis of the polar formulation *(A)*, both the complexing properties of carbodiphosphoranes[13a] and their manifold organic reactions become immediately understandable[13b].

Received: January 31, 1979 [Z 210 IE]
German version: Angew. Chem. *91*, 437 (1979)

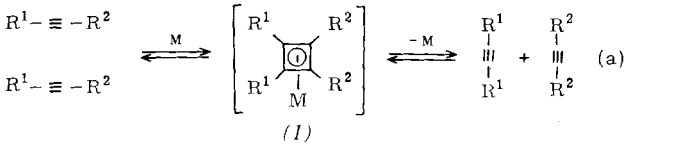
CAS Registry numbers:
(1), 7533-52-0; *(2)*, 57437-91-9; *(3)*, 60798-30-3

[1] *F. Ramirez, N. B. Desai, B. Hansen, N. McKelvie*, J. Am. Chem. Soc. *83*, 3539 (1961).
[2] a) *C. N. Matthews, J. S. Driscoll, J. E. Harris, R. J. Wineman*, J. Am. Chem. Soc. *84*, 4349 (1962); *J. S. Driscoll, D. W. Grisley, J. V. Pustinger, J. E. Harris, C. N. Matthews*, J. Org. Chem. *29*, 2427 (1964); *J. I. Zink, W. C. Kaska*, J. Am. Chem. Soc. *95*, 7510 (1973); *G. E. Hardy, J. C. Baldwin, J. I. Zink, W. C. Kaska, P. H. Lin, L. Dubois, ibid. 99*, 3552 (1977); b) *G. E. Hardy, J. I. Zink, W. C. Kaska, J. C. Baldwin, ibid. 100*, 8001 (1978); c) *J. I. Zink*, Acc. Chem. Res. *11*, 289 (1978).
[3] *A. T. Vincent, P. J. Wheatley*, J. Chem. Soc. Dalton Trans. *1972*, 617.
[4] *H. Schmidbaur, O. Gasser*, J. Am. Chem. Soc. 97, 6281 (1975); *H. Schmidbaur, O. Gasser, M. S. Hussain*, Chem. Ber. *110*, 3501 (1977).
[5] *E. A. V. Ebsworth, T. E. Fraser, D. W. H. Rankin, O. Gasser, H. Schmidbaur*, Chem. Ber. *110*, 3508 (1977).
[6] From diethyl ether, not triboluminescent; monoclinic, space group C2/c, $a=2203(3)$, $b=1020(1)$, $c=1029(1)$ pm, $\beta=109.97(9)°$, $V=2172\times10^6$ pm^3, $Z=4$; 918 structure factors [$F_0=3.0\sigma(F_0)$, $2°\leq2\theta\leq45°$], Syntex $P2_1$/XTL, $Mo_{K\alpha}$ ($\lambda=71.069$ pm, graphite monochromator), $R=0.069$.
[7] a) *M. S. Hussain, H. Schmidbaur*, Z. Naturforsch. *B31*, 721 (1976); b) *H. P. Fritz, H. Gebauer, P. Friedrich, P. Ecker, R. Artes, U. Schubert, ibid. B33*, 498 (1978).
[8] *H. Lumbroso, J. Curè, H.-J. Bestmann*, J. Organomet. Chem. *161*, 347 (1978).
[9] *Y. Dusausoy, J. Protas, P. Renaut, B. Gautheron, G. Tainturier*, J. Organomet. Chem. *157*, 167 (1978).
[10] Not triboluminescent; $a=b=c=1576(2)$ pm, Laue classe m3.
[11] *R. D. Wilson, R. Bau*, J. Am. Chem. Soc. *96*, 7601 (1974), and references cited therein.
[12] *C. Glidewell*, J. Organomet. Chem. *159*, 23 (1978).
[13] a) *W. C. Kaska, D. K. Mitchell, R. F. Reichelderfer, W. D. Korte*, J. Am. Chem. Soc. *96*, 2847 (1974), and references cited therein; b) *H. J. Bestmann*, Angew. Chem. *89*, 361 (1977); Angew. Chem. Int. Ed. Engl. *16*, 349 (1977).

Cyclobutadiene-Metal Complexes as Potential Intermediates in Alkyne Metathesis: Flash Vacuum Pyrolysis of Substituted η^4-Cyclobutadiene-η^5-cyclopentadienylcobalt Complexes[**]

By *John R. Fritch* and *K. Peter C. Vollhardt*[*]

The mechanism of alkyne metathesis [eq. (a)] is a matter of unresolved controversy. The actual process has only been observed at relatively high temperatures in the gas phase[1] and in solution[2] over mostly heterogeneous tungsten and molybdenum catalysts. However, the literature abounds with examples in which the final product of the interaction of an alkyne with a transition metal appears to be derived from initially metathesized or "dichotomized" starting material[3]. The logical intermediate *(1)* in this reaction[1], has been discounted due to the "unusual stability" of cyclobutadienemetal complexes, in addition to the fact that their condensed phase thermal decomposition *fails to give alkyne products*[4].



(1)

We would like to report that: (1) cyclobutadiene-cyclopentadienylcobalt complexes cleanly decompose on heating in the gas phase to regenerate their component acetylenes; (2) these decompositions require intermediate bis(alkyne)cobalt complexes; (3) rotation and reclosure of the complexed alkynes to cyclobutadiene rings competes with decomplexation; and (4) migration of cobalt along the two triple bonds of diyne ligands does not occur.

Flash pyrolyses at short contact times (*ca.* 0.005 s, *ca.* 10^{-5} torr) were carried out as described earlier[5]. Product yields were independent of the amount of material pyrolyzed and of whether or not the pyrolysis tube was cleaned before reuse, thus ruling out wall effects, in particular secondary cobalt-catalyzed wall reactions. η^4-Tetraphenylcyclobutadiene-η^5-cyclopentadienylcobalt *(2)*[6] was pyrolyzed at 726 °C to give (at 47% conversion) 89% of isolated diphenylacetylene. The pyrolyses of the substituted diethynyl derivatives *(3)*—*(6)* summarized in Table 1 are instructive, particularly under conditions of incomplete conversion.

[*] Prof. Dr. K. P. C. Vollhardt, J. R. Fritch
Department of Chemistry, University of California, and the Materials and Molecular Research Division, Lawrence Berkeley Laboratory
Berkeley, California 94720 (USA)

[**] We are grateful for support by the Division of Chemical Sciences, Office of Basic Energy Sciences, U.S. Department of Energy (Contract No. W-7405-Eng-48), NSF, NIH, Chevron Research Company, Pressure Chemical Corporation, and Silar Laboratories, Inc. *K. P. C. V.* is a Fellow of the A. P. Sloan Foundation, 1976—1980, and a Camille and Henry Dreyfus Teacher-Scholar, 1978—1983; *J. R. F.* is the recipient of a Regents' Predoctoral Fellowship (1977) and a Gulf Oil Fellowship (1978).

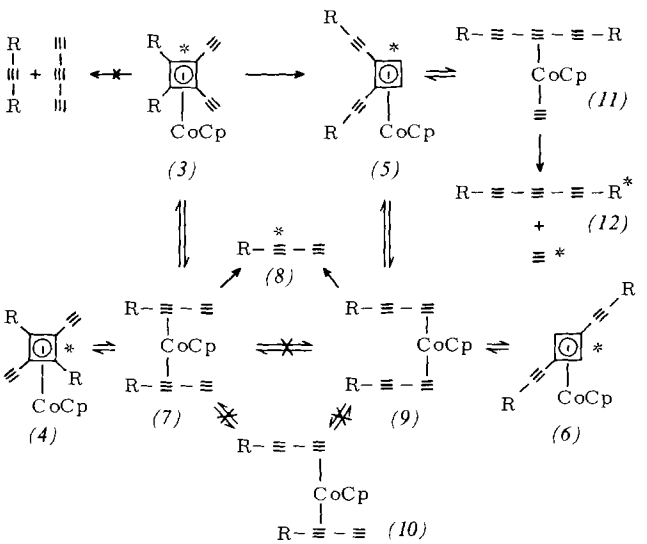
© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0409 $ 02.50/0

Table 1. Alkynes from decomposition of cyclobutadiene complexes *(3)*—*(6)*.

Starting material	T [°C] [c]	Yield [%] [a, d, f] *(3)* [e]	*(4)*	*(5)*	*(6)* [g]	*(8)*	*(12)*
(3) [b, e]	775	[h]	[h]	1.9	0.41	32.0	18.3
	702	[h]	0.04	17.3	1.5	20.5	12.0
	675	[h]	0.04	32.1	2.0	16.3	9.8
(4) [b, i]	780	[h]	0.29	0.06	[h]	74.8	1.1
	682	0.03	17.8	1.1	0.07	59	0.58
	652	0.04	34.7	1.2	0.06	43.7	0.16
	640	0.13	49.2	1.7	0.05	31.9	0.20
(5)	676	[h]	0.02	34.8	2.90	17.4	11.9
(6)	701	≤0.03	[h]	7.17	30.71	30.9	5.70

[a] A cobalt mirror formed on the surface of the pyrolysis tube. Traces of acetylene were (incompletely) trapped in all reactions. In addition to the alkyne products indicated, compounds derived from the cyclopentadienyl moiety were isolated and identified: cyclopentadiene, dihydrofulvalenes, and naphthalene [7]. No cyclobutadiene dimers were detected. [b] These starting materials polymerize on standing and were freshly chromatographed before each run. [c] At the center of the tube. [d] Determined by GC and NMR integration. Polymer forms at both entrance and exit to the oven, accounting for incomplete mass balances. [e] *(3)* leads to *(5)* *via* the diethynylcyclobutadiene rearrangement [5a]. [f] The absence of butadiyne, hexatriyne, trimethylsilylethyne, trimethylsilylhexatriyne, bis(trimethylsilyl)ethyne, and bis(trimethylsilyl)butadiyne was ascertained by FID-GC and GC/mass spectroscopy. [g] Identified by GC mass spectroscopy and independent synthesis [lithiation followed by trimethylsilylation of 1,3-diethynylcyclobutadiene-cyclopentadienylcobalt [5a]: *(6)*: yellow crystals; m.p. 156—158°C; *m/e* 368 (M^+, 100%), 124 (CpCo, 54%); τ (CCl_4) 4.97 (s, 5H), 5.45 (s, 2H), 9.81 (s, 18H); IR: 2135 cm^{-1} (C≡C). [h] Undetectable by GC/mass spectrometry and FID-GC. [i] *(4)* was erroneously reported [5a] to be stable to 700°C under the pyrolysis conditions; correct is 600°C.

Several features are noteworthy. Firstly, efficient conversion of the cyclobutadiene ring to the corresponding alkynes is observed. Second, as demonstrated by the control pyrolysis of *(5)*, *(3)* is decomposed largely *via* the intermediacy of



Scheme 1. Pyrolysis of *(3)*—*(6)*. R = $Si(CH_3)_3$; * = detected compound.

(5) reached by the low-energy and mechanistically totally distinct "diethynylcyclobutadiene rearrangement"[5a]. Third, the free energies of activation[8] for the decomposition of *(2)* and *(4)*—*(6)* ($\Delta G^+ \approx 47$—50 kcal/mol) are appreciably higher than that for the *(3)*→*(5)* rearrangement ($\Delta G^+ = 37$ kcal/mol) but considerably lower than the CpCo-bond strength (64 kcal/mol)[9]. Fourth, unprecedented mutual interconversion (but not complete equilibration) of the cyclobutadiene starting complexes is observed.

The reproducibility of the data, absence of wall effects, known stability of free cyclobutadiene to flash pyrolysis conditions[10] even above 800°C, and the low pressures employed ruling out bimolecular reaction pathways[11] suggest the mechanism in Scheme 1 to rationalize the results.

Isomer *(3)* pyrolyzes *via* *(5)* and the postulated complexes *(9)* and *(11)* to give the observed major products *(8)* and *(12)*, respectively. The new cyclobutadiene isomer *(6)* is derived from *(9)* by rotation and reclosure. The absence of bis(trimethylsilyl)ethyne indicates a relatively high activation energy to decomposition of *(3)* *via* this pathway. The detection of small quantities of *(4)* demonstrates the accessibility of intermediate *(7)* from *(3)*. Isomer *(4)* enters the reaction manifold through *(7)*, giving mainly trimethylsilylbutadiyne *(8)*. It can also reclose to *(3)*, the latter rapidly giving *(5)* and its decomposition products *via* the diethynylcyclobutadiene rearrangement[5a]. The presence of traces of *(6)* shows the possibility of completing two opening-rotation-reclosure sequences in the time scale of the experiment. Decomposition of *(6)* gives products consistent with this picture, again implicating intermediates *(9)* and *(11)*.

The fact that the yield of *(8)* is always much greater than the yield of *(6)* [from *(3)* or *(5)*] and of *(5)* [from *(4)* or *(6)*] indicates that decomplexation from the bisalkyne complexes is more facile than recyclization. The absence of other cyclobutadiene isomers and their ultimate alkyne products in the pyrolyzates of *(3)*—*(6)* (see Table 1, footnote [f]) makes diacetylene shifts (*e.g.* *(7)*⇄*(9)*, *(9)*⇄*(10)*, *etc.*) unlikely.

Scheme 1 suggests that cyclobutadiene-metal complexes are potential intermediates in alkyne methatheses.

Received: January 29, 1979 [Z 202a IE]
German version: Angew. Chem. *91*, 439 (1979)

CAS Registry numbers:
(3), 67378-02-3; *(4)*, 67378-01-2; *(5)*, 67378-03-4; *(6)*, 69991-02-2; *(8)*, 4526-06-1; *(12)*, 21752-86-3

[1] *F. Pennella, R. L. Banks, G. C. Bailey*, Chem. Commun. *1968*, 1548; *A. Mortreux, M. Blanchard*, Bull. Soc. Chim. Fr. *1972*, 1641; *J. A. Moulijn, H. J. Reitsma, C. Boelhouwer*, J. Catal. *25*, 434 (1972); *H. Höcker, R. Musch*, Makromol. Chem. *176*, 3117 (1975).

[2] *A. Mortreux, M. Blanchard*, J. Chem. Soc. Chem. Commun. *1974*, 786; *A. Mortreux, M. Blanchard*, Metathesis Symposium, Mainz, Germany, January 1976; *A. Mortreux, F. Petit, M. Blanchard*, Tetrahedron Lett. *1978*, 4967, and references cited therein.

[3] See, for example, *U. Krüerke, W. Hübel*, Chem. Ber. *94*, 2829 (1961); *W. Hübel, R. Merény*, J. Organomet. Chem. *2*, 213 (1964); *A. J. Hubert*, J. Chem. Soc. *C1967*, 1984; *G. M. Whitesides, W. J. Ehmann*, J. Am. Chem. Soc. *91*, 3800 (1969); *H. Dietl, H. Reinheimer, J. Moffat, P. M. Maitlis, ibid. 92*, 2276 (1970); *R. B. King, I. Haiduc, C. W. Eavenson, ibid. 95*, 2508 (1973), and references cited therein; *H. B. Chin, R. Bau, ibid. 95*, 5068 (1973); *H. Hoberg, R. Krause-Göing, C. Krüger, J. C. Sekutowski*, Angew. Chem. *89*, 179 (1977); Angew. Chem. Int. Ed. Engl. *16*, 183 (1977), and references cited therein; *R. B. King*, Ann. N. Y. Acad. Sci. *295*, 135 (1977); *E. Sappa, A. Tiripicchio, A. M. M. Lanfredi*, J. Chem. Soc. Dalton Trans. *1978*, 552.

[4] *P. M. Maitlis*, Adv. Organomet. Chem. *4*, 95 (1966); *R. C. Dickson, P. J. Fraser, ibid. 12*, 323 (1974); *A. Efraty*, Chem. Rev. *77*, 691 (1977). In the only gas phase study, cyclobutadienetricarbonyliron pyrolyzed to a complex mixture: *E. Hedaya, I. S. Krull, R. D. Miller, M. E. Kent, P. F. D'Angelo, P. Schissel*, J. Am. Chem. Soc. *91*, 6880 (1969).

[5] a) *J. R. Fritch, K. P. C. Vollhardt*, J. Am. Chem. Soc. *100*, 3643 (1978); b) *K. P. C. Vollhardt, L. S. Yee, ibid. 99*, 2010 (1977); *A. J. Barkovich, E. S. Strauss, K. P. C. Vollhardt, ibid. 99*, 8321 (1977).

[6] *M. D. Rausch, R. A. Genetti*, J. Org. Chem. *35*, 3888 (1970).

[7] *E. Hedaya*, Acc. Chem. Res. *2*, 367 (1969).

[8] Approximate free energies of activation (error margin ±2 kcal/mol) were calculated by using four known gas phase pyrolysis reactions (thermolyses of cyclopentadiene dimer, norbornene, cycloheptatriene, and 1,4-cyclohexadiene) as standards to estimate contact times as a function of temperature and molecular weight.

[9] *J. A. Connor*, Top. Curr. Chem. *71*, 71 (1977).

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0410 $ 02.50/0*

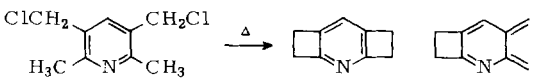
[10] E. Hedaya, R. D. Miller, D. W. McNeil, P. F. D'Angelo, P. Schissel, J. Am. Chem. Soc. 91, 1875 (1969).
[11] G. Seybold, Angew. Chem. 89, 377 (1977); Angew. Chem. Int. Ed. Engl. 16, 365 (1977).

1,2,4,5-Tetrahydrodicyclobuta[*b*,*e*]pyridine[**]

By *Alaric Naiman* and *K. Peter C. Vollhardt*[*]

Benzenoid hydrocarbons fused to strained rings have been the target of recent synthetic efforts aimed at the preparation of aromatic rings in which bond fixation or other perturbations of aromaticity might be observed. So far evidence for the former has been tenuous[1]. The decreased aromaticity of pyridine [estimated at 21 kcal/mol][2] when compared with benzene suggests that it might more easily be subjected to bond localization. Some support for this is found in the physical and chemical properties of cyclobuta[*b*]- and cyclobuta[*c*]pyridine[3]. We report the synthesis of *(2)*, presently the most strained annelated pyridine.

Flash vacuum pyrolysis (800°C, 10^{-4} torr) of dichloride *(1)*[4] proceeds through double HCl-elimination[5], providing on basic workup the pyridine *(2)* in *ca.* 50% yield. Fractional sublimation (40°C, 10^{-3} torr) to separate *(2)* from *(1)* furnished colorless crystals (m.p. 117.5—118.5°C). The structural assignment follows from spectral data and chemical properties[6].



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

Reaction of *(2)* with neat bis(trimethylsilyl)acetylene (200°C, 12h) followed by oxidation with dichlorodicyano-*p*-benzoquinone (in benzene, 80°C, 2h) and desilylation (conc. H_2SO_4, 80°C, 1 min.) gave acridine.

The isolation of *(2)* under conditions conducive to equilibration with the ring-opened *o*-quinodimethane ("*o*-lutidylene") *(3)* suggests appreciable residual aromaticity in *(2)*. This is also indicated by the nuclear magnetic resonance data and the electronic spectrum. As might be expected, the latter shows bathochromic shifts and larger extinction coefficients in comparison with suitable bisannelated models[7]. The significant ring strain experienced by *(2)* is likewise reflected in the ^{13}C-NMR chemical shifts and ^{13}C-H coupling constants[8].

Received: February 2, 1979 [Z 202b IE]
German version: Angew. Chem. 91, 440 (1979)

CAS Registry numbers:
(1), 69961-31-5; *(2)*, 69961-32-6; *(3)*, 69961-33-7

[*] Prof. Dr. K. P. C. Vollhardt, A. Naiman
Department of Chemistry, University of California, and the Materials and Molecular Research Division, Lawrence Berkeley Laboratory, Berkeley, California 94720 (USA)

[**] We are grateful for support by the Division of Chemical Sciences, Office of Basic Energy Sciences, U. S. Department of Energy (contract No. W-7405-Eng-48) and NIH (CA 20713). *K. P. C. V.* is an A. P. Sloan Foundation Fellow (1976—1980) and a Camille and Henry Dreyfus Teacher Scholar (1978—1983); *A. N.* is the recipient of a Regents' Fellowship (1977—1979).

[1] For recent work: *C. Santiago, R. W. Gandour, K. N. Houk, W. Nutakul, W. E. Cravey, R. P. Thummel*, J. Am. Chem. Soc. *100*, 3730 (1978); *R. P. Thummel, W. Nutakul*, J. Org. Chem. *42*, 300 (1977); *43*, 3170 (1978); *D. Davalian, P. J. Garratt, M. M. Mansuri*, J. Am. Chem. Soc. *100*, 980 (1978); *P. Perkins, K. P. C. Vollhardt*, Angew. Chem. *90*, 648 (1978); Angew. Chem. Int. Ed. Engl. *17*, 615 (1978).
[2] *M. J. S. Dewar, A. J. Harget, N. Trinajstic*, J. Am. Chem. Soc. *91*, 6321 (1969); *G. Häfelinger, L. Steinmann*, Angew. Chem. *89*, 48 (1977); Angew. Chem. Int. Ed. Engl. *16*, 47 (1977).
[3] *R. P. Thummel, D. K. Kohli*, J. Org. Chem. *43*, 4882 (1978).
[4] *B. M. Mikhailov, T. K. Kozminskaya*, Zh. Obshch. Khim. *26*, 2042 (1956); Chem. Abstr. *51*, 5072 (1957).
[5] *R. Gray, L. G. Harruff, J. Krymowski, J. Peterson, V. Boekelheide*, J. Am. Chem. Soc. *100*, 2892 (1978); *P. Schiess, M. Heitzmann*, Helv. Chim. Acta *61*, 844 (1978).
[6] MS: $m/e = 131.0732$ (calc. 131.0735, M^+, 84%), 130 (100%), 91 (25%), 65 (42%), 51 (21%), 39 (25%); ^{1}H-NMR ($CDCl_3$): $\delta = 6.96$ (br. s, 1H), 3.30 (m, 4H), 2.98 (m, 4H); ^{13}C-NMR ($CDCl_3$): $\delta = 26.8$ (t, $J_{C,H} = 139.9$ Hz), 34.2 (t, 138.6 Hz), 124.4 (d, 163.5 Hz), 138.6, 161.7; UV (95% ethanol): $\lambda_{max} = 286$ nm sh ($\lg\varepsilon = 3.94$), 289 (3.97), 292 sh (3.95), 299 sh (3.74); IR ($CHCl_3$): $\nu_{max} = 2980$, 2937, 1599, 1369, 1244, 905 cm^{-1}.
[7] *R. P. Thummel, D. K. Kohli*, J. Org. Chem. *42*, 2743 (1977).
[8] For an independent synthesis of *(2)*, see *R. P. Thummel, D. K. Kohli*, Tetrahedron Lett. *1979*, 143.

Cyanohalophosphates(III)—Hypervalent Anions Containing λ^5-Phosphorus(III)[**]

By *Alfred Schmidpeter* and *Franz Zwaschka*[*]

One of the typical reactions of halide ions is their combination with a halogen molecule X_2 to give the linear trihalide ions X_3^-. If different halogen atoms are involved, then the more electropositive one assumes the central position[2]. In accord with its postulated pseudohalogen character[1], the dicyanophosphide ion *(1)* adds bromine and iodine at room temperature to give anions *(3)* of X_3^- type with $P(CN)_2$ as central member. These hypervalent anions are dicyanodihalophosphates(III). Their crown ether-sodium salts can be isolated in crystalline form.

Oxidative addition of halogen to *(1)* can be resolved, at least formally, into two steps:

$$\underset{(1)}{P(CN)_2^-} + X_2 \rightarrow \underset{(2)}{P(CN)_2X} + X^- \rightarrow \underset{(3)}{P(CN)_2X_2^-}$$

It is surprising that the reaction does not lead merely to dicyanohalophosphanes *(2)* but beyond that to the hypervalent species *(3)*[3]. The ion *(3)*, X = Br or I, does not dissociate in solution, as is apparent from the characteristic upfield shift of the ^{31}P-NMR signal (see Table 1). Under the same conditions, addition of chlorine to *(1)* gives only *(2)*, X = Cl.

Addition of cyanogen bromide or iodide instead of halogens gives the tricyanohalophosphates(III) *(4)*, X = Br or I.

$$\underset{(1)}{P(CN)_2^-} + XCN \rightarrow \underset{(4)}{P(CN)_3X^-}$$

These results suggest that phosphorus tricyanide *(5)* ≅ *(2)*, X = CN, might add halide ions to form the hypervalent anions *(4)*:

$$\underset{(5)}{P(CN)_3} + X^- \rightleftharpoons \underset{(4)}{P(CN)_3X^-}$$

Compound *(5)* does indeed react with crown ether-sodium chloride, bromide, and iodide to form mobile equilibria with *(4)* (NMR spectroscopy). The chemical shift δ^{31}P decreases linearly with addition of halide until the equivalence point is reached, and then stays essentially constant. All the equilibria (including that with X = Cl) lie far to the right, and all three crown ether-sodium salts can also be isolated as crystals.

[*] Prof. Dr. A. Schmidpeter, Dipl.-Chem. F. Zwaschka
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

[**] Cyanophosphorus Compounds, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 1: [1].

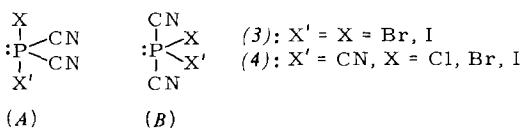
© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0411 $ 02.50/0

Table 1. δ^{31}P data for *(2)*, *(3)*, and *(4)* (in tetrahydrofuran, with H_3PO_4 as standard).

X	*(2)*	*(3)*	*(4)*
Cl	−32 −33.5 [4]		−176
Br	−64.2 [4]	−165	−182
I	−115.8 [4]	−172	−164

In spite of the interest in hypervalent phosphorus(III) compounds as substitution intermediates[5], little is known about their geometry. Although it has not been established to what extent the phosphorus lone pair is sterically effective in *(3)* and *(4)*, we assume a pseudotrigonal-bipyramidal ligand arrangement in these species. The νCN values fail to show any more extensive shift of charge from P to CN than already exists in *(1)*.

There are two possible ligand distributions, *viz. (A)* and *(B)*:



(A) *(B)*

(3): X′ = X = Br, I
(4): X′ = CN, X = Cl, Br, I

Since two CN bands generally appear in the IR spectrum (solid state), *(B)* can be ruled out. The bent $P(CN)_2$ arrangement of *(1)* is retained in *(A)*, which corresponds to the linear structure of a trihalide and is in accord with the structure of $(SeCN)_3^-$ in particular[2].

Procedure

Synthesis of [18]crown-6·Na^+·*(3)*: Solutions of [18]crown-6-sodium dicyanophosphide (20 mmol) and bromine or iodine (20 mmol) in tetrahydrofuran (THF) (20 ml each) are united. The color of the halogen disappears instantaneously and almost completely; only near completion of addition of iodine does the solution remain reddish brown. After evaporation to about half the original volume *in vacuo* and standing for several days at −20 °C, the salt of *(3)* crystallizes. A further crop can be isolated by diluting the mother liquor with diethyl ether. The crystals become opaque *in vacuo*: initially blue-black crystals of the complex of *(3)*, X = I, release iodine and turn pale yellow; 40—85 % yield.

Synthesis of [18]crown-6·Na^+·*(4)*: Solutions of $P(CN)_3$ (10 mmol) in THF (20 ml) and of [18]crown-6-sodium bromide or iodide (10 mmol) in acetonitrile (30 ml) are combined and evaporated to dryness *in vacuo*. The residue is taken up in THF (50 ml), and diethyl ether is added to the solution until it becomes turbid. On cooling to −20 °C the salt of *(4)* precipitates as colorless crystals; yield 40—90 %. For X = Cl, a suspension of finely powdered NaCl in THF and an equivalent amount of crown ether are used. The mixture is filtered after 2d and then evaporated down to half its volume; the initial unidentified fraction is separated off and the solution evaporated to dryness. The residue crystallizes on dissolution in a small volume of THF; yield 20 %. All the crystals turn opaque *in vacuo*.

Received: January 10, 1979 [Z 206a IE]
German version: Angew. Chem. *91*, 441 (1979)

CAS Registry numbers:
[18]crown-6·Na^+·*(3)*, X = Br, 70024-16-7; [18]crown-6·Na^+·*(3)*, X = I, 70024-18-9; [18]crown-6·Na^+·*(4)*, X = Cl, 70024-20-3; [18]crown-6·Na^+·*(4)*, X = Br, 70024-22-5; [18]crown-6·Na^+·*(4)*, X = I, 70024-24-7; [18]crown-6-sodium dicyanophosphide, 70096-16-1; $P(CN)_3$, 1116-01-4; [18]crown-6-sodium bromide, 70024-25-8; [18]crown-6-sodium iodide, 70024-26-9; [18]crown-6-sodium chloride, 63889-63-4

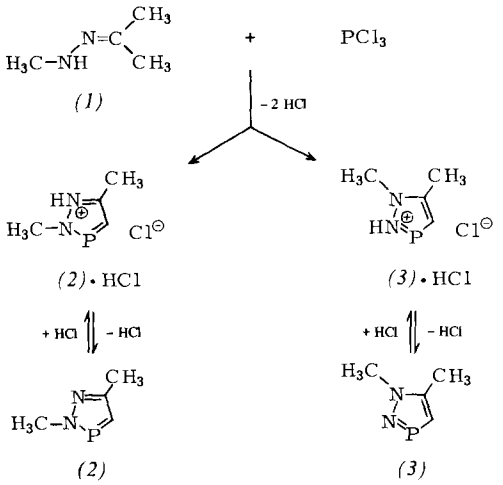
[1] *A. Schmidpeter, F. Zwaschka*, Angew. Chem. *89*, 747 (1977); Angew. Chem. Int. Ed. Engl. *16*, 704 (1977).
[2] Trihalide ions involving a pseudohalogen are still very rare; only (NCSe—SeCN—SeCN)$^-$ is known to contain a central pseudohalogen. *S. Hauge*, Acta Chem. Scand. *25*, 3081 (1971).
[3] The only hypervalent phosphorus(III) compounds known so far are PX_3NMe_3: *R. R. Holmes, R. P. Wagner*, Inorg. Chem. *2*, 384 (1963), and references cited therein; PBr_4^-: *K. B. Dillon, T. C. Waddington*, Chem. Commun. *1969*, 1317.
[4] *K. B. Dillon, M. G. C. Dillon, T. C. Waddington*, J. Inorg. Nucl. Chem. *38*, 1149 (1976).
[5] *R. F. Hudson*, Pure Appl. Chem., Add. Publ. *4*, 81 (1974); *E. P. Kyba*, J. Am. Chem. Soc. *98*, 4805 (1976).

1*H*-1,2,3σ^2-Diazaphospholes — Bond Delocalization in σ^2-Phospholes[**]

By *Josef Helmut Weinmaier, Jörg Luber, Alfred Schmidpeter*, and *Siegfried Pohl*[*]

1*H*- and 2*H*-1,2,3σ^2-diazaphospholes [like *(3)* and *(2)*] having localized π-bonds would correspond to imino- and methylene-phosphanes, respectively, and should accordingly differ in their chemical and physical properties. These differences should diminish if the diazaphospholes qualify as "good phosphapyrazoles", *i.e.* pyrazoles whose 6π delocalization is not interrupted by the σ^2-phosphorus.

So far, only 2*H* isomers such as 2,5-dimethyl-2*H*-1,2,3σ^2-diazaphosphole *(2)*[1] have been reported. This is formed *via* the hydrochloride by condensation of acetone methylhydrazone *(1)* with PCl_3. We have now found that the 1*H* isomer *(3)* is also formed to a lesser extent in this reaction. It can be separated by virtue of its higher boiling point. Subsequent rearrangement of *(2)* to *(3)* was impossible.



(1) + PCl_3 − 2 HCl

(2)·HCl *(3)*·HCl

+ HCl ⇅ − HCl

(2) *(3)*

Reaction of cyclopentanone methylhydrazone and PCl_3 likewise gave not only *(4)*[1] but also a comparable amount of the isomer *(5)*. Separation was possible by fractional sublimation of the hydrochlorides.

[*] Prof. Dr. A. Schmidpeter, Dr. J. H. Weinmaier, Dr. J. Luber
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Dr. S. Pohl
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld 1 (Germany)

[**] Four- and Five-Membered Phosphorus Heterocycles, Part 35. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 34: *A. Schmidpeter, Th. v. Criegern*, Z. Naturforsch. *33b*, 1330 (1978).

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0412 $ 02.50/0*

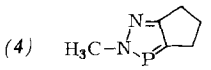
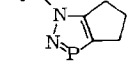
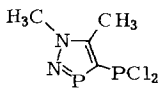
(4)  (5) 

Table 1. Chemical shifts (downfield shifts positive) and coupling constants J [Hz] in $CDCl_3$ (standard: ^{31}P-NMR, H_3PO_4; ^1H-NMR, TMS).

	(3)·HCl	(5)·HCl	(3)	(5)
$\delta^{31}P$	211.0	195.2	223.0	204.1
$\delta^1H(NCH_3)$	4.47 (d)	4.42 (d)	3.86 (d)	3.81 (d)
J_{PNNCH}	2.1	2.6	1.1	1.4
$\delta^1H(CCH_3)$	2.73 (d)		2.38 (d)	
J_{PCCCH}	1.7		1.8	
$\delta^1H(CH)$	8.00 (d)		7.22 (d)	
J_{PCH}	40.2		32.0	

The ^{31}P downfield shift of *(3)* and *(5)* (Table 1) is characteristic of σ^2-phospholes; it approaches the value for *(2)* and *(4)* (228.9 and 204.4, respectively)[1]. While addition of HCl leads to a further downfield shift in the case of *(2)* and *(4)*, an upfield shift is observed for *(3)* and *(5)*. A slight increase in the bond angle at phosphorus due to protonation at N-1 is also observed in *(2)* and *(4)*[2]; this angle should decrease on protonation of *(3)* and *(5)* at N-2. The positions of the methyl groups are established by the phosphorus coupling. The PCH coupling constant in *(3)* is considerably smaller than in *(2)* (43.7 Hz)[1]; the difference expectedly vanishes in the hydrochlorides.

(3) + PCl_3 $\xrightarrow[-HCl]{}$  *(6)*

Like *(2)*, compound *(3)* can be substituted by PCl_3 at C-4[3] to form the dichlorophosphino derivative *(6)* [$\delta^{31}P = 230.5$ (σ^2P), 157.0 (σ^3P), $J_{PCP} = 52.0$ Hz].

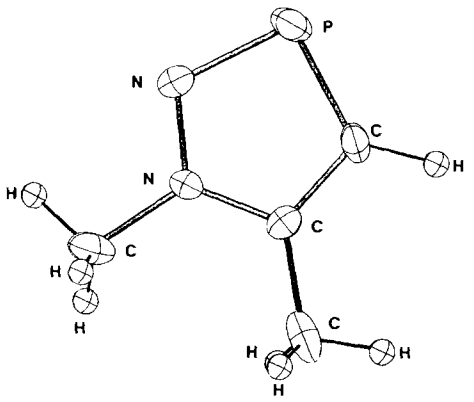


Fig. 1. 1,5-Dimethyl-1*H*-1,2,3σ^2-diazaphosphole *(3)* in the crystalline state at −130°C; vibrational ellipsoids represent 50% probability (except for H atoms) [4]. Bond angles [°] and lengths [pm] in the ring:

NPC	92.9(2)	PN	165.4(3)
PCC	109.3(3)	PC	172.3(3)
CCN	110.6(3)	CC	138.1(5)
CNN	117.0(3)	CN	135.6(4)
NNP	110.2(2)	NN	133.0(4)

Comparison of the molecular structure of *(3)* (Fig. 1) with that of 2*H*-diazaphospholes[2, 5] clearly reveals the shift of the double bond by way of the shortening of the PN and lengthening of the PC bond. However, the differences (about 2 pm) are only about as large as those between the formal C—N/C=N and the C—C/C=C bonds in pyrazole[6]; this suggests similar delocalization in the diazaphospholes. In acyclic σ^2P systems, on the other hand, the P—N/P=N difference is some 12 pm[7, 9] and the P—C/P=C difference some 15 pm[8, 9].

Procedure

Compound *(1)* (43 g, 0.5 mol) is allowed to react with PCl_3 (344 g, 2.5 mol) (for procedure, see [1]). The crude mixture of hydrochlorides is suspended in benzene (300 ml) and triethylamine (50.5 g) is added with vigorous stirring. The triethylammonium chloride is separated off after 2 h, the benzene is stripped off, and the residue is fractionated: 31.1 g (54%) *(2)* at 45—60°C/80—90 mbar; 6.7 g (12%) *(3)* at 40—50°C/10^{-3} mbar, m.p. ≈30°C.

The mixture of hydrochlorides obtained in a similar manner from cyclopentanone methylhydrazone (28 g, 0.25 mol) and PCl_3 (172 g, 1.25 mol) is sublimed: 17.6 g (40%) of *(4)*·HCl at 60°C (bath temperature); 22.0 g (50%) of *(5)*·HCl at 100°C (bath temperature)/10^{-3} mbar; m.p. 156—158°C. *(5)* is liberated therefrom as above: b.p. 82°C/0.2 mbar.

Received: February 22, 1979 [Z 206b IE]
German version: Angew. Chem. *91*, 442 (1979)

CAS Registry numbers:
(1), 5771-02-8; *(2)*, 58298-51-4; *(3)*, 69991-36-2; *(3)*·HCl, 69991-37-3; *(4)*·HCl, 58298-52-5; *(5)*, 69991-38-4; *(5)*·HCl, 69991-39-5; PCl_3, 7719-12-2; cyclopentanone methylhydrazone, 2646-33-5

[1] *J. Luber, A. Schmidpeter*, Angew. Chem. *88*, 91 (1976); Angew. Chem. Int. Ed. Engl. *15*, 111 (1976).
[2] *P. Friedrich, G. Huttner, J. Luber, A. Schmidpeter*, Chem. Ber. *111*, 1558 (1978).
[3] *J. Luber, A. Schmidpeter*, J. Chem. Soc. Chem. Commun. *1976*, 887.
[4] Cell data at −130°C: $a = 734.2(3)$, $b = 742.1(3)$, $c = 1102.5(6)$ pm, $\beta = 103.40(2)°$, $V = 584 \times 10^6$ pm^3, $Z = 4$; space group: $P2_1/n$; 920 independent reflections, of which 815 were observed; $R_1 = 0.049$; Syntex $P2_1$ diffractometer, Syntex XTL program system.
[5] *V. G. Andrianov, Yu. T. Struchkov, N. I. Shvetsov-Shilovskii, N. P. Ignatova, R. G. Bobkova, N. N. Melnikov*, Dokl. Akad. Nauk SSSR *211*, 1101 (1973).
[6] *T. La Cour, S. E. Rasmussen*, Acta Chem. Scand. *27*, 1845 (1973) and earlier determinations.
[7] *S. Pohl*, Angew. Chem. *88*, 723 (1976); Angew. Chem. Int. Ed. Engl. *15*, 687 (1976); Z. Naturforsch. *32b*, 1342 (1977).
[8] *G. Becker, O. Mundt*, Z. Anorg. Allg. Chem. *443*, 53 (1978).
[9] Compared to the bond lengths in acyclic σ^2P systems, the PN bonds of azaphospholes are long and the PC bonds short.

syn-Anthracene 4a,10:9,9a-Dioxide

By *Jean Rigaudy, Albert Defoin*, and *Joële Baranne-Lafont*[*]

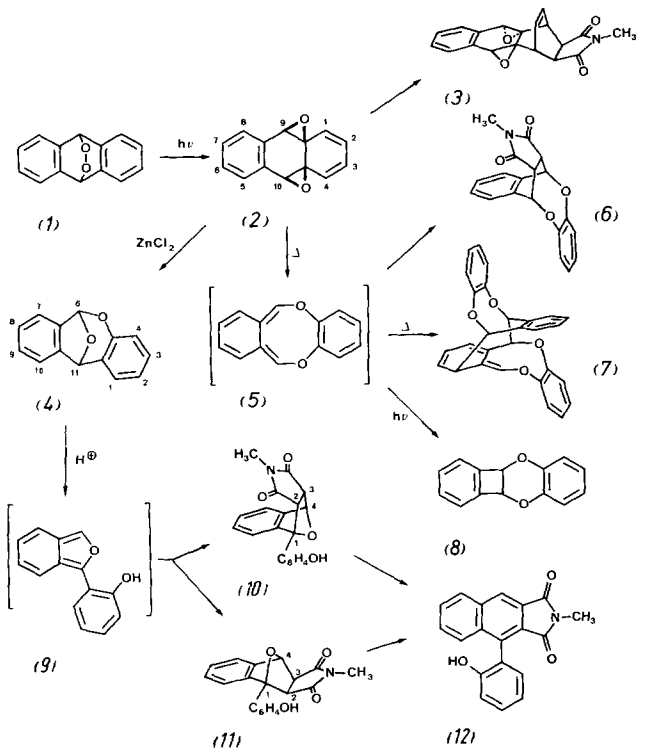
Dedicated to Professor Egbert Havinga on the occasion of his 70th birthday

The rearrangement of epidioxides (endoperoxides) to compounds having two epoxide groups is a well-known reaction in cycloalkadiene chemistry; it can be induced either thermally or photochemically[1]. Thermolabile 1,4-endoperoxides of anthracenes (and naphthalenes) with bridgehead alkoxy groups have also been shown to give isolable isomeric dioxides on irradiation[2]. In contrast, dioxides could not be isolated on rearrangement of *meso*-endoperoxides (*e.g.* 9,10-anthracene endoperoxide) but only trapped with dienophiles such as *N*-methylmaleimide (NMM). This is exemplified by the rather unstable diepoxide arising from 9,10-diphenyl-9,10-anthracene endoperoxide by photoisomerization[3], and most clearly by the *syn*-dioxide *(2)* which is the primary product of thermal

[*] Prof. J. Rigaudy, A. Defoin, J. Baranne-Lafont
Laboratoire de Recherches Organiques de l'ESPCI
et de l'Université Pierre et Marie Curie
10, rue Vauquelin, F-75231 Paris Cedex 05 (France)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0413 $ 02.50/0*

isomerization of 9,10-anthracene endoperoxide *(1)*. At the temperature required for reaction, *(2)* affords the dimer *(7)* or the tetracyclic compound *(8)* *via* the *o*-quinodimethane diether *(5)*[4].



It has now proved possible to prepare the dioxide *(2)* by prolonged irradiation of *(1)* with light of wavelength $\lambda > 435$ nm.

A solution of *(1)* (0.5 g, 2.4 mmol) in dry benzene (120 ml) is irradiated in a water-cooled Pyrex flask at 5—6 °C for 40 h with an external xenon lamp (Philips CSX 1600 W); wavelengths below $\lambda = 435$ nm are cut off by a Schott GG 455 filter[5]. After irradiation, a small amount of sodium carbonate is added, and the mixture is shaken, filtered, and cooled until it freezes. The solvent is stripped off at 0.5 torr. The residual colorless flakes are washed twice with cold benzene and once with cold ether; yield 0.39 g (78 %) of dioxide *(2)* (Table 1). Compound *(2)* prepared in this way is pure and must be stored at −20 °C.

Dropwise addition of *(2)* to boiling benzene leads instantaneously to the dimer *(7)*[4] (yield 70 %). In the presence of NMM [1.1 mol per mol of *(2)*] a mixture of *(3)* (8 %) and *(6)* (79 %) results; thermal isomerization of *(1)* under the same conditions leads to the same mixture[4]. The half-lifetime of *(2)* is 6.5 h at 28 °C. Thus *(2)* is less stable than benzene dioxide[6].

Addition of protic acids or Lewis acids to *(2)* effects immediate isomerization. Thus *(2)* is transformed by picric acid or $ZnCl_2$ (in dry benzene) into the bicyclic acetal *(4)* (Table 1). Acetals of this type have already been obtained from 9,10-disubstituted 9,10-anthracene endoperoxides[7]. Strong acids such as trifluoroacetic acid isomerize *(4)* further to the unstable isobenzofuran derivative *(9)* which can be trapped with NMM in chloroform [1.5 mol NMM per mol of *(9)*] as a mixture of *endo*- and *exo* adducts [*(10)* and *(11)* respectively] with the *in-situ* dehydration product *(12)*[8] (Table 1).

Table 2. Yields [%] of compounds isolated after photoisomerization of *(1)*; c = 20 mmol l^{-1} in benzene, 10—15 °C; source, Philips S.P.500; $\lambda > 435$ nm; irradiation time, 40 h. NMM = *N*-methylmaleimide, An = anthraquinone, Hy = 10-hydroxyanthrone.

Run	NMM [a]	Yield [%] *(1)*	*(2)*	*(3)*	*(6)*	*(7)*	*(8)*	An	Hy
1	3 [b]	—	—	94	2	—	—	3	1
2	3 [c]	9	—	64	1	—	4	4	—
3	0	—	60	13 [d]	—	—	4	6	—
4 [e]	0	—	83	7.5 [d]	—	—	2.5	2	1

[a] Moles of NMM per mole of *(1)*. [b] NMM added prior to irradiation. [c] NMM added after irradiation. [d] With addition of NMM to the mother liquors after isolation of *(2)*. [e] Irradiation carried out at 5—6 °C, source, Philips CSX 1600 W xenon lamp.

The results obtained under various irradiation conditions are compiled in Table 2. It is seen that the behavior of *meso*-acene endoperoxides such as *(1)* closely parallels that of endoperoxides of cyclic dienes as long as retrodienic dissociation remains unimportant[1].

Received: November 28, 1978 [Z 197 IE]
German version: Angew. Chem. *91*, 443 (1979)

CAS Registry numbers:
(1), 4741-24-6; *(2)*, 69961-07-5; *(3)*, 66964-85-0; *(4)*, 69927-54-4; *(6)*, 42896-22-0; *(7)*, 67042-83-5; *(8)*, 42896-18-4; *(10)*, 69927-55-5; *(11)*, 69979-94-8; *(12)*, 69927-56-6

Table 1. Physical data of the new compounds.

	Yield [%]	M.p. [°C]	UV [a] λ [nm] (logε)	IR [b] [cm^{-1}]	^{1}H-NMR (δ values) [c]
(2)	78	145—150 (dec.)	284.5 (3.49), 278.5 (3.51), 273 (3.48)		5.61 (H-1,4, m), 6.34 (H-2,3, m), 4.07 (H-9,10, s), 7.65 (H-5,8, m), 7.46 (H-6,7, m); $J_{1,2} = 9.7$, $J_{1,3} = 1.1$, $J_{1,4} = 0.9$, $J_{2,3} = 5.8$, $J_{5,6} = 7.65$, $J_{5,7} = 1.2$, $J_{5,8} = 0.5$, $J_{6,7} = 7.6$ Hz
(4)	55 68	100—101	285.5 (3.52), 278 (3.48)	1610, 1602, 1580	7.07, 6.82, 7.12, 6.69 (ABCD-spectrum, H-1,2,3,4, m), 6.65 (H-6, s), 5.81 (H-11, s), 7.48, 7.26, 7.27 (H-7,(8,9),10, m); $J_{1,2} = 7.4$, $J_{1,3} = 1.7$, $J_{1,4} = 0.4$, $J_{2,3} = 7.6$, $J_{2,4} = 1.1$, $J_{3,4} = 8.2$ Hz
(10)	34	188.5—189.5	283 (3.47), 276 (3.50)	3380, 3340, 1780, 1710, 1620	4.07, 4.00, 5.98 (ABX spectrum, H-2,3,4), 2.45 (N—Me, s), 7.55 (OH-2', s), 8.28 (H-6', m), 7.2 ± 0.2 (7 H_{ar}, m); $J_{2,3} = 8.5$, $J_{3,4} = 5.9$ Hz
(11)	10	273—274	281 (3.35), 272.5 (3.40), 271 (3.39)	3420, 1765, 1680, 1610	3.95 (H-2, d), 3.23 (H-3, d), 5.91 (H-4, s), 2.98 (N—Me, s), 7.3 ± 0.4 (8 H_{ar}, m); $J_{2,3} = 6.8$, $J_{3,4} = 0$ Hz
(12)	10—20	273—274	357 (3.61), 340 (3.51), 292 (3.93), 257 (4.77)	3360, 1758, 1710, 1610, 1600	8.38 (H-4, s), 3.15 (N—Me, s), 7.6 ± 0.5 (8 H_{ar}, m)

[a] In diethyl ether. [b] In Nujol. [c] In $CDCl_3$; TMS internal standard.

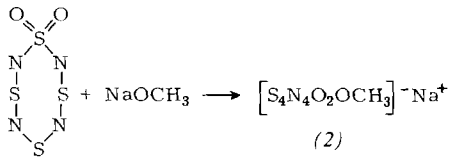
© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0414 $ 02.50/0

[1] *W. Adam*, Angew. Chem. *86*, 683 (1974); Angew. Chem. Int. Ed. Engl. *13*, 619 (1974).
[2] *J. Rigaudy, N. C. Cohen, Nguyen Kim Cuong*, C. R. Acad. Sci. *264C*, 1851 (1967); *J. Rigaudy, C. Delétang, J. J. Basselier, ibid. 268C*, 344 (1969).
[3] *J. Rigaudy, C. Brelière, P. Scribe*, Tetrahedron Lett. *1978*, 687.
[4] *J. Rigaudy, J. Baranne-Lafont, A. Defoin, Nguyen Kim Cuong*, C. R. Acad. Sci. *280C*, 527 (1975); Tetrahedron *34*, 73 (1978); *A. Defoin, J. Baranne-Lafont, J. Rigaudy, J. Guilhem, ibid. 34*, 83 (1978).
[5] At wavelengths *below* $\lambda = 435$ nm, *(1)* gives mainly anthraquinone and its derivatives instead of *(2)* (*N. Sugiyama, M. Iwata, M. Yoshioka, K. Yamada, H. Aoyama*, Chem. Commun. *1968*, 1563). In solvents such as toluene, acetone, tetrahydrofuran, CH_2Cl_2, or CS_2, the yield of *(2)* falls considerably in favor of these compounds.
[6] *H.-J. Altenbach, E. Vogel*, Angew. Chem. *84*, 985 (1972); Angew. Chem. Int. Ed. Engl. *11*, 937 (1972); the half-lifetime of *syn*-benzene dioxide calculated for 28 °C is 112 h.
[7] a) *J. Rigaudy, M. Moreau, Nguyen Kim Cuong*, C. R. Acad. Sci. *274C*, 1589 (1972); b) *J. Rigaudy, D. Sparfel*, Tetrahedron *34*, 113 (1978); c) *34*, 2263 (1978). Supporting evidence for the structure of *(4)* came from comparison of spectral data with those of the 6,11-dimethyl derivative [7a] and of the naphthacene homolog [7b].
[8] The configurations of *(10)* and *(11)* were deduced by comparison of the NMR data with those of analogous compounds, cf. *R. N. Warrener*, J. Am. Chem. Soc. *93*, 2346 (1971); *M. P. Cava, N. M. Pollack, O. A. Mamer, M. J. Mitchell*, J. Org. Chem. *36*, 3932 (1971); *U. E. Wiersum, C. D. Eldred, P. Vrijhof, H. C. van der Plas*, Tetrahedron Lett. *1977*, 1741.

SN Ring with Di-, Tri-, and Tetra-Coordinated Sulfur Atoms by Nucleophilic Substitution[**]

By *Herbert W. Roesky, Michael Witt, Bernt Krebs*, and *Hans-Jürgen Korte*[*]

Although the chemistry of cyclic sulfur-nitrogen compounds has long been a topic of study, nucleophilic substitution reactions have remained in the realm of speculation[1]. We have now succeeded, for the first time, in trapping the product of such a reaction of the S_4N_4 derivative *(1)*[2] with sodium methoxide and isolating it.



(1)

$$+ \ NaOCH_3 \longrightarrow \underset{(2)}{\left[S_4N_4O_2OCH_3\right]^-Na^+}$$

Which atom of the ring system suffers nucleophilic attack? The electron-withdrawing action of the SO_2 group would strongly suggest that this role is assumed by the adjacent sulfur atoms. A corresponding charge distribution also results from a CNDO/2 calculation, in which the S_3N_4 structure is regarded as a 10π-electron system coupled to an SO_2 group[3]. On the other hand, electron density changes are known to be favored in SN systems when the sulfur and nitrogen atoms are di-coordinated. Thus the sulfur atom most distant from the SO_2 might also be attacked by the nucleophile; the resulting product would then have a symmetrical electron distribution. The sodium of salt *(2)* was replaced by a tetraphenylphosphonium ion for single crystal structure analysis.

$[(C_6H_5)_4P]^+[S_4N_4O_2(OCH_3)]^-$ forms monoclinic crystals (space group $P2_1/n$) with $a = 15.866(8)$, $b = 11.277(6)$, $c = 15.907(8)$ Å, $\beta = 108.78(4)°$, $Z = 4$. X-Ray structure analysis (diffractometer data, $R = 4.7\,\%$) gave a conformation of the eight-membered ring resembling that of S_4N_4 and revealed almost ideal C_s symmetry of the anion, in which one of the two transannular interactions (2.482(2) Å) is still present (Fig. 1). The S_4N_4 skeleton can therefore be regarded as consisting of two annelated five-membered rings with a weak central S—S bond. The bond angles in the ring are ($\sigma = 0.2°$): N—$S(O_2)$—N 101.7, N—S—N 116.6 (average value), N—S(OR)—N 107.1, $S(O_2)$—N—S 116.0 (average value), S(OR)—N—S 122.9° (average value). Many reactions in the SN field can readily be explained on the basis of this contribution.

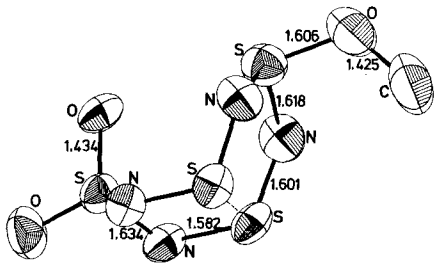


Fig. 1. Structure of the $[S_4N_4O_2(OCH_3)]^-$ ion in the crystal, bond lengths in Å ($\sigma = 0.002$—0.006 Å).

Procedure

A solution of $NaOCH_3$ (0.02 mol) in a small volume of methanol is added dropwise to a cooled suspension of *(1)* (0.02 mol) in anhydrous methanol (50 ml). The reaction product *(2)* can be isolated from the deep-violet mixture either by precipitation with benzene or by crystallization at −70 °C. The reaction is practically quantitative.—The salt *(2)* can be converted into the corresponding phosphonium salt by treatment with tetraphenylphosphonium chloride in methanol or cold water; this salt was purified by recrystallization from methanol at −70 °C (yield 60 %).

Received: January 15, 1979 [Z 209 IE]
German version: Angew. Chem. *91*, 444 (1979)

[1] *H. W. Roesky, M. Witt, M. Diehl, J. W. Bats, H. Fuess*, Chem. Ber., in press.
[2] *H. W. Roesky, W. Schaper, O. Petersen, T. Müller*, Chem. Ber. *110*, 2695 (1977).
[3] Calculations performed by Prof. *C. Furlani*, Rome.

[*] Prof. Dr. H. W. Roesky, Dipl.-Chem. M. Witt
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. B. Krebs, Dipl.-Chem. H. J. Korte
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

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

$(-)_{579}$-Bis[(*S*)-(+)-*O,O'*(1,1'-binaphthyl-2,2'-diyl)-dithiophosphato]nickel(II) — The First Dithiophosphato Complex to Have Axial Chirality

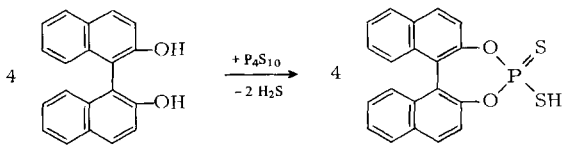
By *Ernst W. Hoffmann, Wilhelm Kuchen, Wolfgang Poll*, and *Hartmut Wunderlich*[*]

Metal complexes of dithiophosphoric acids $[(RO)_2P(S)S]M/n$ and dithiophosphinic acids $[R_2P(S)S]M/n$ are of interest mainly on account of their potential industrial applications[1], *e.g.* as additives to mineral oils[2], and have proved to be valuable adsorbents for chromatographic separation of Lewis bases[3]. We have now obtained the first axially chiral complex of this class in optically active form, *viz.* the title compound, and determined its absolute configuration by X-ray structure analysis.

[*] Prof. Dr. W. Kuchen, Dipl.-Chem. E. W. Hoffmann, Dr. H. Wunderlich, W. Poll
Institut für Anorganische Chemie und Strukturchemie der Universität
Universitätsstrasse 1, D-4000 Düsseldorf (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* 0570-0833/79/0505-0415 $ 02.50/0

Reaction of stoichiometric amounts of tetraphosphorus decasulfide and the axially chiral compound 2,2'-dihydroxy-1,1'-binaphthyl *(1)* in boiling chlorobenzene (1 h) gives *O,O'*-(1,1'-binaphthyl-2,2'-diyl)dithiophosphoric acid ("bndtpH") *(2)*, m. p. 242—243 °C (toluene/hexane), in about 80 % yield.



(1) *(2)*

Fractional crystallization of the (+)-methylbenzylammonium ("MBA") salt of the racemic acid *(2)* from isopropyl alcohol/water (1:3, v/v) permitted its resolution into the less soluble (+)MBA-(+)bndtp *(3a)* and its diastereomer (+)MBA-(−)bndtp *(3b)* from which the enantiomeric acids (+)-*(2)* and (−)-*(2)* could be liberated by the action of 8 N HCl. The ORD spectrum of (+)-*(2)* showed a negative Cotton effect at $\tilde{\nu}=35000\,cm^{-1}$, which suggested that this enantiomer has the (*S*) configuration[4, 5].

Reaction of *(3a)* and nickel(II) acetate in glacial acetic acid afforded the title compound (*S,S*)-*(4)* (Fig. 1), whose absolute ligand configuration could be confirmed by X-ray methods.

Hence it follows that the rules proposed by *Mislow, Djerassi, et al.*[4] for the configurational assignment of variously bridged biaryls on the basis of their ORD spectra are also applicable to [*d,f*]-annelated 1,3,2-dioxaphosphepin derivatives.

Acid-catalyzed trans-esterification with isopropyl alcohol[6] transforms *(3b)* in essentially quantitative yield into optically pure (*R*)-(+)-2,2'-dihydroxy-1,1'-binaphthyl (+)-*(1)*[7], m. p. 207—209 °C, $[\alpha]^{25}=+33°$ ($c=0.103$, THF), which thus becomes readily accessible.

Synthesis and crystal structure analysis of (S,S)-(4)

A 0.1 M solution of nickel(II) acetate in glacial acetic acid (1 ml) is added to a solution of optically pure MBA salt *(3a)*, $[\alpha]_{578}^{25}=+1404°$ ($c=0.01$, ethanol) (100 mg, 0.2 mmol) in the same solvent (10 ml). The precipitate of (*S,S*)-*(4)* formed in *ca.* 80 % yield is purified by dissolution in a small volume of hot toluene and, after filtration, reprecipitation by addition of hexane. Diamagnetic, brownish violet crystals which darken above *ca.* 320 °C. ^{31}P-NMR ($CDCl_3$, $c=0.1$ %): $\delta_P=+104.0$; $[\alpha]^{25}$ ($c=0.0187$ and 0.00187, $CHCl_3$; λ [nm] in parentheses): +57° (750), −600° (579), −96° (500), −17700° (330), +44000° (280); UV/VIS: $\tilde{\nu}$ (logε): 14000 (1.98), 18700 (2.05), 25500 (3.05, sh), 31400 (4.69) cm^{-1}.

The nickel complex forms rhombic crystals, space group $P2_12_12_1$ (D_2^4), $a=963.0(3)$, $b=1017.1(4)$, $c=3748.9(13)$ pm, $Z=4$, $\rho=1.48$ mg/mm^3. The crystal structure was determined from diffractometer data ($Cu_{K\alpha}$ radiation, ω scan, 2928 significant reflections) and refined to an *R* value of 0.053. The absolute configuration could be unequivocally determined by considering the anomalous dispersion of the Ni, P, and S atoms (Fig. 1).

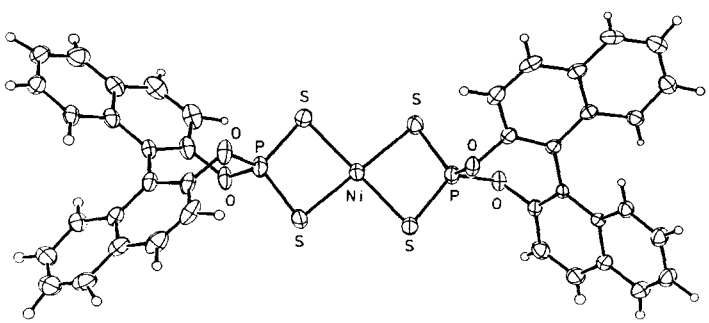


Fig. 1. Molecular structure [8] of (−)$_{579}$-bis[(*S*)-(+)-*O,O'*-(1,1'-binaphthyl-2,2'-diyl)dithiophosphato]nickel(II), (*S,S*)-*(4)* in the crystal.

The Ni atom is in a square-planar environment of four S atoms. The average bond lengths and angles in the four-membered rings are: Ni—S 224.1 and P—S 197.0 pm, and SNiS 89.5, NiSP 81.0, and SPS 106.5°. In the two halves of the molecule, the dihedral angles at the CC bond linking the naphthyl groups are found to be +53.5 and +52.1°.

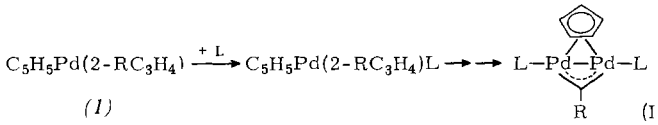
Received: January 30, 1979 [Z 211 IE]
German version: Angew. Chem. *91*, 448 (1979)

[1] *J. R. Wasson, G. M. Woltermann, H. J. Stoklosa*, Top. Curr. Chem. *35*, 65 (1973); *W. Kuchen, H. Hertel*, Angew. Chem. *81*, 127 (1969); Angew. Chem. Int. Ed. Engl. *8*, 89 (1969).
[2] *H. Bannuscher, M. Rossenbeck, U. Hasserodt* in *J. Falbe, U. Hasserodt*: Katalysatoren, Tenside und Mineralöladditive. Thieme, Stuttgart 1978, p. 235.
[3] *J. Delventhal, H. Keck, W. Kuchen*, J. Chromatogr. *95*, 238 (1974); *W. Kuchen, R. Philipp*, Z. Anorg. Allg. Chem. *443*, 241 (1978); *W. Kuchen, H. F. Mahler*, Z. Naturforsch. *B33*, 1049 (1978).
[4] *K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, J. Weiss, C. Djerassi*; J. Am. Chem. Soc. *84*, 1455 (1962).
[5] *R. S. Cahn, C. Ingold, V. Prelog*, Angew. Chem. *78*, 413 (1966); Angew. Chem. Int. Ed. Engl. *5*, 385 (1966).
[6] *S. V. Larionov, L. A. Il'ina, V. E. Taraban'ko, L. A. Patrina*, Zh. Neorg. Khim. *20*, 1812 (1976).
[7] *E. P. Kyba, G. W. Gokel, F. de Jong, K. Koga, L. R. Sousa, M. G. Siegel, L. Kaplan, G. D. Y. Sogah, D. J. Cram*, J. Org. Chem. *42*, 4173 (1977).
[8] *C. K. Johnson* (1976). Program ORTEP II, ORNL-5138, Oak Ridge National Laboratory, Tenn., USA.

Structural Isomers of Palladium Complexes of Type $C_5H_5Pd(2\text{-}RC_3H_4)L$ — A Case of Simultaneous π/σ and σ/π Rearrangement of Two Organic Ligands[1]

By *Helmut Werner* and *Alfred Kühn*[*]

Synthesis of the dinuclear complexes *(3)* according to Scheme (I)[2a] involves a 1:1 adduct *(2)* which can be isolated in some cases[2]:



(1) (I) *(3)*

(2a), R = *t*Bu, L = $P(iPr)_3$
(2b), R = *t*Bu, L = $P(cC_6H_{11})_3$
(2c), R = *t*Bu, L = $P(tBu)Ph_2$
(2d), R = Me, L = $P(iPr)_3$
(2e), R = Me, L = $P(cC_6H_{11})_3$
(2f), R = Me, L = $P(cC_6H_{11})_2Ph$

Investigation of the properties and the structure of compounds *(2)* surprisingly revealed that the two organic ligands C_5H_5 and $2\text{-}RC_3H_4$ are coordinated to the metal in a differing fashion depending upon R and L.

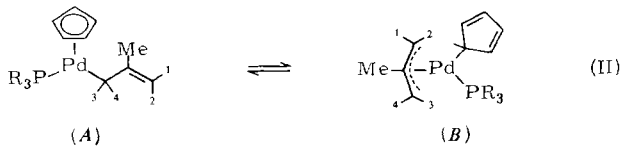
The ^{1}H-NMR spectra of the yellow crystalline complexes *(2a)*—*(2c)* show the cyclopentadienyl ligand to be *monohapto*- or σ-bonded and the allyl ligand to be *trihapto*- or π-bonded. The data of the allylic protons corresponds to those of the known compounds $(2\text{-}RC_3H_4)Pd(L)X$ (X=Cl,

[*] Prof. Dr. H. Werner, Dr. A. Kühn
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* 0570-0833/79/0505-0416 $ 02.50/0

Br, I)[3]. The C_5H_5 protons give rise to one sharp doublet (J_{PH} = 1.3—1.5 Hz) in the temperature range −60 to +90 °C, from which we deduce that *(2a)*—*(2c)* possess a fluxional structure *in solution*, *i.e.* undergo a very fast metallotropic rearrangement [migration of the (2-RC_3H_4)PdL group around the ring according to a 1,2-shift[4]]. The *monohapto* coordination of the cyclopentadienyl ring *in the crystal* has been established by X-ray structure analysis in the case of *(2a)*[5].

The room-temperature ^{1}H-NMR spectra of the complexes *(2d)*—*(2f)* closely resemble those of *(2a)*—*(2c)*. However, if their solutions in [D_8]toluene are cooled to −60 °C, the picture changes completely: *Two* signals now appear in the region of the C_5H_5 protons, and more than four signals for the protons of the allyl ligands. Detailed analysis of the low-temperature spectra demonstrates the presence of two isomers in equilibrium [eq. (II)].



(A) (B) (II)

Isomer *(A)* contains, together with L, a *pentahapto*-bonded cyclopentadienyl and a *monohapto*-bonded allyl ligand, resulting in an 18-electron configuration of the metal atom. In contrast, *(B)* has a *monohapto*-bonded five-membered ring and a *trihapto*-bonded allyl ligand, and the metal thus possesses a 16-electron configuration.

The intensity of the proton signals of *(A)* and *(B)* (Table 1) show that *(B)* predominates at −60 °C. This isomer ratio alters with rising temperature. Since the coalesced C_5H_5 proton signal observed at room temperature lies roughly half-way between the two peaks observed at −60 °C, we assume a 1:1 ratio of *(A)* and *(B)* to hold under these conditions. The data recorded for the allyl protons of *(2d)* at −60 and +35 °C support this result.

Detailed analysis of the C_5H_5 signal of *(2f)* at various temperatures (Table 2)[6] provided quantitative information about the ligand reorientation process of eq. (II).

π/σ rearrangements of organic ligands have repeatedly been observed both for π-cyclopentadienyl- and for π-allyl-metal complexes. Addition of a new ligand L to the metal is generally regarded as the initiating step. The reverse reaction is also known, *i.e.* rearrangement of a σ-C_5H_5 to a π-C_5H_5 ligand, and of a σ-2-RC_3H_4 to a π-2-RC_3H_4 ligand[7]. However, to our knowledge, the process described in eq. (II) is the first example of an isomerization reaction in which π/σ and σ/π rearrangement of a cyclopentadienyl ring and an allyl group, respectively, occur *simultaneously*.

Received: January 17, 1979 [Z 208 IE]
German version: Angew. Chem. *91*, 447 (1979)

CAS Registry numbers:
(2d)(A), 63511-32-0; *(2d)(B)*, 70072-33-2; *(2e)(A)*, 70072-34-3; *(2e)(B)*, 70072-35-4; *(2f)(A)*, 70072-36-5; *(2f)(B)*, 70101-45-0

[1] Studies on the Reactivity of Metal π-Complexes, Part 28. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 27: *H. Werner, A. Kühn*, Z. Naturforsch. *B33*, 1360 (1978).

[2] a) *H. Werner, D. Tune, G. Parker, C. Krüger, D. J. Brauer*, Angew. Chem. *87*, 205 (1975); Angew. Chem. Int. Ed. Engl. *14*, 185 (1975); *H. Werner, A. Kühn, D. J. Tune, C. Krüger, D. J. Brauer, J. C. Sekutowski, Yi-Hung Tsay*, Chem. Ber. *110*, 1763 (1977); b) *A. Kühn*, Dissertation, Universität Würzburg 1979.

[3] *J. Powell, B. L. Shaw*, J. Chem. Soc. *A1967*, 1839; *K. Vrieze, H. C. Volger, P. W. N. M. van Leeuwen*, Inorg. Chim. Acta Rev. 3, 109 (1969).

[4] *A. Bonny, S. R. Stobart, P. C. Angus*, J. Chem. Soc. Dalton Trans. *1978*, 938.

[5] *C. Burschka, A. Kühn, H. Werner*, unpublished.

[6] We thank Prof. *L. M. Jackman*, Pennsylvania State University, for the FORTRAN program DNRAX 1 to perform line shape analyses; it was adapted to a TR 440 computer.

[7] *F. A. Cotton, G. Wilkinson:* Advanced Inorganic Chemistry, 3rd Edit. Wiley-Interscience, New York 1972, Chap. 23.

Table 1. ^{1}H-NMR data of the complexes *(2d)*—*(2f)* at −60 °C in [D_8]toluene (δ values, TMS as int. standard, *J* in Hz).

	Ratio of isomers [a]	C_5H_5	H^1	H^2	H^3	H^4	Me
(2d)	*(A)*: 21	5.53 bs	5.05 s	4.75 bs	2.9 bs	2.9 bs	2.12 s
	(B): 79	6.42 bs	3.56 d J_{PH} = 9	—	1.81 s	2.54 s	1.49 s
(2e)	*(A)*: 18	5.66 bs	[b]	[b]	[b]	[b]	2.22 s
	(B): 82	6.60 bs	3.62 d J_{PH} = 10	—	[b]	2.59 s	1.54 s
(2f)	*(A)*: 21	5.67 bs	5.12 s	4.80 bs	2.3 bs	2.3 bs	2.18 s
	(B): 79	6.58 bs	3.72 d J_{PH} = 11	—	1.97 s	2.52 s	1.58 s

[a] Percentages of *(A)* and *(B)*, determined from the intensity ratio of the C_5H_5 signals.
[b] Signals not observed owing to insufficient solubility of the compound at −60 °C.

Table 2. Thermodynamic and kinetic data for the isomer equilibrium *(B)*⇌*(A)* of *(2f)*.

T[K]	p_A [a]	p_B	K	T[K]	k ((A)→(B)) [s^{-1}]	k ((B)→(A)) [s^{-1}]
213	0.21	0.79	0.26	233	10.4	23.7
233	0.26	0.74	0.35	242	27.8	52.6
245	0.28	0.72	0.39	255	69.4	146
260	0.32	0.68	0.46	265	422	599
273	0.48	0.52	0.94	275	1084	1267
292	0.58	0.42	1.39	287	2401	2243
308	0.61	0.39	1.53	297	3772	3025
335	0.70	0.30	2.33			

$\Delta H = 11.6 \pm 0.2$ kJ/mol
$\Delta S = 40.9$ J/mol·K
E_a ((B)→(A)) = 56.1 ± 1.5 kJ/mol
E_a ((A)→(B)) = 46.5 ± 1.5 kJ/mol

[a] The populations of the two isomers *(A)* and *(B)*, *i.e.* p_A and p_B, were determined from the relative intensities of the C_5H_5 signals of *(A)* and *(B)* below the coalescence point and from the position of the coalescence signal relative to the signals of *(A)* and *(B)* at −60 °C above the coalescence point. Division of p_A by p_B affords the equilibrium constant *K*.

© *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0505-0417 $ 02.50/0*

Catalysis of Hydrogen Formation from an Organic Radical in Aqueous Solution by Colloidal Silver[**]

By *Arnim Henglein*[*]

Reactions between free radicals in homogeneous solution, such as combination, disproportionation, and dismutation, proceed with minimum rearrangement. Such reactions are usually very fast. Organic radicals having a high negative redox potential[1] should be capable of reducing water or of eliminating hydrogen among themselves. Reactions of this kind have not yet been observed because they are too slow to compete with the above-mentioned radical-radical reactions.

It has now been found that 1-hydroxy-1-methylethyl radicals form hydrogen in the presence of colloidal silver Ag_n in aqueous solution:

$$2(CH_3)_2\dot{C}OH \xrightarrow{Ag_n} 2(CH_3)_2CO + H_2 \quad (1)$$

The yellow colloidal silver was produced by complete reduction of 5×10^{-4} M Ag^+[2], the solution also containing 1×10^{-3} M sodium dodecylsulfate as stabilizer. In order to generate the organic radicals, acetone and 2-propanol (each 0.1 M) are added and the solution exposed to γ-radiation with exclusion of air. The primary radicals resulting from radiolysis of the water react under these conditions according to

$$e_{aq}^- + (CH_3)_2CO + H^+ \rightarrow (CH_3)_2\dot{C}OH \quad (2)$$

$$\dot{O}H + (CH_3)_2CHOH \rightarrow (CH_3)_2\dot{C}OH + H_2O \quad (3)$$

$$H + (CH_3)_2CHOH \rightarrow (CH_3)_2COH + H_2 \quad (4)$$

The yield of hydrogen corresponds to formation of one molecule of H_2 per two 1-hydroxy-1-methylethyl radicals (corrected for the small amount of H_2 liberated from the water by the action of the radiation). The effects observed can be interpreted in terms of the following mechanism:

$$2(CH_3)_2\dot{C}OH + Ag_n \rightarrow 2(CH_3)_2CO + 2H^+ + Ag_n^{2-} \quad (5)$$

$$Ag_n^{2-} + 2H_2O \rightarrow Ag_n + H_2 + 2OH^- \quad (6)$$

$$2H^+ + 2OH^- \rightarrow 2H_2O \quad (7)$$

$$2(CH_3)_2\dot{C}OH \rightarrow H_2 + 2(CH_3)_2CO \quad (1)$$

The organic radicals charge the silver particles by electron transfer, more than two electron being transferred [eq. (5)], until decomposition of water occurs [eq. (6)]. The silver particles thus assume the role of a pool of electrons which can be released, singly or pairwise, on demand to suitable acceptors[3]. Reaction (5) appears reasonable because 1-hydroxy-1-methylethyl radicals exhibit an anodic polarographic wave which extends to more than -1.0 V[1] at negative potentials (*vs.* standard hydrogen electrode). A negatively charged colloidal particle is to be regarded as a microelectrode at a negative potential according to the above mechanism.

These experiments show that short-lived free radicals can be forced to undergo unusual reactions if they are generated in the presence of a metal colloid catalyst in aqueous solution.

Received: March 2, 1979 [Z 212 IE]
German version: Angew. Chem. *91*, 449 (1979)

[*] Prof. Dr. A. Henglein
Radiation Laboratory, University of Notre Dame
Notre Dame, Ind. 46556 (USA)
Permanent address: Hahn-Meitner-Institut für Kernforschung, Berlin GmbH, Bereich Strahlenchemie,
Glienicker Strasse 100, D-1000 Berlin 39 (Germany)

[**] This work was supported by the Office of Basic Energy Sciences of the US Department of Energy (Doc. No. NDRL-1953, Notre Dame Radiation Laboratory).

[1] *A. Henglein*, Electroanal. Chem. *9*, 164 (1976).
[2] *J. Voigt*: Das kolloidale Silber. Akademische Verlagsgesellschaft, Leipzig 1929, p. 24.
[3] *A. Henglein*, J. Phys. Chem., in press.

BOOK REVIEWS

Intermolecular Interactions: From Diatomics to Biopolymers. Edited by *B. Pullman*. John Wiley & Sons, London 1978, 1st edit., ix, 447 pp., bound, £ 19.50.

The book begins with a contribution by *D. Buckingham*, which is chiefly concerned with multipole expansion and its role in the theory of intermolecular forces, treating other aspects of the theory very briefly. We sense a little of the fascination of the theory of intermolecular forces, with its unexpected snares and its problems which are in part still unsolved or have only recently been solved, when we turn to *P. Claviere*'s report, and in particular to the first part, which deals with the basic aspects of the theory. The author can in part refer to his own work here. The second part is concerned with the derivation of approximate formulas for individual contributions to intermolecular forces in large molecules. The bibliography is impressive. In *R. Rein*'s article, so broad is the theme of the book, he describes the interactions of nucleic acids, and in particular hydrogen bridges and dispersion forces between superimposed base pairs. Finally, *P. Schuster* gives a very useful survey of *ab initio* calculations for hydrogen bridges. He begins with a critical assessment of calculations on isolated components, and goes as far as hydrogen fluoride polymers $(HF)_n$. A whole series of physical properties and the way in which they are affected by hydrogen bridges are discussed; much attention is paid to an analysis of the calculations and to a qualitative interpretation of the results.

In all, the book can be recommended to anyone interested in the theory of intermolecular forces.

Werner Kutzelnigg [NB 454 IE]

Fourier Transform Infrared Spectroscopy. Vol. 1. Applications to Chemical Systems. Ed. by *J. R. Ferraro* and *L. J. Basile*. Academic Press, New York 1978, 1st edit., viii, 311 pp., bound, $ 25.00.

This is the combined work of a series of well-known authors. It is divided into seven chapters, which are largely concerned with applications:

1. Study of matrix-isolated species (*D. W. Green, G. T. Reedy*);
2. Study of synthetic and biological macromolecules (*L. D'Es-*

© Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0505-0418 $ 02.50/0

posito, J. L. Koenig); 3. Emission measurements (*J. B. Bates*); 4. GC/IR Coupling (*P. R. Griffiths*); 5. Study of materials under high pressures (*J. L. Lauer*); 6. Far infrared spectroscopy (*J. R. Durig, A. W. Cox*); 7. Environmental protection, space research and energy research (*J. R. Ferraro, L. J. Basile*).

Each chapter describes the application of IR spectroscopy to the solution of specific and demanding problems, and is illustrated with many examples. Most of these problems have been known for some time, and were dealt with in the sixties and earlier by means of conventional dispersive IR spectrophotometry. To do this, it was often necessary to operate at or beyond the capability limits of the instruments. The introduction of the Fourier technique considerably extended the possible applications of IR spectroscopy. The aim of the present book is to demonstrate these wider applications, and this is certainly achieved qualitatively. The book also offers many valuable technical tips not directly connected with the Fourier technique (cell construction, sample preparation, evaluation of the spectra, *etc.*). However, it is a pity that there is no chapter dealing in general terms with the advantages and disadvantages of the Fourier technique as opposed to the conventional dispersive method, where the various problems (microsamples, FIR range, heavy background losses, rapid measurements, *etc.*) could be considered. Without such a chapter an impartial reading of this quite heterogeneous work could lead to the conclusion that any problem which can fit into any of the seven chapters requires the use of the Fourier technique. Such a conclusion is undoubtedly valid in the case of GC/IR coupling and in the problems of space research, to name but two examples, but it is completely unjustified *e.g.* in the case of the study of matrix-isolated species and of synthetic macromolecules in the medium IR range. This is shown by the flood of excellent papers which describe work in this field, where the conventional dispersive instruments are used just as much as ever. The book should have provided a clearer answer to the question when a user might need, or be able to exploit, the dearly bought advantages of the Fourier technique.

Erich Knözinger [NB 449]

Stereochemie und Konformationsanalyse (Stereochemistry and Conformational Analysis). By *J. Dale*. Verlag Chemie, Weinheim 1978. xii, 208 pp., bound, DM 38.00.

From its title the book promises to be a comprehensive presentation on these two important sectors of chemistry; the promise, however, is fulfilled only as far as the second part of the title is concerned. Conformational analysis is treated in detail taking as a basis the physical methods used. Almost half of the book is devoted to the conformational analysis of cyclic compounds. This section is logically arranged, and both students and experienced scientists and lecturers can learn something from it.

In the first part of the book, however, the geometric foundations of stereochemistry are missing. No effort is made to present clear definitions. The use of models, a requirement in all scientific work, is especially important in stereochemistry. This certainly does not mean that rigid geometric objects can give a true-to-life representation of molecules (or of large numbers of molecules), but geometric models do make it possible, with the necessary degree of caution, to work out the fundamentals of modern stereochemistry. This is true not only for the structure, configuration, and conformation of molecules, but also for the symmetry relationships of constitutionally identical groups within a molecule. These relationships play an important role, for example, in NMR spectroscopy and in enzymology. When we find the assertion on page 32 that "The presence of a chirality center allows the geminal protons or groups to be nonequivalent (*diastereotopic* or *prochiral*)" then we understand why clear definitions of these expressions have been avoided.

On the other hand, the physical methods, and in particular the spectroscopic techniques used to determine molecular properties, are described carefully and in detail. The section on asymmetric induction is inserted somewhat unexpectedly after the section on cyclization of polyenes (p. 100).

Although the book is not written in such a way as to arouse any great enthusiasm, it can be recommended to interested readers. One should not, however, be under the illusion that the long-awaited standard work on stereochemistry has at last arrived.

Janos Rétey [NB 465 IE]

Surfactants and Interfacial Phenomena. By *M. J. Rosen*, John Wiley & Sons, New York 1978. 1st edit., 304 pp., bound, $ 30.45.

Because of the increasing importance of interfacial phenomena, particularly in connection with detergents, the literature concerned with these problems has increased markedly over the past few years.

The present book attempts to provide a compact summary of the most important interfacial and colloid chemistry aspects of the use of surfactants. In ten chapters the author discusses the general properties and structures of surfactants, their adsorption at interfaces, micelle formation, solubilization, reduction of surface tension, wetting, foam properties, emulsification, dispersion, and washing.

The author has succeeded very well in his aim of providing the essential information for the interested reader in a restricted space. Careful selection of the material permits the important relationships to be recognized; the book is not weighed down with marginal data and information.

The work is intended for advanced students and for practising scientists who want a compact guide to the properties of surfactants. At the end of each section there is a selection of literature references to enable the topic to be studied further. It is worth noting that the literature references cover the appropriate European and Japanese literature, which is not always the case with English-language monographs.

The present book will completely fulfil its purpose of offering both the interested subject specialist in the chemical industry and also the advanced student the opportunity of obtaining the essential information on surfactants and their behavior at interfaces.

M. J. Schwuger [NB 447 IE]

Internal Rotation and Inversion. An Introduction to Large Amplitude Motions in Molecules. By *D. G. Lister, J. N. Macdonald* and *N. L. Owen*. Academic Press, London 1978, 1st edit., xii, 246 pp., £, 11.50.

This book attempts (in itself a praiseworthy aim) to present the multiplicity of specific experimental and theoretical methods for the investigation of the internal mobility of molecules, together with the results and insights gained therefrom, to a broad non-specialist audience. Vibration and rotation spectroscopy, and also small rotation barriers, are treated in comparative detail, while the methods for the barrier range of 25 to 100 kJ mol^{-1} are only mentioned cursorily. One chapter contains a few remarks about empirical force-field and quantum-chemical calculations of barriers. The book closes with a discussion of atomic inversions, pseudorotations, and other motions in rings, and with a brief look at macromolecules of biological significance.

Within a compass of 240 text pages we might have expected, in view of the profusion and diversity of the material, a purely descriptive treatment. The authors strive for more and manage to achieve less. They feel the need to protect the chemist, as far as possible, from the hardships of a coherent mathematical treatment, but on the other hand they do not wish to forego embellishing their work with mathematical decorations. The results of such an approach are of necessity unsatisfactory. There remain about 130 pages which the non-specialist may read with some profit; provided, however, that he is not disturbed by the many imprecise formulations, *e.g.* statements that a secular determinant and secular equations mean the same thing, that Hamiltonian eigenfunctions behave either in a symmetric or antisymmetric fashion with respect to symmetry operations, that a methyl group attached to nitrogen is an electron attractor, that the inversion barrier in NH_3 is 5.8 kJ mol^{-1}, or that the barrier to restricted rotation in *N*,*N*-disubstituted amides has a typical value of 40 kJ mol^{-1}.

There has long been an urgent need for a modern survey of this extensive and important field. The book that will satisfy this need is yet to be written.

Gerhard Binsch [NB 453 IE]

Transform Techniques in Chemistry. Edited by *P. R. Griffiths*. Plenum Press, New York 1978. xviii, 385 pp., bound, $ 47.40.

The present new volume from the series "Modern Analytical Chemistry" offers, for the first time in one volume, a survey of the entire range of applications of transform techniques in chemistry. Several authoritative writers describe the specific applications in concise review articles. It thus becomes clear that Fourier transform techniques in particular have an astonishing degree of universality. Some emphasis is of course given to spectroscopic applications, but there are also interesting possibilities in the fields of the processing and analysis of chemical data.

The book is intended for non-specialists and is therefore written in an easily understandable style. Because of the enormous range of applications, only the basic features could be covered; however, the book is suitable as a first survey of the many possibilities. Up to now the applications of transform techniques have largely developed independently of one another. It is therefore particularly good to see that an attempt has been made here to interrelate the individual fields of application.

R. R. Ernst [NB 461 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Annual Reports on Fermentation Processes, Vol. 2. Edited by *D. Perlman* and *G. T. Tsao*. Academic Press, New York 1978. viii, 338 pp., paper, $ 19.00.—ISBN 0-12-040302-1

Fortschritte der Verfahrenstechnik, Band 16, Abt. F. Published by VDI-Verlag, Düsseldorf 1978. xiv, p. 547—665, paper—ISBN 3-18-400402-3

VDI-Berichte 322. Wirbelschichtfeuerung. Fluidized Bed Combustion. Published by VDI-Verlag, Düsseldorf 1978. iv, 145 pp., paper, DM 75.00.—ISBN 3-18-090322-8

Annual Reports, Vol. 74, 1977, Section A, Physical and Inorganic Chemistry. The Chemical Society, London 1978. xiv, 289 pp., bound, £ 18.00.—ISBN 0-85186-100-8

Annual Reports, Vol. 74, 1977, Section B, Organic Chemistry. The Chemical Society, London 1978. xv, 471 pp., bound, £ 20.00.—ISBN 0-85186-101-6

Additives for Plastics, Vol. 2. New Developments. Edited by *R. B. Seymour*. Academic Press, New York 1978. x, 125 pp., bound, $ 9.50.—ISBN 0-12-637502-X

Annals of The New York Academy of Sciences, Vol. 313. Synthesis and Properties of Low-Dimensional Materials. Edited by *J. S. Miller* and *A. J. Epstein*. The New York Academy of Sciences, New York 1978. 828 pp., bound, $ 80.00—ISBN 0-89072-069-X

Organic Chemistry, A Series of Monographs, Vol. 38. Strained Organic Molecules. By *A. Greenberg* and *J. F. Liebman*. Academic Press, New York 1978. xi, 406 pp., bound, $ 41.50.—ISBN 0-12-299550-3

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979. - Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstraße 12, D-6940 Weinheim, Germany, Telephone (06201) 14036. Telex 465516 vchwh d.

Editor: *O. Smrekar* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*). Pappelallee 3. P.O. Box 1260/1280, D-6940 Weinheim, Germany. Telephone Weinheim (06201) 14031. Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English

Volume 18 · Number 6
June 1979
Pages 421–492

Triphase Catalysis

New synthetic methods (27)

By Steven L. Regen[*]

Triphase catalysis (TC) has recently been introduced as a unique form of heterogeneous catalysis in which the catalyst and each of a pair of reactants are located in separate phases. Based on this concept, new synthetic methods have been developed for aqueous phase–organic phase reactions using a solid phase catalyst. Although it is only at an early stage of development, TC shows considerable potential for practical use. Our mechanistic understanding of these highly complex catalytic systems is at present very limited and detailed examination will be required before their relationship to phase-transfer, micellar, and interfacial catalysis becomes clear.

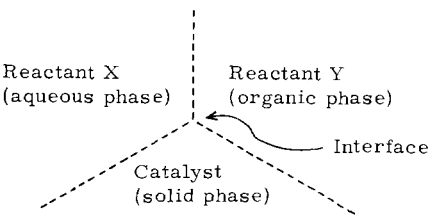
1. Introduction

A significant and recurring problem facing the synthetic organic chemist is how to effectively carry out reaction between a water-soluble reagent and a water-insoluble substrate. When reaction is attempted as an aqueous–organic biphase process, very low rates are usually observed due to the low concentration of at least one of the compounds in each phase. Rapid stirring has been shown, in certain cases, to have an accelerating effect by increasing the surface contact between the layers and thereby increasing the interfacial component of the reaction[1]. Alternatively, reaction rates may be increased by the use of a cosolvent which, by conferring homogeneity upon the system, increases the effective concentration of the reactants. As a consequence of the third solvent, however, the organic reactant is not only more accessible to the reagent, but at the same time has greater contact with water. This situation can lead to undesired by-products by furnishing a competing hydrolytic pathway. Furthermore, work-up and product isolation are made more difficult when a cosolvent is employed. Finally, soluble ammonium and phosphonium salts[2] as well as crown ethers[3], cryptands[4], and surfactants[5] have proven extremely useful in catalyzing aqueous–organic biphase reactions. Interest in such phase-transfer and related two-phase catalytic techniques continues to grow in synthetic and mechanistic organic chemistry[6]. This topic has been the subject of recent comprehensive reviews and will not be discussed here[7].

2. Concept of Triphase Catalysis (TC)

It occurred to us that the development of a technique which used insoluble catalysts to accelerate aqueous–organic phase reactions would not only be an interesting possibility but could also provide the basis for synthetic methods competitive with or even superior to existing ones (Scheme 1).

Two immediate advantages would be (1) simplified product work-up and (2) easy and quantitative catalyst recovery. From the standpoint of industrial applications, this concept is a



Scheme 1. Triphase catalysis.

[*] Prof. S. L. Regen
Department of Chemistry, Marquette University
Milwaukee, Wisconsin 53233 (USA)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0421 $ 02.50/0

very attractive one due to low energy and capital requirements for processing. In addition, such a technique would be ideally suited for continuous flow methods.

3. Development of Triphase Catalysts

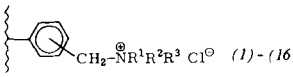
Crosslinked polystyrene resins and silica gel have received considerable attention as supports for insolubilizing synthetically important catalysts and reagents[8]. Thus far, all of the triphase catalysts introduced are based on these materials. In the following discussion we have divided the catalysts into three different categories based on the nature of the active site: 1) ion-exchange groups; 2) crown ethers and cryptands; and 3) cosolvents.

3.1. Classes of Catalysts

3.1.1. Insolubilized Ammonium and Phosphonium Salts

The feasibility of triphase catalysis was first demonstrated by the reaction of cyanide ion with 1-bromo- and 1-chlorooctane in water–benzene systems using a crosslinked polystyrene resin *(1)* bearing quaternary ammonium groups as the catalyst (Scheme 2)[9, 10]. Control experiments showed that in the absence of *(1)* or in the presence of its unfunctionalized counterpart no reaction took place and that *(1)* did not dissolve in the medium or decompose to yield a soluble catalyst. The experimental set-up is shown schematically in Figure 1. A series of related polystyrene-based catalysts *(2)*—*(16)* were prepared and tested for their ability to catalyze the reaction of sodium cyanide with 1-bromooctane (Table 1)[11].

Table 1. Dependence of catalyst activity in the triphase reaction (a) upon resin structure [11]. DVB = divinylbenzene.



(1)-*(16)*

Catalyst	Polystyrene backbone	DVB [%]	Ring substitution [%]	$R^1=R^2$	R^3	k [s^{-1}] [a]
(1)	Microporous	2	10	CH_3	n-C_4H_9	2.2
(2)			1			1.9
(3)			21			2.2
(4)			10	CH_3	CH_3	3.0
(5)			46			0.015
(6)			76			≤0.015
(7)			10	CH_3	n-C_8H_{17}	4.4
(8)			10	CH_3	n-$C_{12}H_{25}$	3.0
(9)			9	CH_3	n-$C_{14}H_{29}$	3.7
(10)			8	C_2H_5	C_2H_5	1.5
(11)			9	CH_3	$CH_2C_6H_5$	2.6
(12)			8	CH_3	C_2H_4OH	1.1
(13)	Microporous	1	10	CH_3	n-C_4H_9	2.2
(14)	Microporous	4	9			2.7
(15)	Macroporous	8	8			0.22
(16)	"Popcorn"		10			2.5

[a] Observed first-order rate constant divided by the molar amount of quaternary ammonium groups.

From this work it was concluded that:

1) At 8—10% ring substitution, the structure of the quaternary ammonium group and the type of support material used (microporous, macroporous, and "popcorn") are not of major importance in determining the catalyst's activity.

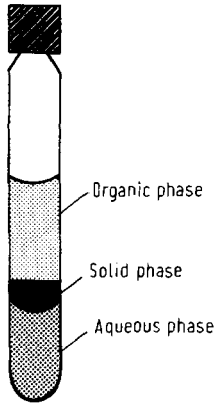
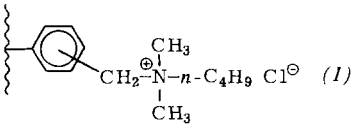
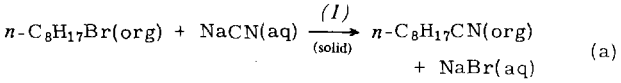


Fig. 1. Experimental set-up for triphase catalytic reaction of sodium cyanide (in water) with 1-bromooctane (in benzene); catalyst *(1)*. Corning No. 9826 culture tube containing organic, aqueous, and solid phases.



(1)



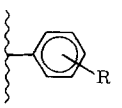
(a)

Scheme 2. Microporous polystyrene resin *(1)*, crosslinked with 2% divinylbenzene and with 10% ring substitution, as catalyst for the triphase reaction (a).

2) Commercial ion-exchange resins which swell extensively in water and have little or no compatibility with organic solvents appear to be very poor triphase catalysts. Thus, commercial Bio-Rad AG1-X2 whose structure is nearly identical with *(6)* failed to show any triphase activity.

In a similar study, *Cinquini et al.*[12] examined resins *(17)*—*(22)* for their usefulness in converting 1-bromooctane into 1-iodooctane and octanecarbonitrile in toluene/resin/water systems. Polymer-anchored phosphonium salts exhibited greater activity than analogous ammonium-based resins. Moreover, all the triphase reactions proceeded slower than comparable transformations carried out using a phase-transfer catalyst. The crosslink density of the support was also shown to be important: more extensive crosslinking led to lower catalytic activity.

Brown and *Jenkins*[13] prepared resins *(23)*—*(27)* and used them for triphase catalysis of the *O*-alkylation of 2-naphthoxide with benzyl bromide [reaction (b)].



(17)-*(22)*

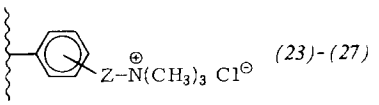
Microporous polystyrene resin crosslinked with 2% divinylbenzene

(17), R = $CH_2\overset{\oplus}{N}(CH_3)_3Cl^{\ominus}$; 50% ring substitution

(18), R = $CH_2\overset{\oplus}{N}(n\text{-}C_4H_9)_3Cl^{\ominus}$; 7% ring substitution

(19), R = $CH_2\overset{\oplus}{N}(n\text{-}C_8H_{17})_3Cl^{\ominus}$; 10% ring substitution

(20)—*(22)*, R = $CH_2\overset{\oplus}{P}(n\text{-}C_4H_9)_3Cl^{\ominus}$; 7, 10, and 50% ring substitution, respectively

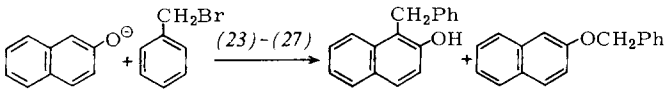


(23)-(27)

Polystyrene-based catalyst; microporous catalysts crosslinked with 2% divinylbenzene

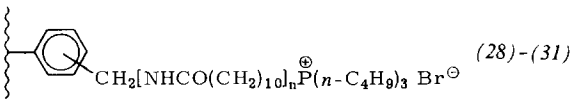
(23), $Z = CH_2OCO[CH_2]_{11}$; 98% ring substitution, microporous
(24), $Z = CH_2OCO[CH_2]_{11}$; 46% ring substitution; Rohm and Haas XE305, macroporous
(25), $Z = CH_2OCO[CH_2]_5$; 100% ring substitution, microporous
(26), $Z = CH_2OCO[CH_2]_5$; 40% ring substitution, Rohm and Haas XE305, macroporous
(27), $Z = CH_2$; ring substitution not specified, microporous

Lengthening the alkyl chain between the support and the onium groups significantly improved the yield of *O*-alkylated product. Also, macroreticular resins were found to be more active than microporous ones. Catalysts *(23)* and *(24)* were also effective in promoting cyanide displacement [eq. (a)].



(b)

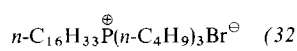
In a systematic study, *Molinari et al.*[14] examined how the length of the pendant chain used to attach phosphonium groups to polystyrene influenced the activity of the resulting catalyst. Resins *(28)*—*(31)* were synthesized and tested as



(28)-(31)

Microporous polystyrene-based catalyst, crosslinked with 2% divinylbenzene, 33% ring substitution

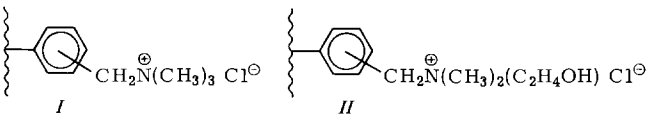
(28), $n = 0$; *(29)*, $n = 1$; *(30)*, $n = 2$; *(31)*, $n = 3$



(32)

catalysts for the displacement reaction between iodide and thiophenoxide and 1-bromooctane. The order of catalyst activity was *(31)* > *(30)* > *(29)* > *(28)*. With resin *(31)*, observed rates approached those measured under similar conditions using phase-transfer catalyst *(32)*.

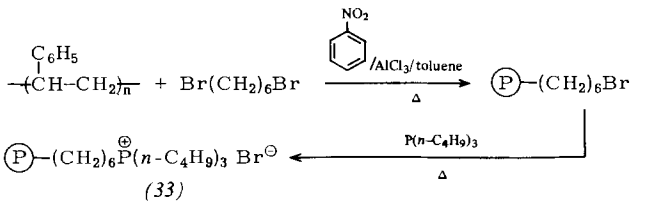
Zadeh et al.[15] have applied triphase procedures to the *C*-alkylation of nitriles using commercial ion-exchange polymers of structures *I* and *II* [cf. *(27)* and *(12)*]. Although



I *II*

it was demonstrated that triphase catalysis was possible, direct comparison with phase-transfer catalysis using soluble ammonium and phosphonium salts showed the latter to be the preferred method. This is not surprising, however, since commercial ion-exchange resins similar to those used in this study have already exhibited very poor triphase catalytic activity in nucleophilic substitution reactions[11,12].

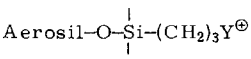
Recently, *Tundo* reported a readily available and economically attractive triphase catalyst, *(33)* (Scheme 3)[16]. This resin swells extensively in dichloromethane and has a catalytic capacity comparable with the analogous phase-transfer catalyst *(32)* for alkylation of ketones as well as some simple nucleophilic displacement reactions (Table 2).



(33)

Scheme 3. Synthesis of the triphase catalyst *(33)*. Ⓟ = polystyrene.

Silica-based triphase catalysts have been reported by two groups. *Rolla et al.*[17] demonstrated that solids derived from ammonium and phosphonium salts covalently attached to glass surfaces [*(34)*—*(43)*] could be used to convert 1-bromohexane into 1-iodohexane under triphase conditions [eq. (c)].

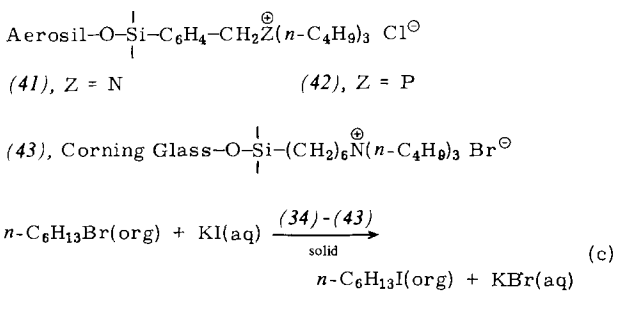


(34), Y = NH_3; X = Cl
(35), Y = $N(CH_3)_3$; X = I
(36), Y = $N(C_2H_5)_3$; X = Br(Cl)
(37), Y = $N(n\text{-}C_4H_9)_3$; X = Br(Cl)
(38), Y = $N(n\text{-}C_8H_{17})_3$; X = Br
(39), Y = $N(n\text{-}C_{16}H_{33})_3$; X = Br
(40), Y = $P(n\text{-}C_4H_9)_3$; X = Cl

Table 2. Catalytic activity of *(32)* and *(33)* in phase-transfer and triphase catalysis [16] (0.01 mol of catalyst per mol of substrate).

(32) $n\text{-}C_{16}H_{33}\overset{\oplus}{P}(n\text{-}C_4H_9)_3Br^{\ominus}$ Ⓟ$\text{-}(CH_2)_6\overset{\oplus}{P}(n\text{-}C_4H_9)_3Br^{\ominus}$ *(33)*

Substrate	Reagent	Product	Catalyst	Organic solvent	Conditions *T*/*t*	Conversion [%]
$n\text{-}C_8H_{17}Br$	KI	$n\text{-}C_8H_{17}I$	*(33)*	toluene	90°C/2.3 h (24 min)	98 (50)
			(32)	toluene	90°C/36 min	50
	KCN	$n\text{-}C_8H_{17}CN$	*(33)*	toluene	90°C/1.6 h (17 min)	98 (50)
			(32)	toluene	90°C/13 min	50
	C_6H_5SK	$n\text{-}C_8H_{17}SC_6H_5$	*(33)*	CH_2Cl_2	20°C/2 h	97
			(32)	CH_2Cl_2	20°C/0.25 h	97
$C_6H_5CH_2COCH_3$	$n\text{-}C_4H_9Br$	$n\text{-}C_4H_9CH(C_6H_5)COCH_3$	*(33)*	none	20°C/2.5 h	98
			(32)	none	20°C/2.5 h	90



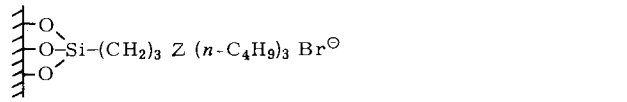
(41), Z = N *(42)*, Z = P

(43), Corning Glass–O–Si–$(CH_2)_6\overset{\oplus}{N}(n\text{-}C_4H_9)_3\ Br^{\ominus}$

$$n\text{-}C_6H_{13}Br(org) + KI(aq) \xrightarrow[\text{solid}]{(34)\text{-}(43)} n\text{-}C_6H_{13}I(org) + KBr(aq) \quad (c)$$

Dilute solutions and vigorous stirring were required to achieve catalysis. The size of the alkyl groups bonded to nitrogen did not significantly influence catalyst activity. Not surprisingly, *(34)*—*(43)* were unstable in alkaline solution.

Tundo similarly showed that *(44)* and *(45)* were effective in catalyzing halogen exchange reactions and reduction of ketones by $NaBH_4$ under triphase conditions[18]. Interestingly,

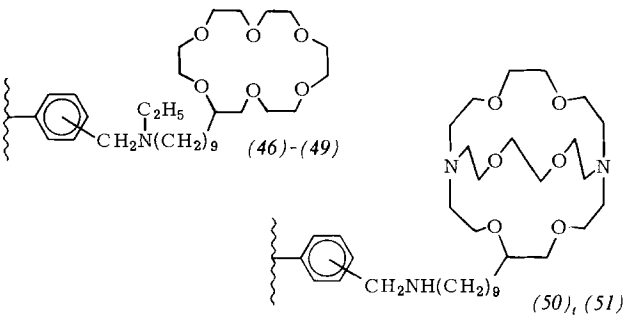


(44), Z = $P^{\oplus}$; *(45)*, Z = $NHCO(CH_2)_{10}\ P^{\oplus}$

(44) and *(45)* exhibited *greater* activity than the analogous phase-transfer agent *(32)* in the reduction of 2-octanone.

3.1.2. Insolubilized Crown Ethers and Cryptands

This class of catalyst has received limited attention thus far. Only nine resins have been described in the literature for use in triphase systems. *Cinquini et al.*[12] have reported the preparation of polymers *(46)*—*(51)* and their use as

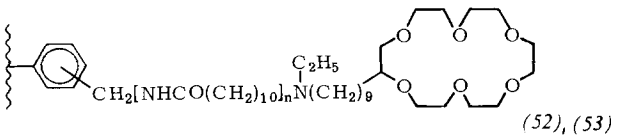


(46)-*(49)* *(50)*, *(51)*

Microporous polystyrene-based catalyst, crosslinked with 2% divinylbenzene [4% for *(49)*]

(46), 5% ring substitution
(47), 10% ring substitution
(48), 33% ring substitution
(49), 20% ring substitution
(50), 3% ring substitution
(51), 5% ring substitution

catalysts in the reaction of cyanide and iodide with 1-bromooctane. Polymer-anchored crown ethers and cryptands, like supported phosphonium salts, were more useful than supported ammonium salts owing to their higher activity and thermal stability. Related studies using resins *(52)* and *(53)* for the

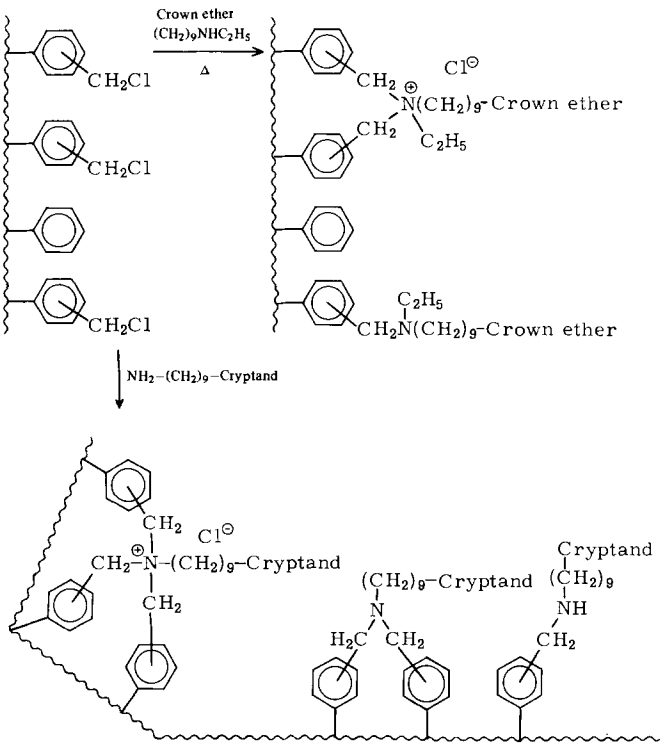


(52), *(53)*

Microporous polystyrene-based catalysts, crosslinked with 2% divinylbenzene, 17% ring substitution *(52)*, $n=1$; *(53)*, $n=2$

conversion of 1-bromooctane into 1-iodooctane and *n*-octyl phenyl sulfide indicated that increasing the length of the pendant chain used to bind the crown ether to the polymer backbone led to increased catalytic activity[14].

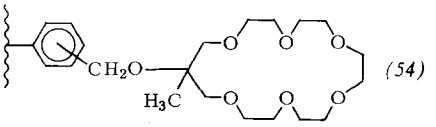
There is a certain ambiguity associated with these catalysts, however, which must be recognized. Polymers *(46)*—*(51)* were synthesized by reaction of the appropriate amine form of the crown ether or cryptand with a chloromethylated polystyrene resin. Since the polymer backbone is flexible[19,20], and since there must be a certain percentage of neighboring chloromethylstyryl units in the copolymer, there is a high probability that these resins contain at least a small fraction of ammonium groups (Scheme 4).



Scheme 4. Side reactions in the production of catalysts of type *(46)*—*(51)*.

Furthermore, quaternization may also occur during the catalysis by alkylation of amine groups by one of the reactants (1-bromooctane). A similar ambiguity is present with catalysts *(52)* and *(53)*. Thus, a clear assessment of the participation of the crown ether and cryptand moieties in these systems is not possible.

That a polymer-supported crown ether could function as a triphase catalyst was firmly established in very recent work by *Tomoi et al.*[21]. Polymer *(54)* was shown to have significant activity for the triphase conversion of 1-bromooctane into 1-iodooctane.

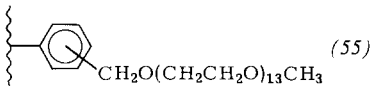


(54)

Macroreticular polystyrene resin, crosslinked with 10% divinylbenzene; 1.8 mmol of crown ether units/g of polymer

3.1.3. Insolubilized Cosolvents

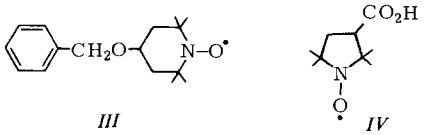
In an effort to expand the utility of TC, catalysts having cosolvent-like properties have been developed. Thus, a graft copolymer *(55)* derived from poly(ethylene glycol monomethyl ether) and microporous crosslinked polystyrene proved effective for the hydrolysis of *tert*-butyl chloride and 1-bromoadamantane and also for the reaction between phenoxide and 1-bromobutane in water–toluene systems[22].



(55)

Microporous polystyrene-based catalyst, crosslinked with 2 % divinylbenzene, 11 % ring substitution

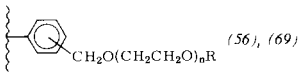
Studies using spin-labeled *III* and *IV* showed that *(55)* can act as a cosolvent by influencing the polarity and motional freedom of the microenvironment within the solvent channels[23]. Additional support for cosolvent behavior has recently come from a kinetic comparison of the closely related graft copolymers *(56)*—*(69)* used in catalyzing the hydrolysis of 1-bromoadamantane[24]. The activation parameters summarized in Table 3 indicate a considerable variation in $\Delta H^{\neq}$



III *IV*

accompanied by a compensating fluctuation in $\Delta S^{\neq}$. The free energy of activation, $\Delta G^{\neq}$, for all the catalytic systems was nearly identical ($\Delta G^{\neq} = 30.1$ kcal mol^{-1}) and approximately 2 kcal mol^{-1} lower than for the uncatalyzed reaction.

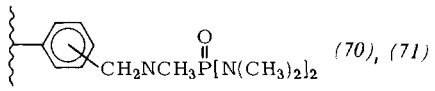
Table 3. Graft polymers as triphase catalysts for hydrolysis of 1-bromoadamantane [24].



(56), (69)

Cat.	n	R	Ring substitution [%]	$\Delta H^{\neq}$ [kcal mol^{-1}]	$\Delta S^{\neq}$ [kcal K^{-1} mol^{-1}]
(56)	1	CH_3	17	16.58 ± 0.87	−35.01 ± 2.33
(57)	2			17.82 ± 1.87	−31.73 ± 4.96
(58)	3			16.85 ± 0.06	−34.24 ± 0.18
(59)	16			16.19 ± 0.22	−37.53 ± 0.60
(60)	1		45	19.01 ± 0.49	−30.88 ± 1.30
(61)	2			15.59 ± 0.13	−39.26 ± 0.34
(62)	3			16.58 ± 0.25	−36.62 ± 0.66
(63)	2		92	17.35 ± 0.73	−34.41 ± 1.92
(64)	3			22.27 ± 0.49	−20.64 ± 1.30
(65)	1	H	17	17.06 ± 0.81	−33.72 ± 2.19
(66)	4			19.82 ± 0.19	−27.48 ± 0.51
(67)	13			16.81 ± 0.61	−35.83 ± 1.61
(68)	1		92	18.37 ± 0.39	−31.85 ± 1.03
(69)	4			21.14 ± 0.53	−24.96 ± 1.41

Another type of solid phase cosolvent has been prepared by attachment of hexamethylphosphoramide to a polymer support[25]. Resins *(70)* and *(71)* proved useful in triphase catalytic displacement reactions by cyanide and chloride ion on 1-bromooctane. These copolymers also catalyzed the hydrolysis of 1-bromoadamantane under triphase conditions.



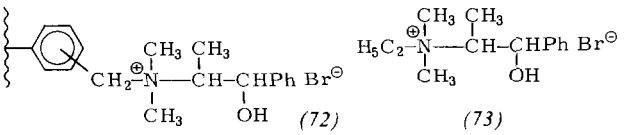
(70), (71)

Microporous polystyrene-based catalyst, crosslinked with 1 % divinylbenzene *(70)*, *(71)* with 92 and 17 % ring substitution, respectively

3.2. Chiral Triphase Catalysts

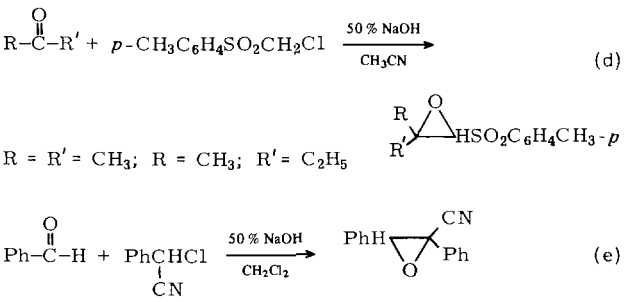
Colonna et al.[26] have prepared an ephedrinium-based chiral triphase catalyst *(72)* and used it to perform Darzens condensations [eq. (d) and (e)]. Asymmetric induction was achieved with optical yields as high as 23 %. Although the products derived from *(72)* were of lower optical rotation than those from the soluble analog *(73)*, the polymer-supported catalyst had the advantage of being easily and completely removed from the product mixture by filtration.

In a brief report, *Chiellini* and *Solaro* confirm the feasibility of asymmetric induction using chiral triphase catalysts[27].



(72) *(73)*

Microporous polystyrene-based catalyst, crosslinked with 1 % divinylbenzene, 12 % ring substitution



(d)

(e)

3.3. Catalyst Stability

In order for TC to be of real practical value, the catalysts must be reasonably stable. *Dou et al.*[28] have examined the stability of two commercial ammonium ion-exchange resins (Dowex 1 × 8 and Dowex 11) in the presence of anions of thiophenol and phenylacetonitrile generated under triphase conditions. Significant polymer decomposition occurred, apparently through a dequaternization process. In order to put the significance of these results into proper perspective, however, two additional points must be considered. Firstly, these experiments were performed *in the absence of a competing alkylating reagent* (normally a desired reactant). *Herriott* and *Picker* have made kinetic measurements of the alkylation of thiophenol by 1-bromooctane using several ammonium catalysts and failed to find any evidence of catalyst decomposition[29]. Second, it has been shown[11–13,15] that commercial anion exchange resins of this type are very poor triphase catalysts. What relevance these stability data have with regard to *active* triphase catalysts is unclear.

Present indications are that many of the useful ammonium and phosphonium-based catalysts have stabilities ranging from good to excellent[12,14,16,17,21,26,30]. For this class of catalysts, stability will depend on the exact structure of the phosphonium or ammonium group and also the inherent reactivity of the reagent and substrate.

From the standpoint of stability, insolubilized crown ethers, cryptands, and cosolvents are more attractive since they avoid the potential dequaternization problem; however, their synthetic scope has not yet been established. More studies with these catalysts are needed.

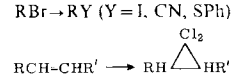
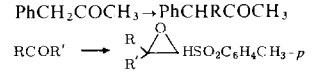
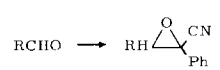
3.4. Selectivity Features of Polystyrene-Based Catalysts

Polystyrene resins are known to impart a modest size-selectivity to attached catalysts and reagents in solid/liquid biphase reactions[31,32]. Preliminary studies in our laboratory indicate that similar selectivity is possible with polystyrene-based triphase catalysts in liquid/solid/liquid reactions. The magnitude of the selectivity observed for triphase catalyzed reactions of phenoxide ion with a homologous series of primary organic bromides was high for cosolvent and modest for ion-exchange type catalysts[33]. Both diffusional barriers imposed by the polymer matrix and absorption equilibria appear to be important factors. Comparable phase-transfer experiments yielded no detectable selectivity.

4. Synthetic Applications

Table 4 summarizes most of the synthetic applications of TC which have appeared in the literature.

Table 4. Triphase catalysis, synthetic applications.

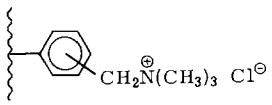
Reaction	Solvent	Catalyst	Ref.
RX→RCN (X=Br, Cl)	benzene/H_2O	*(1)*, *(70)*, *(71)*	[10, 25]
RX→RY (X=Cl, Br, I; Y=Cl, Br, I)	toluene/H_2O	*(1)*	[34]
RBr→ROR′	toluene/H_2O	*(1)*	[34]
RBr→ROR′	toluene/H_2O	*(59)*	[22]
RBr→RY (Y=I, CN)	toluene/H_2O	*(17)*—*(22)*, *(46)*—*(51)*	[12]
RBr→RY (Y=I, SPh)	toluene, chlorobenzene or heptane/H_2O	*(28)*—*(31)*, *(52)*, *(53)*	[14]
RBr→ROR′	substrate/H_2O	*(23)*—*(27)*	[13]
RBr→RI	substrate/H_2O	*(44)*, *(45)*	[18]
RBr→RI	toluene/H_2O	*(34)*—*(43)*	[17]
RBr→RY (Y=I, CN, SPh)	toluene or CH_2Cl_2/H_2O	*(33)*	[16]
	$CHCl_3/H_2O$	*(1)* and related resins	[27, 34]
RCHBrCHBrR′→RCH=CHR′	toluene/H_2O	*(1)*	[34]
ROH→RCl	$CHCl_3/H_2O$	*(1)*	[34]
$R_2CHOH→R_2CO$	toluene/H_2O	*(1)*	[34]
$RCH_2CN→RCHR'CN$	substrate/H_2O	various ammonium polymers	[27]
$RCH_2CN→RCHR'CN$	substrate/H_2O	commercial anion exchange resins	[15]
$PhCH_2COCH_3→PhCHRCOCH_3$	substrate/H_2O	*(33)*	[16]
	substrate/H_2O	*(72)*	[26]
	CH_2Cl_2/H_2O	*(72)*	[26]

5. Mechanistic Studies

Our mechanistic understanding of triphase catalysis is still very limited. Only one kinetic investigation of a triphase system has been reported; *i.e.*, reaction of cyanide ion with 1-bromooctane in the presence of catalyst *(1)* [eq. (a)][11]. The rate of displacement exhibited a first-order dependency on the 1-bromooctane concentration and was linearly dependent on the amount of catalyst used. Comparison of the catalytic activity for similar resins having 1, 10, and 21 % ring substitution indicated that, within this range, resin activity is directly related to the number of quaternary groups present. The catalyst isolated after triphase reaction had undergone complete ion-exchange to the cyanide form.

In this study it was assumed that chemical reaction is rate limiting; no consideration was given to diffusion. In principle, the overall rate for such transformations could be limited by film diffusion, chemical reaction throughout the polymer matrix, and/or chemical reaction at the particle surface.

We have since examined the kinetic features of the triphase reaction between cyanide ion, benzyl chloride, and the resin *(74)*. Taken together, the data obtained favor chemical reaction as being the rate limiting step[35].



(74)

Microporous polystyrene, crosslinked with 1 % divinylbenzene, 17 % ring substitution

A rate-limiting chemical reaction occurring throughout the resin should be characterized by: 1) a first-order dependence on benzyl chloride concentration; 2) a rate which is directly proportional to the amount of catalyst used; 3) a rate which is independent of stirring; 4) a significant activation energy ($>10\,kcal\,mol^{-1}$); and 5) a rate which is independent of particle size.

For a diffusion-controlled process, 1) and 2) should apply along with the *converse* of 3), 4), and 5)[36]. Thus, examination of stirring and particle size effects on rate along with activation energy measurements provide a means of identifying the rate-controlling step. For the reaction of cyanide with benzyl chloride we have observed a first-order dependence on benzyl chloride and a rate constant, k_{obs}, which is directly proportional to the amount of resin used. The apparent activation energy was 19.9 ± 1.6 kcal mol^{-1}. Changing the stirring speed from 0 to 750 RPM produced only a slight increase in rate ($\approx 20\,\%$). Increasing the resin surface area by grinding to a fine powder resulted in a *decrease* in catalyst activity. Although these observations are most consistent with a rate-limiting chemical reaction, the decrease in activity on reducing particle size is puzzling and leads to some uncertainty in establishing whether reaction takes place throughout the matrix or just on the bead surface. It should be noted that the fact that triphase catalysts can, at least in certain cases, exhibit close to maximum activity as an unstirred system may have important technological consequences. Minimal stirring is important in order to maintain the physical stability of the catalyst; it is also desirable for continuous flow methods.

6. Factors Affecting Catalyst Activity

Although TC is very simple from a synthetic standpoint, it is highly complex mechanistically. It incorporates a multitude of parameters, many of which are likely to be interdependent. This technique is still in its infancy and much more work will be required before a complete understanding is possible. The discussion presented in this section is not intended to furnish the potential investigator with a critical mass of information necessary for the rational design of new catalysts, but is instead aimed at stimulating further synthetic and mechanistic research.

6.1. Resin-Based Catalysts

Crosslinked polystyrene resins in microporous form have received the most attention as support material in TC[37]. The following applies not only to this specific class of resins but to solvent-swellable crosslinked polymers in general.

The rate-limiting step for TC using resin-based catalysts should be: 1) diffusion of reactants across a thin liquid layer surrounding the solid phase (Nernst or film diffusion); 2) chemical reaction at the particle surface; or 3) chemical reaction throughout the polymer matrix. If chemical reaction proceeds at a much higher rate than the diffusion of reactants through the Nernst layer, 1) will control the rate. In contrast, if chemical reaction is much slower, then the rate would be governed by either 2) or 3). When diffusion of reactants through the resin (matrix diffusion) is very slow relative to chemical reaction and film diffusion is rapid, then reaction takes place exclusively at the particle surface; if matrix diffusion is fast, chemical reaction occurs throughout the polymer.

If the rate of a triphase process is controlled by chemical reaction, three principal factors will influence the observed activity of the catalyst: 1) the effective concentration of catalytically active sites; 2) the effective concentration of reactants; and 3) the free energy of activation for the reaction. In terms of efficient TC, it is desirable that all or as many as possible of the active sites located within the polymer participate in the catalysis. Experimentally, this can be controlled by adjusting the swelling of the resin. The greater the degree of swelling, the faster the rate of diffusion of reactants through the matrix and thus the greater the efficiency of the catalyst. Swelling is determined by the nature of the liquid solvents used, the composition of the polymer, and the crosslink density. Organic solvents having a structure similar to that of the resin tend to swell the resin to a greater extent. Also, for any given choice of solvents, swelling varies inversely with the crosslink density. It is important to realize that slight structural modification of a resin can lead to pronounced changes in its swelling properties.

The effective concentration of neutral reactants within the resin will depend on their concentration in the external liquid phases and their coefficient of absorption. For ionic reactants, complexation and ion-exchange equilibria will also be important factors when catalysts bearing crown ether, cryptand, quaternary ammonium or phosphonium groups are used. Activation parameters for TC depend on the type of active site, the nature of the reactants, and the microenvironment.

6.2. Inorganic-Based Catalysts

Only two reports have appeared thus far describing inorganic-based (silica gel) triphase catalysts[17,18]. Although it is somewhat premature to speculate on these systems, factors which would seem likely to be important in affecting their activity are surface area, coefficient of adsorption of the reactants, complexation and ion-exchange equilibria (for ionic reactants when crown ether, cryptand, quaternary ammonium or phosphonium groups are employed), and also the free energy of activation of the reaction as defined by the type of reactive site and nature of the reactants and microenvironment.

6.3. Location of Catalyst Relative to the Liquid/Liquid Interface

Another factor which may be relevant to a catalyst's activity is its location relative to the liquid/liquid interface. All of the polymers prepared in our laboratory which have proven active as triphase catalysts reside at the liquid phase boundary, some protruding more into the organic phase than others (cf. Fig. 1). Resins which could not be maintained as a suspension between layers (in the absence of stirring) were found to be inactive. How resin distribution at the interface affects triphase activity needs to be clarified. Interestingly, the inorganic solids *(34)—(43)* required vigorous stirring in order to achieve catalysis. This fact suggests that agitation is needed to mechanically shuttle this type of catalyst from one liquid phase to the other.

6.4. Surface Area Catalysis

Finally, we wish to mention a simple physical phenomenon which, if present, may make important contributions to certain TC transformations. We shall refer to it as "surface area catalysis". Figure 2 is a schematic representation of a polymer generating microscopic aqueous and organic pools, the composition of which is either similar or identical to the external bulk phases.

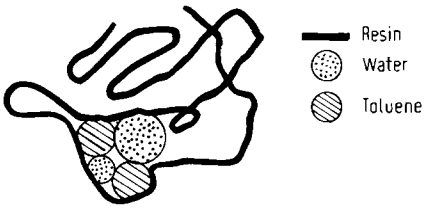


Fig. 2. Schematic representation of "surface area catalysis" for a toluene/resin/water system.

Resins used in TC may operate in part by generating extensive "pool/pool phase boundaries" thereby increasing the rate of interfacial reaction. In effect, the polymer serves as a *pseudo high speed stirrer*. Although this concept is highly speculative and there is no existing evidence which supports it, there is, similarly, no firm data to rule it out.

6.5. Empirical Observations

From the available experimental data, two factors appear to be particularly important in the design of useful triphase catalysts: 1) a high compatibility of the resin with organic solvents, and 2) a long pendant chain used to anchor the catalytic site. More studies, however, are needed to understand these observations.

7. Relationship of Triphase to Phase-Transfer Catalysis

The term, "phase-transfer catalysis", was originally introduced by *Starks* to characterize a process in which: "reaction is brought about by the use of small quantities of an agent which transfers one reactant across the interface into the other phase so that reaction can proceed"[38]. It is an attractive phrase, but one which carries with it clear mechanistic implications. Some elegant work by *Starks et al.*[39] and *Landini et al.*[40] provide very strong support for this concept. Recently, however, there has been some concern over its appropriateness in describing certain aqueous–organic phase reactions using a soluble catalyst[6] (*e.g.*, evidence is beginning to appear in support of an interfacial process for dihalocarbene reactions[1b]). Reference to the solid phase catalysts reviewed here as heterogeneous or immobilized phase-transfer catalysts is unwarrantable on the basis of the limited data available and their classification as such should be avoided. All of these systems will require detailed examination before their relationship to phase-transfer[7], micellar[41], and interfacial[1b,42] catalysis becomes clear. The term triphase catalysis transmits no mechanistic information, yet it serves as an adequate description of the technique. We encourage its use[*].

[*] Note added by Prof. *E. Dehmlow*, Berlin: A detailed discussion took place at the Euchem Conference held at Gargnano [6] whether only mechanistically unequivocal phase transfer catalyst reactions should be designated as such, as proposed by *Regen* and others. It was held that this would not receive the support of most chemists; in particular, the proliferation of new concepts with only minor differences of meaning would not be in the interests of utilizable documentation and literature search systems. Accordingly, the term phase transfer catalysis should embrace all reactions between solid or aqueous ionic compounds and organic compounds in organic solvents, provided that these reactions are made possible or accelerated by catalysts and are not unequivocally classifiable as mere surface catalysis or micellar catalysis. This definition would characterize triphase catalysis as a subcategory of phase transfer catalysis. It remains to be seen which definition becomes accepted.

8. Outlook

Triphase catalysis has been established as a synthetic technique for accelerating aqueous–organic phase reactions. The inherent complexity associated with three phase catalytic systems makes this a particularly challenging and intriguing new area for the mechanistic chemist who is interested in testing his ingenuity for designing meaningful experiments in unconventional systems. Moreover, the practical potential of this technique for laboratory as well as industrial applications is great. Active, economically attractive and reasonably stable catalysts have already been prepared [*e.g. (33)*] and should find immediate use. Preliminary studies in our laboratories further reveal that a high degree of selectivity toward reactants is possible using certain polystyrene-based triphase catalysts. In brief, it appears highly probable that TC will expand significantly over the next few years along synthetic and mechanistic lines.

The author wishes to thank the Division of Basic Energy Sciences of the Department of Energy, the Army Research Office, and the National Science Foundation for support of his work. The author is also grateful to co-workers listed in the references for their contributions and to Drs. Jacques Besse and Alok Nigam for critical discussions and their assistance with the preparation of this article.

Received: September 5, 1978 [A 272 IE]
German version: Angew. Chem. *91*, 464 (1979)

[1] a) *F. M. Menger*, J. Am. Chem. Soc. *92*, 5965 (1970); *A. Tomita, N. Ebina, Y. Tamai, ibid. 99*, 5725 (1977); b) *M. Mąkosza, E. Bialecka*, Tetrahedron Lett. *1977*, 183; *F. Yamashita, A. Atsumi, H. Inoue*, Nippon Kegaku Kaishi *6*, 1102 (1975); *S. L. Regen, J. J. Besse*, unpublished work; *S. L. Regen, J. McLick, J. Heh*, unpublished work.

[2] *C. M. Starks*, J. Am. Chem. Soc. *93*, 195 (1971); *M. Mąkosza, M. Wawrzyniewicz*, Tetrahedron Lett. *1969*, 4659.

[3] *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 2495 (1967); *D. J. Sam, H. E. Simmons, ibid. 94*, 4024 (1972).

[4] *J. M. Lehn*, Struct. Bonding *16*, 1 (1973).

[5] *F. M. Menger, J. U. Rhee, H. K. Rhee*, J. Org. Chem. *40*, 3803 (1975).

[6] Euchem Conference on Phase-Transfer Catalysis and Related Topics, Gargnano (Italy), 1978.

[7] *W. P. Weber, G. W. Gokel*: Phase-Transfer Catalysis in Organic Synthesis. Springer, Berlin 1977; *E. V. Dehmlow*, Angew. Chem. *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *16*, 493 (1977); *A. Brändström*, Adv. Phys. Org. Chem. *15*, 267 (1977).

[8] *C. C. Leznoff*, Chem. Soc. Rev. *3*, 65 (1974); *C. U. Pittman, Jr., G. O. Evans*, Chem. Tech. *1973*, 560; *E. C. Blossey, D. C. Neckers*: Solid Phase Synthesis. Halsted Press, New York 1975; *C. G. Overberger, K. N. Sannes*, Angew. Chem. *86*, 139 (1974); Angew. Chem. Int. Ed. Engl. *13*, 99 (1974); *R. H. Grubbs*, Chem. Tech. *1977*, 512.

[9] Anion-exchange resins have previously been found to catalyze certain cyanide displacement reactions: *H. B. Copelin, G. B. Crane*, US Pat. 2779781 (1957). Although such systems bear a resemblance to triphase catalysis we believe the fact that these reactions proceed at a significant rate in the absence of a catalyst makes such a relationship appear questionable.

[10] *S. L. Regen*, J. Am. Chem. Soc. *97*, 5956 (1975).

[11] *S. L. Regen*, J. Am. Chem. Soc. *98*, 6270 (1976).

[12] *M. Cinquini, S. Colonna, H. Molinari, F. Montanari, P. Tundo*, J. Chem. Soc. Chem. Commun. *1976*, 394.

[13] *J. M. Brown, J. A. Jenkins*, J. Chem. Soc. Chem. Commun. *1976*, 458.

[14] *H. Molinari, F. Montanari, P. Tundo*, J. Chem. Soc. Chem. Commun. *1977*, 639.

[15] *H. Komeili-Zadeh, H. J.-M. Dou, J. Metzger*, J. Org. Chem. *43*, 156 (1978).

[16] *P. Tundo*, Synthesis *1978*, 315.

[17] *F. Rolla, W. Roth, L. Horner*, Naturwissenschaften *64*, 377 (1977).

[18] *P. Tundo*, J. Chem. Soc. Chem. Commun. *1977*, 641.

[19] *S. L. Regen, D. P. Lee*, Macromolecules *10*, 1418 (1977), and references cited therein.

[20] S. L. Regen, D. P. Lee, J. Am. Chem. Soc. 96, 294 (1974).
[21] M. Tomoi, O. Abe, M. Ikeda, K. Kihara, H. Kakiuchi, Tetrahedron Lett. 1978, 3031.
[22] S. L. Regen, L. Dulak, J. Am. Chem. Soc. 99, 623 (1977).
[23] S. L. Regen, J. Am. Chem. Soc. 99, 3838 (1977).
[24] S. L. Regen, J. J. Besse, J. McLick, J. Am. Chem. Soc., in press.
[25] S. L. Regen, A. Nigam, J. J. Besse, Tetrahedron Lett. 1978, 2757; M. Tomoi, T. Takubo, M. Ikeda, H. Kakiuchi, Chem. Lett. 1976, 473.
[26] S. Colonna, R. Fornasier, U. Pfeiffer, J. Chem. Soc. Perkin Trans. 1 1978, 8.
[27] E. Chiellini, R. Solaro, J. Chem. Soc. Chem. Commun. 1977, 231.
[28] H. J.-M. Dou, R. Gallo, P. Hassanaly, J. Metzger, J. Org. Chem. 42, 4275 (1977).
[29] A. W. Herriott, D. Picker, J. Am. Chem. Soc. 97, 2345 (1975).
[30] S. L. Regen, J. Heh, unpublished work.
[31] R. H. Grubbs, L. C. Kroll, J. Am. Chem. Soc. 93, 3062 (1971); R. H. Grubbs, L. C. Kroll, C. M. Sweet, J. Macromol. Sci. Chem. 7, 1047 (1973); R. H. Grubbs: Catalysis in Organic Synthesis. Academic Press, New York 1976, p. 153.
[32] S. L. Regen, D. P. Lee, Isr. J. Chem., in press.
[33] S. L. Regen, A. Nigam, J. Am. Chem. Soc., in press.
[34] S. L. Regen, J. Org. Chem. 42, 875 (1977).
[35] S. L. Regen, J. McLick, J. Heh, unpublished work.
[36] F. Helfferich: Ion Exchange. McGraw-Hill, New York 1962, p. 525.
[37] For a brief description of the different types of crosslinked polystyrene, see: J. M. J. Frechet, M. J. Farrall in: Chemistry and Properties of Cross-linked Polymers. Academic Press, New York 1977, p. 59.
[38] C. M. Starks, J. Am. Chem. Soc. 93, 195 (1971).
[39] C. M. Starks, R. M. Owens, J. Am. Chem. Soc. 95, 3613 (1973).
[40] D. Landini, A. Maia, F. Montanari, J. Am. Chem. Soc. 100, 2796 (1978).
[41] E. H. Cordes, R. B. Dunlap, Acc. Chem. Res. 2, 329 (1969); C. A. Bunton, Prog. Solid State Chem. 8, 239 (1973); E. J. Fendler, J. H. Fendler, Adv. Phys. Org. Chem. 8, 271 (1970).
[42] F. M. Menger, J. Am. Chem. Soc. 92, 5965 (1970).

Key Building Blocks of Natural Product Biosynthesis and Their Significance in Chemistry and Medicine[**]

By Burchard Franck[*]

The principal features of the biosynthesis of natural products have been elucidated during the past thirty years by the use of isotopic methods. It was discovered that large groups of natural products originate from the same biosynthetic precursor—the key building block. The conversion of key building blocks into biologically active natural products serves as a model for the development of more efficient syntheses in chemistry. In medicine, information about key building blocks permits the elucidation and therapy of metabolic diseases.

1. Introduction

Natural products are defined as carbon compounds which are formed in plants, microorganisms, animals, and man. Many of these natural products, *e. g.* vitamins and antibiotics, are indispensable for man's existence.

The number of structurally elucidated natural products has increased greatly in recent years. This is due, on the one hand, to the great interest shown in biologically active substances and, on the other hand, to the highly developed methods available for their isolation and structural determination. Thus, approximately 20000 natural products are known[1]; that is less than 1% of all organic compounds. From the point of view of man and other organisms, however, they are an elite group of compounds which have been selected out during the course of evolution for the necessities of life.

Natural product biosynthesis is an important field of research in modern natural product chemistry[3-6]. Work in this field led, primarily, to an understanding of the diversity of organic natural products, gave an insight into metabolism and induced the development of simpler syntheses[4,6-10].

The biosynthesis of natural products was elucidated by isotopic labeling[8]. Surprisingly, it was discovered that entire groups of natural products originated from the same biosynthetic precursor. These precursors are the *key building blocks* of natural product biosynthesis. Information about a few key building blocks is sufficient to obtain an overall view of the diversity of natural products.

The key building blocks of biosynthesis occupy an important position in the metabolism of living organisms. Numerous diseases are caused by a modification of the biosynthetic steps involving the key building blocks[9]. In medicine, information about a few key building blocks thus allows elucidation and treatment of several metabolic diseases.

A knowledge of the key building blocks led to a revolutionary development in the chemical synthesis of natural products. Many natural products can be synthesized in the laboratory by using key building blocks as starting materials[4,5,10,11]; such syntheses, which utilize biosynthesis as a model, are often superior to the customary natural product syntheses.

In the following, a greatly simplified survey of natural product biosynthesis will first be given. The application of biogenetic findings to chemical syntheses and in medicine will then be dealt with using topical examples. Finally, it will be discussed why natural product biosynthesis proceeds *via* certain key building blocks.

2. Biosynthesis of the Main Groups of Natural Products

The 20000 natural products can be divided into four large groups according to their biosyntheses. Three typical compounds of each of these groups are given as examples in Table 1.

[*] Prof. Dr. B. Franck
Organisch-Chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

[**] Based on a plenary lecture given to the 110th Meeting of the Gesellschaft Deutscher Naturforscher und Ärzte on September 19, 1978 in Innsbruck (Austria).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0429 $ 02.50/0

Table 1. The four main groups of natural products (with examples).

1. Carbohydrates	2. Arenes
D-Glucose	Flower pigments
Vitamin C	Vitamin K_1
Cellulose	Lignin
3. Acetogenines	**4. Nitrogen-containing natural products**
Fatty acids	Nucleosides
Vitamin D	Blood pigment
Caoutchouc	Proteins

The biosynthesis of all these natural products starts with atmospheric carbon dioxide, water and nitrogen (Fig. 1). Carbon dioxide and water are converted, with the assistance of sunlight and chlorophyll, into D-glucose by the process of photosynthesis elucidated by *Calvin*[12]. This simple sugar (D-glucose) not only acts as a key building block for the very large group of carbohydrate natural products, but also for the three other groups. These three other groups result from D-glucose *via* the key building blocks shikimic, acetic, and amino acids. Ammonia is formed from atmospheric nitrogen in a reaction sequence—nitrogen fixation[13]—which is only found in a few microorganisms. D-Glucose is thus the central key building block of natural product biosynthesis. The quantities of glucose produced annually in photosynthesis far exceed those of any other technically or biologically synthesized organic compound.

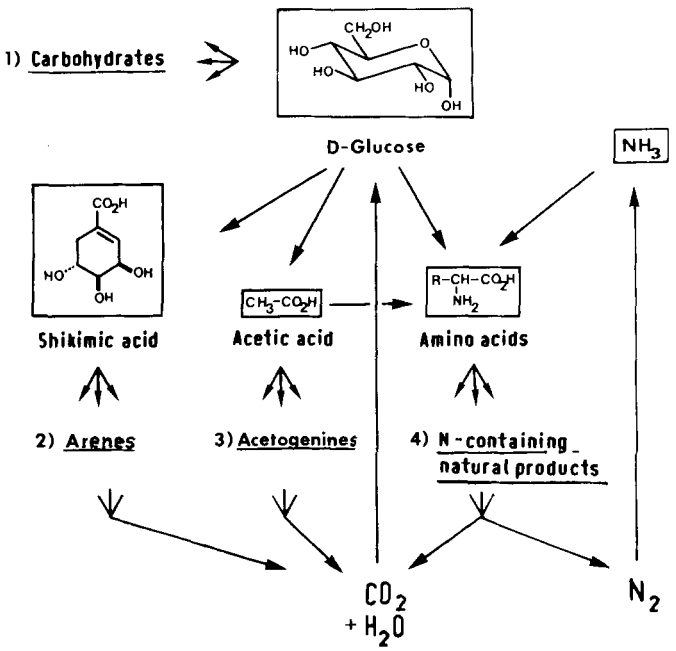


Fig. 1. Biosynthesis of the four main groups of natural products *via* the key building blocks D-glucose, shikimic acid, acetic acid and amino acids.

During the course of biosynthesis, the key building blocks shown in Figure 1 are followed by further key building blocks which are precursors for smaller natural product groups. All of these natural products undergo reactions which finally end in biological degradation and reformation of carbon dioxide, water and nitrogen. Thus, there is a fluent transition between biosynthesis and biological degradation.

Figures 2 and 3, respectively, show situations in which the first step of biosynthesis and the last step of biological degradation proceed at their highest possible intensities.



Fig. 2. Rice plantation on the Philippines in a state of full photosynthesis (photograph: BASF).

3. Problems in Natural Product Synthesis

The first synthesis of a natural product was accomplished 150 years ago by *Friedrich Wöhler* in Berlin; this was his famous urea synthesis[14]. The then current dogma that natural products could only be formed in living organisms was thus refuted. Chemical natural product synthesis has made a great deal of progress since then. This is apparent if urea *(1)* is compared, for example, with erythronolide B *(2)*. The complete synthesis of erythronolide was recently achieved by *Corey* and co-workers[15]. Erythronolide B is an aglycon of the erythromycin antibiotics. As it contains ten chiral carbon atoms in a relatively flexible ring system, its total synthesis was regarded as an almost "hopelessly complex" task twenty years ago[*].

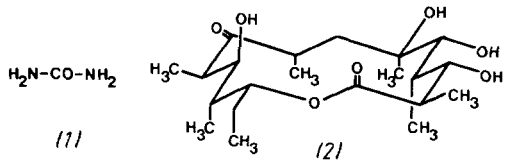


Figure 4 shows a sample of *Wöhler*'s first urea together with his publication in Poggendorffs Annalen[14]; the urea was sealed and labeled by *Wöhler* himself; he gave it to his friend *Emanuel Merck* in Darmstadt. *Wöhler* had purified his preparation so thoroughly that, according to its modern IR spectrum, it is as pure as "Merck" analytical urea (Fig. 5).

[*] *R. B. Woodward* (1956) [16]: "Erythromycin, with all our advantages, looks at present quite hopelessly complex, particularly in view of its plethora of asymmetric centers...".



Fig. 3. Degradation of residual substances of natural product biosynthesis by bacteria in a modern sewage plant (photograph: BASF).

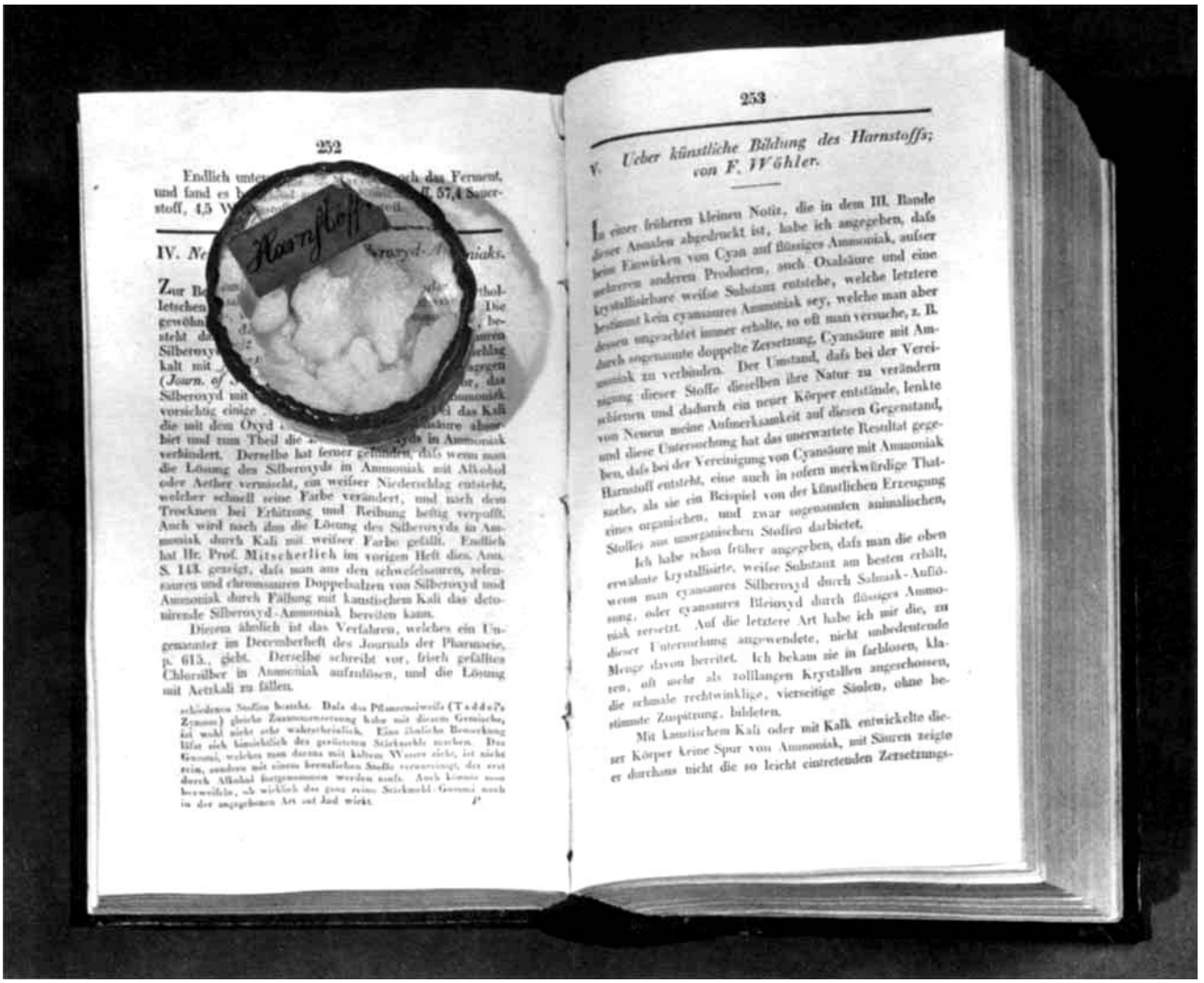
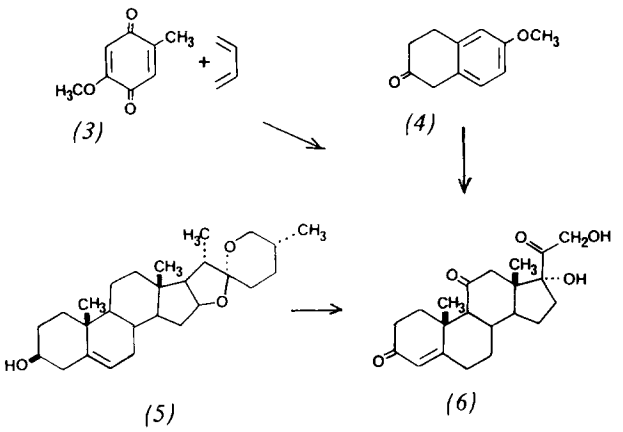


Fig. 4. Original sample of *Wöhler*'s first synthetic urea and his publication in Poggendorffs Annalen [14] (photograph: Merck).

Despite the development of impressive total syntheses, natural product synthesis is still in a dilemma. Syntheses suitable for the technical production of natural products are only available in relatively few cases. Most total syntheses of the more complicated natural products require so many reaction steps that the total yield becomes vanishingly low. This can best be illustrated by the example of the medically important steroid hormone, cortisone *(6)*.



Woodward[17] was the first to succeed in performing the sensational, total synthesis of this natural product with its six chiral carbon atoms in 1952. The synthesis started with methoxytoluquinone *(3)* and proceeded *via* 49 steps, the total yield was less than 10^{-5}%. This does not detract in any way from the great scientific significance of this achievement. The further efforts of industrial laboratories were then directed towards improving yields by reducing the number of steps. The 27-step synthesis developed by Roussel in France from a tetralone (4) gave a technically interesting total yield of 1%[18]. A synthesis performed by Syntex in the USA[19] (13 steps, 3.3% total yield) starts with the readily available steroid natural product, diosgenin *(5)*, and is thus not a total synthesis.

Table 2 shows the relationship between the number of reaction steps and the total yields in multistep syntheses. If the average yield is 70% per reaction step—which can be considered as very good—the total yield decreases drastically as the number of reaction steps increases. As multistep syntheses with such yields are of no use in practice, either the average yield must be increased (to 99%) or the number of reaction steps must be greatly reduced. These requirements can be met if natural syntheses are based on biosynthetic models with the utilization of key building blocks. Such *biomimetic syntheses* are generally characterized by a small number of steps and a high total yield. Furthermore, it is generally important that they are carried out under mild conditions and that the formation of by-products is avoided by means of high selectivity.

Table 2. The dependence of the total yields [%] in multistep syntheses on the average yields and number of steps.

Steps \ Average Yield [%]	99	90	70
1	99	90	70
10	90	35	2.8
20	82	12	0.08
30	74	4.2	0.0023
40	67	1.5	0.000064
50	61	0.52	0.0000016

The first definitive example of a natural product synthesis based on a biosynthetic model was the laboratory synthesis of the alkaloid, tropinone *(8)*. *Willstätter*[20] synthesized this, then regarded as problematic, bridged heterocycle from suberic acid *(7)* in a 15-step total synthesis. The yield was only 0.76%. The one-step synthesis based on biosynthetic concepts developed by *Robinson* and *Schöpf* provided an impressive

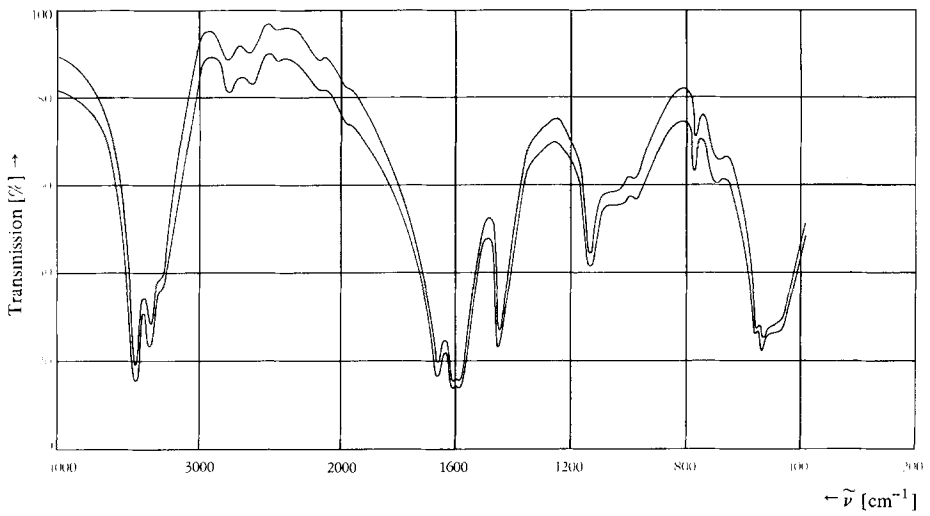
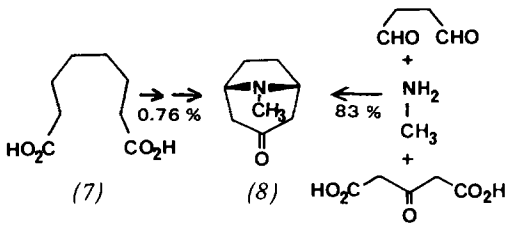


Fig. 5. IR spectra of *Wöhler's* urea (upper spectrum) and "Merck" analytical urea (lower spectrum) in KBr (photograph: Merck).



comparison; the yield was over 80%[21]. Stimulated by this success, intensive efforts were then initiated to work out simple, efficient syntheses for alkaloids and other natural products using the key building blocks of biosynthesis.

4. Elucidation of the Key Building Blocks

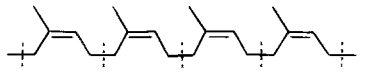
Isotopic methods are indispensable for the elucidation of the key building blocks of natural product biosynthesis. The four isotopes of carbon are most important; these are available as a result of highly developed enrichment and nuclear transformation techniques (Table 3). The two most important, the stable ^{13}C and the radioactive ^{14}C, complement one another with respect to their possible applications[22]. Biosynthetic experiments in which the reliable determination of labeled products at high dilutions is important can be performed with ^{14}C due to its extremely low natural abundance. ^{13}C allows (with, however, a considerably lower detection sensitivity) very simple determination of labeling positions in molecules by means of ^{13}C-NMR spectroscopy. The short-lived ^{11}C is utilized in medicine for metabolic investigations.

Table 3. Radioactive and stable isotopes of carbon.

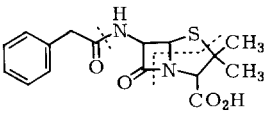
C isotope	Abundance [%]	Half-life
^{11}C	—	20.4 min
^{12}C	98.89	∞
^{13}C	1.11	∞
^{14}C	10^{-10}	5600 years

The main features of the biosynthesis of natural products have been elucidated over the past 30 years by using isotopic methods[8]. With the help of this information, it is now usually simple to recognize the key building blocks of a natural product and the main group to which it belongs. This is illustrated by the formulas for rubber *(9)* (isoprene)[23] and the antibiotic, penicillin *(10)* (cysteine and valine)[24]. The biosynthesis of some novel natural products from marine organisms, *e. g.* the extremely toxic saxitoxin *(11)*[25], is less evident.

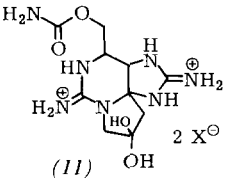
The synthesis and function of more complex key building blocks are still under intensive investigation. Although these compounds give rise to smaller natural product groups than do the basic key building blocks, they furnish very useful information for chemistry and medicine. This topic will be discussed for four groups of biologically active natural products in the following sections. The unsaturated hydrocarbon, squalene *(12)*, is the key building block for the steroids and triterpenes[26,27]. Numerous, structurally related compounds (anthraquinoids) are derived from the anthraquinone emodin *(13)*[28]. Many isoquinoline alkaloids, *e. g.* morphine, are formed from the key building block reticulin *(14)*[29]. The structurally complex uroporphyrinogen III *(15)* is the precursor for heme[30], vitamin B_{12}[31] and similar natural products.



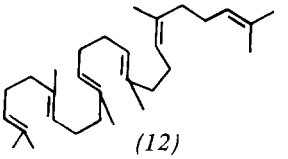
(9)



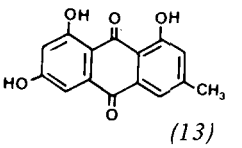
(10)



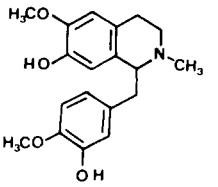
(11)



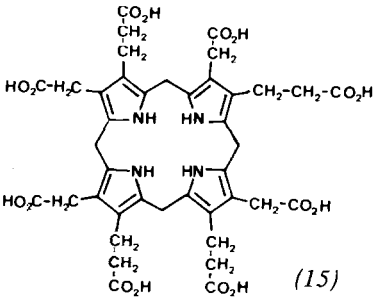
(12)



(13)



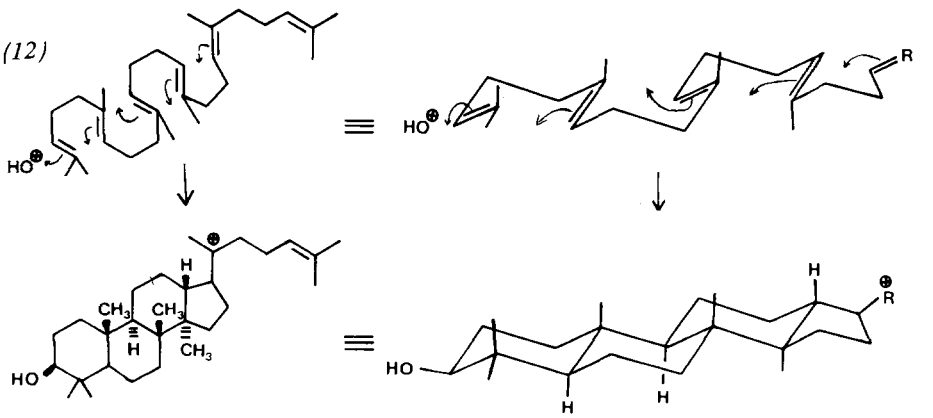
(14)



(15)

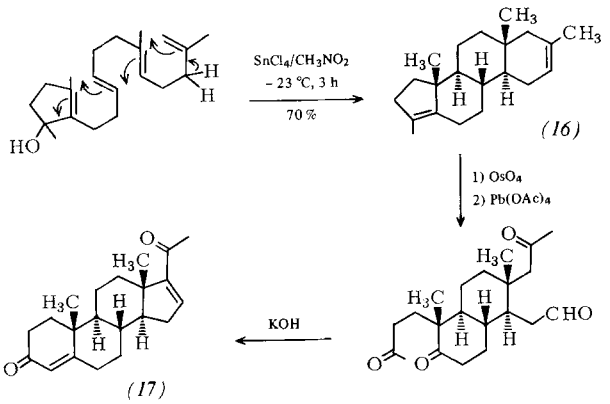
5. Key Building Blocks of Acetogenine Biosynthesis

The cyclization of squalene *(12)* to the tetracyclic steroid molecule is a fascinating biosynthetic reaction. Four rings are closed and eight centers of chirality are formed in a concerted reaction; this is triggered by hydroxy cation *via* a terminal epoxidation. In order to account for the stereospecific-



(12)

ity of such a complicated reaction sequence, it is assumed that the carbon chain of the squalene in solution prefers an arrangement in which the individual rings of the steroid molecule are, as it were, preformed[32]. The cyclization of the key building block, squalene, understandably represented a challenge to the chemist to synthesize the medically valuable steroids in a similar fashion. *W. S. Johnson et al.*[32] have achieved remarkable results; the simple biomimetic synthesis of 16,17-didehydroprogesterone *(17)* is shown as an example. The elegant construction of a steroid-like ring system *(16)* was accomplished under mild conditions starting with a precursor similar to the key building block, squalene. The steroid hormone *(17)* was obtained from this in three further steps. This strategy of biomimetic synthesis has already proved to be of value in other steroid syntheses.



Emodin *(13)*, a key building block which, like squalene *(12)*, is formed from acetic acid, is involved in the biosynthesis of a group of toxins produced by mold fungi. Many molds found in food contain poisonous substances whose danger is partially increased by their accumulation in the organism and their lingering action[33]. Figure 6 shows a pure culture of such a fungus on bread. The strongly active aflatoxin B_1 *(18)* from *Aspergillus flavus* and the weakly active roquefortin *(19)* from *Penicillium roqueforti* are examples of fungal toxins from food molds[34,35].

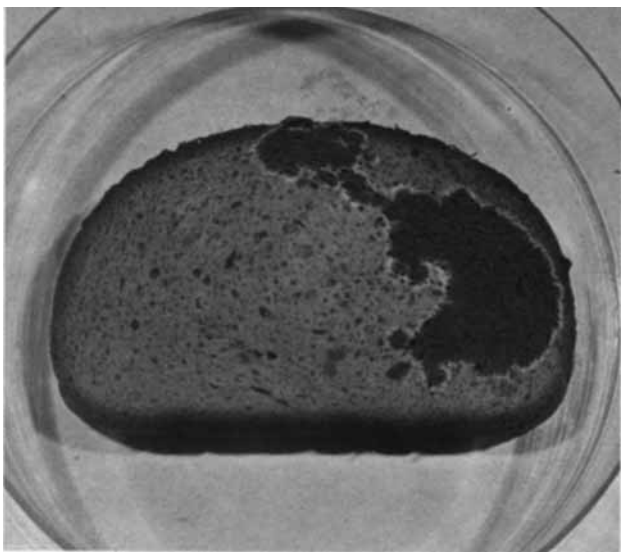
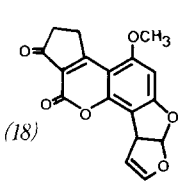
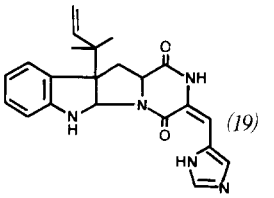
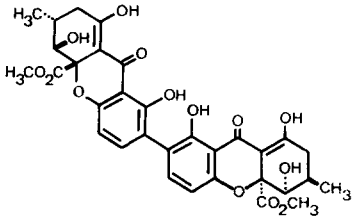


Fig. 6. A pure culture of *Penicillium islandicum* on bread (from [36]).

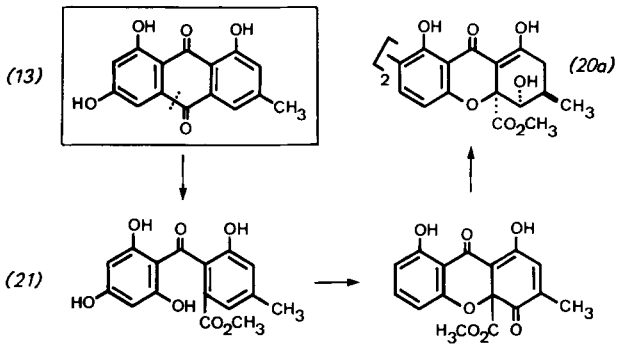

(18)


(19)

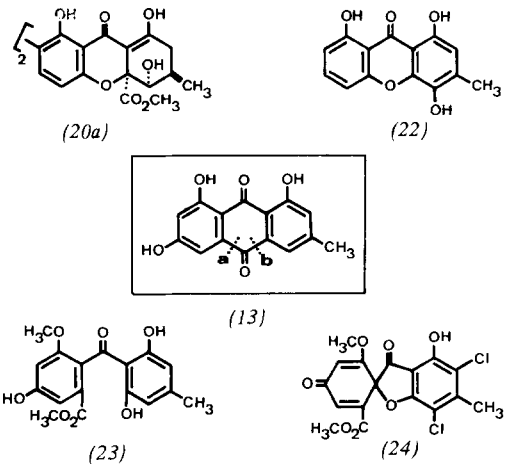
Our laboratory has also been very involved with work on one of these groups of fungal toxins, the ergochromes. The ergochromes[37] are produced by molds mainly found in rye, maize and rice. In rye they form the sclerotia known as ergot. As the structure of the most important ergochrome secalonic acid A *(20)* shows, these compounds are dimeric xanthone derivatives[38,39].


(20)

13 ergochromes have so far been isolated from molds and lichens[38,40-45]. It appeared likely that these ergochromes could be prepared *via* a novel biosynthetic route in which emodin *(13)* is the key building block. Each half of the ergochrome molecule might be formed in a few steps in which



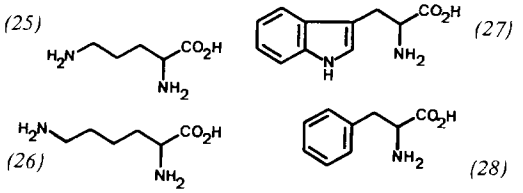
emodin is first cleaved oxidatively to give benzophenone *(21)*. Subsequent cyclization, together with reductive reactions, would then furnish the xanthone derivative *(20a)*



found in the ergochromes. We have studied this hypothesis using emodin derivatives labeled with C and H isotopes. After feeding molds with labeled anthraquinones, these compounds were indeed converted into ergochromes in high yields *via* a benzophenone intermediate [cf. *(21)*][46-48]. This is the first evidence for oxidative ring opening of an anthraquinone in biosynthesis[49]. It was later discovered that further natural products, are also derived from emodin *(13)*, which is thus an especially versatile key building block, by ring cleavage at a or b. *Gatenbeck et al.*[50] demonstrated that the benzophenone sulochrin *(23)* is a seco-anthraquinone[46]. Using isotopically labeled precursors, we were further able to show that the antibiotic geodin *(24)*[51] and ravenelin *(22)*[52] can also be classed as seco-anthraquinones. Emodin *(13)* could be converted into *(21)* and products of type *(20a)* in biomimetic syntheses[53,54]. The formulas again show how completely different structures can be related to one another by means of their origin from the same key building block in biosynthesis.

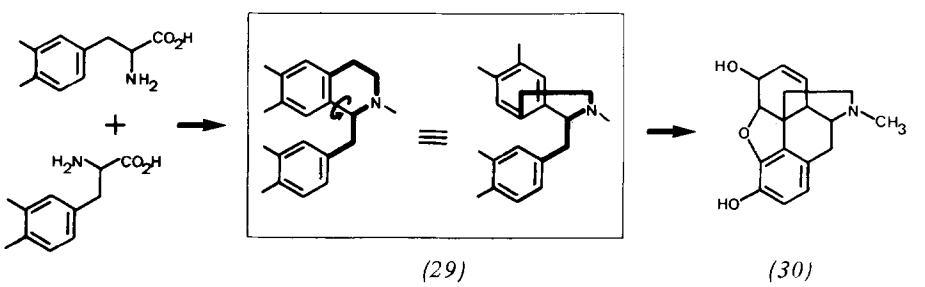
6. Key Building Blocks of Alkaloid Biosynthesis

Alkaloids, as the name suggests, are natural products with basic properties. They are mainly produced by plants and are distinguished by their specific pharmacological effects on human and animal nervous systems. This fact has long been made use of by man. Approximately 5000 alkaloids are known. Considering their varied structures, it is surprising that almost all of them are formed from only four amino acids or their derivatives[55]; these are ornithine *(25)*, lysine *(26)*, tryptophan *(27)* and phenylalanine *(28)*.



The biosynthesis of morphine will be taken as an example. Two phenylalanine derivatives split off carbon dioxide and ammonia to form benzyltetrahydroisoquinoline *(29)* as key building block[55,56] which can undergo especially diverse reactions [cf. reticulin *(14)*]. The three-dimensional ring system of morphine *(30)* results after 180° rotation around the bond indicated and subsequent ring linkage.

The key building block *(29)* enclosed within the rectangle gives rise to additional basic skeletons from which a total of approximately 2000 alkaloids are derived (Fig. 7).



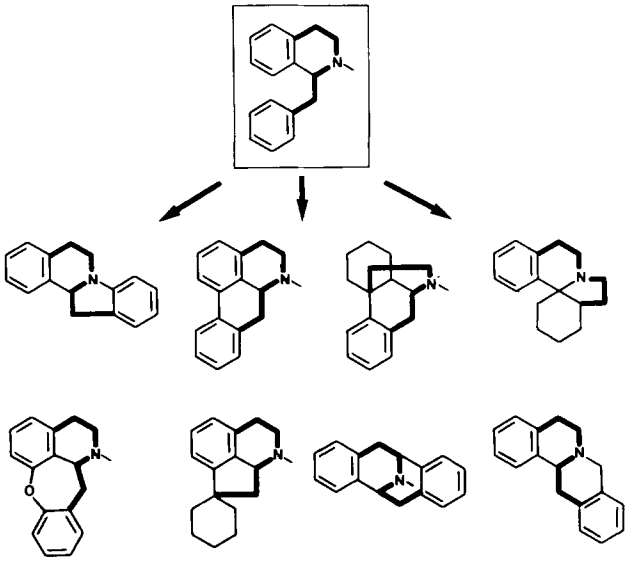
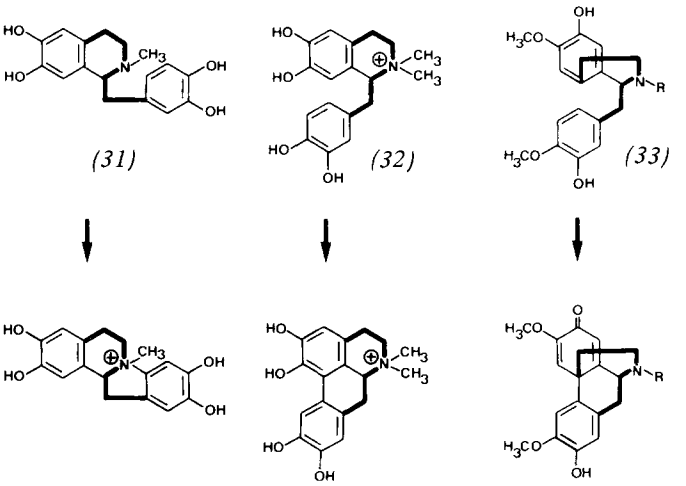


Fig. 7. Eight basic alkaloid skeletons which are derived from derivatives of the key biosynthetic building block, benzyl tetrahydroisoquinoline (enclosed within the rectangle). The alkaloids are of the following types (upper row): crytaustoline, aporphine, morphine, erythrinane; (lower row): cularine, proaporphine, pavine, protoberberine (from left to right in each case).

The economy of this biosynthetic scheme is impressive and it is an ideal model for the technical production of a range of chemical products. In the past 40 years, numerous groups of workers have thus tried to simulate this scheme in the laboratory. The first experiments were carried out independently by *Schöpf*[57] and *Robinson*[58]. They oxidized ben-



zyl tetrahydroisoquinoline *(31)* in the hope that they would obtain an aporphine or a morphinane. Ring closure with a 70% yield was achieved but resulted in a cryptaustoline de-

rivative. We later found that the oxidative ring closure could be steered to give the desired aporphine in 62% yield by quaternization at the nitrogen [*(31)*→*(32)*][59]. This was the first biomimetic synthesis of the basic aporphine skeleton from which numerous alkaloids with diverse pharmacological effects are derived.

Biomimetic synthesis of the basic morphinane skeleton was more difficult. *Barton*[60] first demonstrated that ring closure could be achieved by oxidative condensation of the key building block *(33)*. The yield could be increased to 4% by using a two-phase oxidation system[61] and to 40% by utilizing vanadium oxide trichloride as oxidizing agent[62], thus making this reaction suitable for synthetic purposes. It should be mentioned in this context that morphine, which is indispensable in medicine, is still obtained from poppy plants. Misuse cannot be ruled out. It is therefore urgent that a method be found in which morphine can be produced industrially under supervisable conditions.

The finding that aporphine and morphine alkaloids can be relatively easily produced from their key building blocks raises the question as to whether this synthesis can also take place spontaneously or undesirably in living organisms. According to recent results, this is indeed the case in chronic alcoholism. The first reports of a connection between alcohol and opium addiction first appeared several years ago[63]. It is now certain that the similarity between the disease symptoms in alcoholism and opium addiction is of chemical origin[64-66] (Fig. 8). The alcohol consumed is dehydrated in the liver to

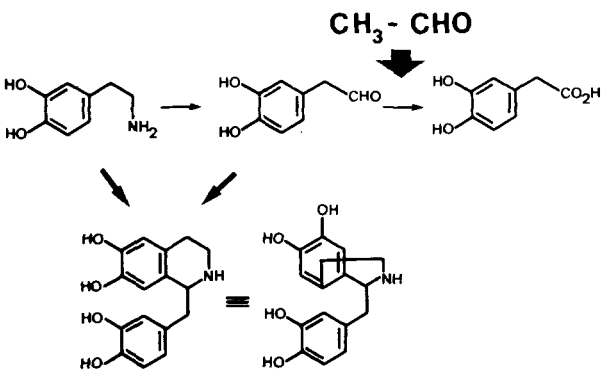
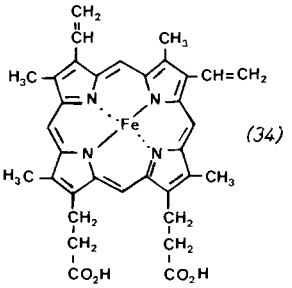


Fig. 8. Opiate formation in chronic alcoholism.

acetaldehyde which, depending on its quantity, then blocks to a lesser or greater extent the normal degradation of phenylalanine in the organism. Phenylethylamine and phenylacetaldehyde derivatives are thus produced in higher concentrations which then condense spontaneously to give the key building block for aporphine and morphine biosynthesis [see *(29)*]. Formation of the key building block and the alkaloids derived from it have been clearly demonstrated in experiments on animals. These results are extremely important for the preventive, psychological, and medicinal therapy of chronic alcoholism[66].

7. Key Building Blocks of Porphyrin Biosynthesis

Key building blocks have an especially impressive role in the biosynthesis of the blood pigment heme and related compounds. The basic heme skeleton is a porphyrin. The porphyrins belong to the most interesting systems which nature has produced. Porphyrins existed on the surface of the earth 2.5 billion years ago[67], they catalyze vital metabolic processes in almost all organisms. As far as man is concerned, heme *(34)* is the most important porphyrin[68]. It is a component of the proteid hemoglobin, which is responsible for the transport of oxygen from the lungs to the cells within the body. Minor modifications in heme biosynthesis cause lethal blood diseases[9, 70].



(34)

The blood pigment heme and related natural products originate from two very simple compounds—glycine and succinic acid. The first information concerning heme biosynthesis is to be found in the pioneering studies of *Shemin*[69]. This work started 30 years ago with an experiment which, on the basis of the then current knowledge, was rather risky. *Shemin* synthesized 66 g glycine labeled with ^{15}N and swallowed it. He subsequently showed that the glycine nitrogen was directly incorporated into the heme of his blood. Further biosynthetic experiments—with duck blood—demonstrated that heme is produced from eight molecules of glycine and eight of succinic acid (Fig. 9).

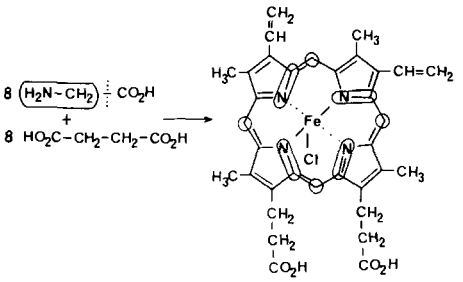
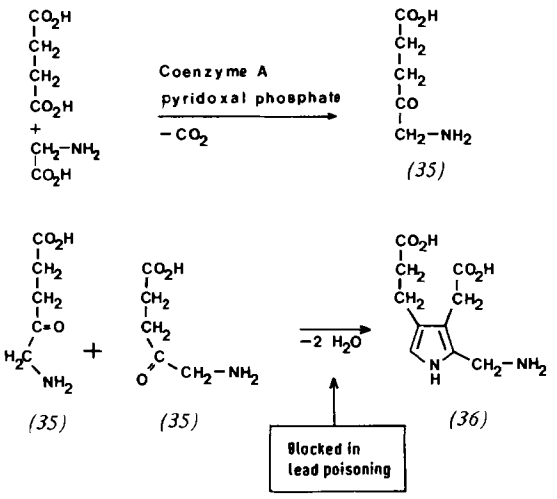


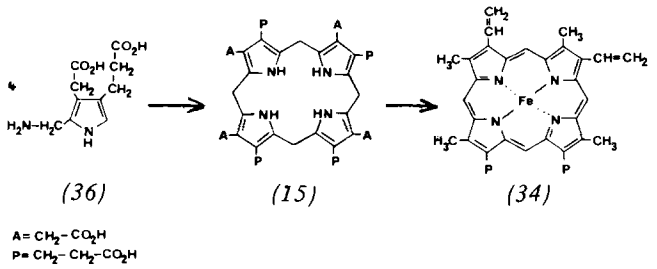
Fig. 9. Biosynthesis of heme from glycine and succinic acid [69]. The encircled atoms are derived from glycine, the others from succinic acid.

Succinic acid and glycine first condense with decarboxylation to give 5-aminolevulinic acid *(35)*. Two molecules of 5-aminolevulinic acid then give the pyrrole derivative, porphobilinogen *(36)*. This reaction step is inhibited, for example, in lead poisoning[70]; the detectable concentration of 5-aminolevulinic acid in urine is a direct calibration of the degree of lead poisoning. In this way, less heme is synthesized. This results in damage due to oxygen deficiency which first affects the brain[71]. Four molecules of the very reactive porphobilinogen *(36)* are then assumed to condense to form the porphyrin.

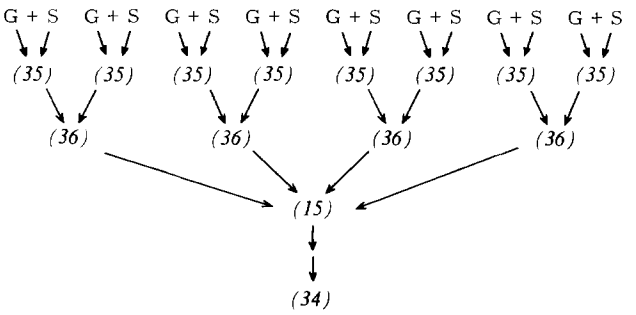
Until fairly recently, there were many possible explanations for this condensation[72]. Several years ago we were able to show for the first time by total synthesis of radioactively labeled uroporphyrinogen III *(15)*[73] and its conversion to heme by enzymes in duck blood, that uroporphyrinogen III is the direct biosynthetic precursor of the blood pigment



heme *(34)*[30]. *Scott et al.*[31] subsequently found that the vitamin B_{12} ring system is also formed from uroporphyrinogen III. Chlorophyll is probably synthesized in a similar way. Uroporphyrinogen III may thus be a biogenetic key building block which is of central importance for all organisms. Its synthesis from the monopyrrole porphobilinogen *(36)* is now



being intensively investigated by several groups of workers[74-77]. A simplified scheme containing the most important parts of heme biosynthesis starts with eight molecules of both glycine and succinic acid ("G + S"). These condense in pairs to give aminolevulinic acid *(35)*, two molecules of which then furnish the monopyrrole building block, porphobilinogen *(36)*. After this, the reaction pathway leads to uroporphyrinogen III *(15)* and heme *(34)*. This biosynthetic scheme constitutes an ideal model for a rational natural product synthesis. This embodies perfectly the important principle of "converging" synthesis in which a high total yield is attained with as small a number of successive, linear synthesis steps as possible (Fig. 10).



As is the case with alkaloids and steroids[78], there are also biomimetic syntheses for the porphyrins which are distinguished by their simplicity and good yields. Porphobilinogen *(36)* in dilute acid can be converted in high yields into porphyrins[79]. The main product is uroporphyrinogen III *(15)*, the key building block of heme biosynthesis[80]. The reaction product contains, however, smaller quantities of the three other isomers of this key building block. The high specificity of reaction is surprising; for example, open-chained condensation products or ring systems with more than four pyrrole units are not produced[81]. Simple syntheses for known, biologically active and also novel porphyrins have been developed with the help of these very efficient, biomimetic porphyrin syntheses[31-33]. Examples[82] are the highly strained,

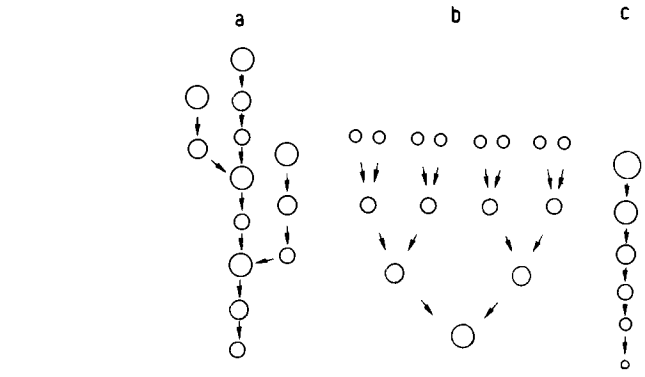
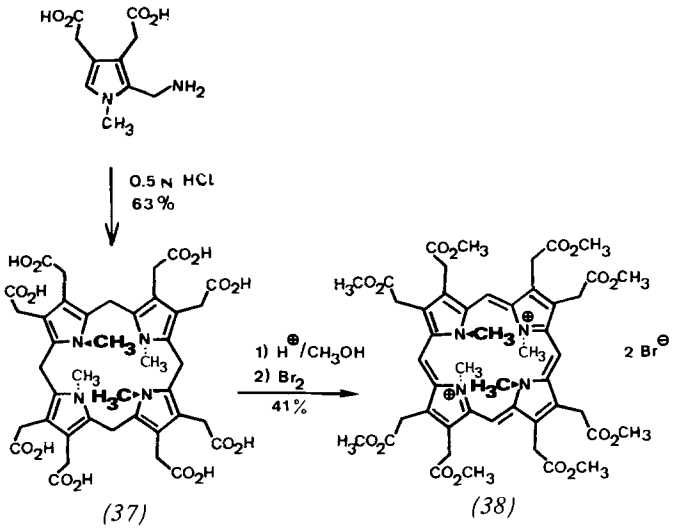


Fig. 10. Strategies for multistep syntheses: a) branched, b) converging, c) linear (taken from [89]).



non-planar[84] *N,N,N,N*-tetramethylporphyrinogen *(37)* and its green dehydration product called *N,N,N,N*-tetramethylporphyrin *(38)*[82] whose syntheses have been attempted for 40 years.

8. Conclusion

The question as to why natural product biosynthesis proceeds *via* relatively few key building blocks and in essentially a similar fashion in all organisms deserves special attention. One reason may be that it would be rational if a large range of natural products were formed *via* as few as possible versa-

tile intermediates. Organisms whose metabolism did not develop in accordance with this principle would then be inferior and would disappear during evolution. A further possible explanation may be that most of the key building blocks of natural product biosynthesis already existed on the surface of the earth over three billion years ago.

In experiments on the simulation of the "primeval atmosphere"[85, 86] (water, methane, hydrogen, ammonia), it was shown that, under the influence of radiant energy, a "primeval soup" was formed. This "primeval soup" contained prac-

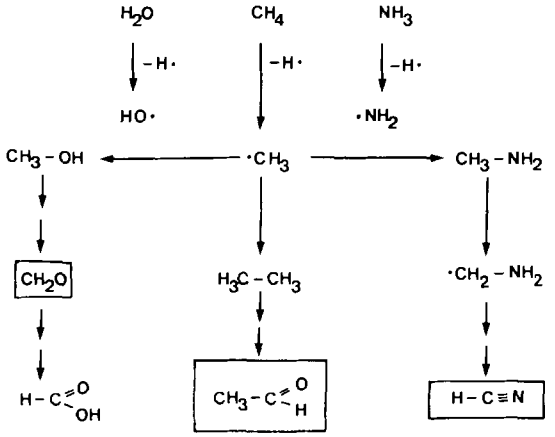


Fig. 11. Fundantental prebiotic reactions.

tically all the substances (amino acids, fatty acids, sugars, purine bases, porphyrins *etc.*) which, as is now known, are necessary for the metabolism of living organisms. Synthesis of all these compounds is, according to modern mechanistic concepts, easy to explain (see *e. g.* Fig. 11, 12[86–88]).

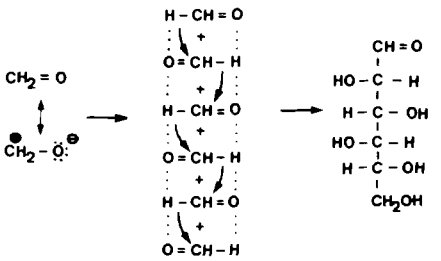


Fig. 12. The synthesis of hexoses from formaldehyde in a simulation experiment.

The aim of this article has been to show what the key building blocks of natural product biosynthesis are and their significance in chemistry and medicine. Research on key building blocks in natural product chemistry has led to a plethora of interesting results with many different applications. Many—even complex—natural products are apparently compounds which were selected out during evolution not only for their biological activity but also on account of their especially simple mode of formation. An understanding and simulation of this mode of formation could, in the future, lead to simple total syntheses of useful, biologically active natural products.

I am especially indebted to the co-authors of our publications cited. Their enthusiasm for thematically and methodically multifarious problems made possible the exploration of the relationships described. Generous support by the Deutsche Forschungsgemeinschaft, the Landesamt für Forschung in Nordrhein-Westfalen, and the Fonds der Chemischen Industrie is gratefully acknowledged.

Received: November 23, 1978 [A 262 IE]
German version: Angew. Chem. 92, 453 (1979)

[1] Up until 1961, 4423 plant products (excluding alkaloids) had been registered in the handbook of *Karrer et al.* [2]; of these, 1754 were recorded in the period 1956–1961. Thus an increase of approximately 1800 over a five-year period, or of 6000 from 1961 to 1978 may be assumed for these products, giving a total number of 10000 plant products. The number of alkaloids and animal products so far known are each estimated to be approximately 5000. The total number of natural products is thus approximately 20000.

[2] *W. Karrer, E. Cherbuliez, C. H. Eugster:* Konstitution und Vorkommen der organischen Pflanzenstoffe (exclusive Alkaloide). Hauptwerk und Ergänzungsband I. Birkhäuser, Basel 1958 und 1977.

[3] *R. Robinson:* The Structural Relations of Natural Products. Clarendon Press, Oxford 1955.

[4] *D. H. R. Barton, T. Cohen* in: Festschrift für Arthur Stoll. Birkhäuser, Basel 1957, p. 122.

[5] *D. Ranganathan, S. Ranganathan:* Art in Biosynthesis, the Synthetic Chemist's Challenge. Vol. I. Academic Press, New York 1976.

[6] *A. J. Birch* in: Further Perspectives in Organic Chemistry. Elsevier, Amsterdam 1978, p. 5.

[7] *B. Franck,* Naturwissenschaften *47*, 169 (1960).

[8] *P. Bernfeld:* Biogenesis of Natural Compounds. Pergamon, Oxford 1967.

[9] *W. Siegenthaler:* Klinische Pathophysiologie. Thieme, Stuttgart 1976; *P. K. Bondy, L. E. Rosenberg:* Diseases of Metabolism. Saunders, Philadelphia 1974.

[10] *E. E. van Tamelen,* Fortschr. Chem. Org. Naturst. *19*, 242 (1961).

[11] *B. Franck, G. Blaschke, G. Schlinghoff,* Angew. Chem. *75*, 957 (1963); Angew. Chem. Int. Ed. Engl. *3*, 192 (1964).

[12] *M. Calvin,* Angew. Chem. *74*, 165 (1962); Angew. Chem. Int. Ed. Engl. *1*, 65 (1962).

[13] *D. Kleiner,* Angew. Chem. *87*, 97 (1975); Angew. Chem. Int. Ed. Engl. *14*, 80 (1975).

[14] *F. Wöhler,* Poggendorffs Ann. *12*, 253 (1828).

[15] *E. J. Corey, S. Kim, S. Yoo, K. G. Nicolaou, L. S. Melvin, D. J. Brunelle, J. R. Falck, E. J. Trybulski, R. Lett, P. W. Sheldrake,* J. Am. Chem. Soc. *100*, 4620 (1978).

[16] *R. B. Woodward* in: Perspectives in Organic Chemistry. Interscience, New York 1956, p. 160.

[17] *R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, W. M. McLamore,* J. Am. Chem. Soc. *73*, 4057 (1951); *74*, 4223 (1952).

[18] *L. Velluz, G. Nominé, J. Mathieu,* Angew. Chem. *72*, 725 (1960).

[19] *O. Mancera, H. J. Ringold, C. Djerassi, G. Rosenkranz, F. Sondheimer,* J. Am. Chem. Soc. *75*, 1286 (1953).

[20] *R. Willstätter,* Justus Liebigs Ann. Chem. *326*, 23 (1903).

[21] *R. Robinson,* J. Chem. Soc. *111*, 762 (1917); *C. Schöpf,* Justus Liebigs Ann. Chem. *518*, 1 (1935).

[22] *E. Buncel, C. C. Lee:* Carbon-13 in Organic Chemistry; Isotopes in Organic Chemistry. Vol. 3. Elsevier, Amsterdam 1977; *H. Simon:* Messung von radioaktiven und stabilen Isotopen: Anwendung von radioaktiven und stabilen Isotopen in der Organischen Chemie und Biochemie. Band II. Springer, Berlin 1974.

[23] *F. Lynen, U. Henning,* Angew. Chem. *72*, 826 (1960).

[24] *H. R. V. Arnstein, M. E. Clubb,* Biochem. J. *65*, 618 (1957).

[25] *J. Bordner, W. E. Thiessen, H. A. Bates, H. Rapoport,* J. Am. Chem. Soc. *97*, 6008 (1975).

[26] *N. M. Packter:* Biosynthesis of Acetate-derived Compounds. Wiley, London 1973, p. 143.

[27] *R. B. Clayton,* Q. Rev. Chem. Soc. *19*, 168 (1965).

[28] *R. H. Thomson:* Naturally Occurring Quinones. Academic Press, London 1971.

[29] *D. H. R. Barton, G. W. Kirby, W. Steglich, G. M. Thomas, A. R. Battersby, T. A. Dobson, H. Ramuz,* J. Chem. Soc. *1965*, 2423.

[30] *B. Franck, D. Gantz, F.-P. Montforts, F. Schmidtchen,* Angew. Chem. *84*, 433 (1972); Angew. Chem. Int. Ed. Engl. *11*, 421 (1972).

[31] *A. I. Scott, N. Georgopapadakou, K. S. Ho, S. Klioze, E. Lee, S. L. Lee, G. H. Temme, C. A. Townsend, I. M. Armitage,* J. Am. Chem. Soc. *97*, 2548 (1975).

[32] *W. S. Johnson,* Angew. Chem. *88*, 33 (1976); Angew. Chem. Int. Ed. Engl. *15*, 9 (1976); *W. S. Johnson, T. Li, C. A. Harbert, W. R. Bartlett, T. R. Herrin, B. Staskun, D. H. Rich,* J. Am. Chem. Soc. *92*, 4461 (1970).

[33] *I. F. H. Purchase:* Mycotoxins. Elsevier, Amsterdam 1974.

[34] *L. A. Goldblatt:* Aflatoxin. Academic Press, New York 1969.

[35] P. M. Scott, M.-A. Meerien, J. Polonsky, Experientia *32*, 140 (1976).
[36] *B. Franck*, Abh. Rhein.-Westf. Akad. Wiss. N 219 (1972).
[37] *B. Franck, H. Flasch*, Fortschr. Chem. Org. Naturst. *30*, 151 (1973); *B. Franck*, Angew. Chem. *81*, 269 (1969); Angew. Chem. Int. Ed. Engl. *8*, 251 (1969).
[38] *B. Franck, E. M. Gottschalk, U. Ohnsorge, F. Hüper*, Chem. Ber. *99*, 3842 (1966).
[39] *J. W. Hooper, W. Marlow, W. B. Whalley, A. D. Borthwick, R. Bowder*, J. Chem. Soc. Part C *1971*, 3580.
[40] *A. Freeburn*, Pharm. J. *88*, 568 (1912).
[41] *I. Yosioka, T. Nakanishi, S. Izumi, I. Kitagawa*, Chem. Pharm. Bull. *16*, 2090 (1968).
[42] *P. S. Steyn*, Tetrahedron *26*, 51 (1970).
[43] *M. Yamazaki, Y. Maebayashi, K. Miyaki*, Chem. Pharm. Bull. *19*, 199 (1971).
[44] *C. C. Howard, R. A. W. Johnstone*, J. Chem. Soc. Perkin Trans. 1 *1973*, 2440.
[45] *R. Andersen, G. Büchi, B. Kobbe, A. L. Demain*, J. Org. Chem. *42*, 352 (1977).
[46] *B. Franck, F. Hüper, D. Gröger, D. Erge*, Angew. Chem. *78*, 752 (1966); Angew. Chem. Int. Ed. Engl. *5*, 728 (1966).
[47] *B. Franck, F. Hüper, D. Gröger, D. Erge*, Chem. Ber. *101*, 1954 (1968).
[48] *D. Gröger, D. Erge, B. Franck, U. Ohnsorge, H. Flasch, F. Hüper*, Chem. Ber. *101*, 1970 (1968).
[49] *B. Franck* in *P. S. Steyn:* The Biosynthesis of Mycotoxins. Academic Press, New York, in press.
[50] *S. Gatenbeck, L. Malmström*, Acta Chem. Scand. *23*, 3493 (1969).
[51] *H. Fujimoto, H. Flasch, B. Franck*, Chem. Ber. *108*, 1224 (1975).
[52] *G. Breipohl*, Diplomarbeit, Universität Münster 1978.
[53] *B. Franck, J. Stöckigt, U. Zeidler, G. Frankowiak*, Chem. Ber. *106*, 1198 (1973).
[54] *B. Franck, B. Berger-Lohr*, Angew. Chem. *87*, 845 (1975); Angew. Chem. Int. Ed. Engl. *14*, 818 (1975).
[55] *K. Mothes, H. R. Schütte:* Biosynthese der Alkaloide. VEB Deutscher Verlag der Wissenschaften, Berlin 1969.
[56] *A. R. Battersby, R. Binks, R. J. Francis, D. J. McCaldin, H. Ramuz*, J. Chem. Soc. *1964*, 3600.
[57] *C. Schöpf, K. Thierfelder*, Justus Liebigs Ann. Chem. *497*, 22 (1932).
[58] *R. Robinson, S. Sugasawa*, J. Chem. Soc. *1932*, 789.
[59] *B. Franck, G. Schlinghoff*, Justus Liebigs Ann. Chem. *659*, 123 (1962).
[60] *D. H. R. Barton, G. W. Kirby, W. Steglich, G. M. Thomas*, Proc. Chem. Soc. *1963*, 203; J. Chem. Soc. *1965*, 2423.
[61] *B. Franck, G. Dunkelmann, H. J. Lubs*, Angew. Chem. *79*, 1066 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1075 (1967).
[62] *S. M. Kupchan, C.-K. Kim, J. T. Lynn*, J. Chem. Soc. Chem. Commun. *1976*, 86.
[63] *V. E. Davis, M. J. Walsh*, Science *167*, 1005 (1970).
[64] *G. Cohen*, Biochem. Pharmacol. *25*, 1123 (1976).
[65] *K. Bum:* Alcohol and Opiates. Academic Press, New York 1977.
[66] *G. Bringmann*, Naturwissenschaften *66*, 22 (1979).
[67] *G. W. Hodgson, B. Hitchon, B. Taguchi, B. L. Baker, E. Peake*, Geochim. Cosmochim. Acta *32*, 737 (1968).
[68] *K. M. Smith:* Porphyrins and Metalloporphyrins. Elsevier, Amsterdam 1975.
[69] *D. Shemin*, Naturwissenschaften *57*, 185 (1970); *D. Shemin, D. Rittenberg*, J. Biol. Chem. *166*, 621 (1946).
[70] *L. Heilmeyer:* Die Störungen der Bluthämsynthese. Thieme, Stuttgart 1964, p. 115.
[71] *Th. Haas, K. H. Schaller, H. Valentin*, Dtsch. Ärztebl. *69*, 1803 (1972).
[72] *J. Lascelles:* Tetrapyrrole Biosynthesis and its Regulation. Benjamin, New York 1964, p. 38.
[73] *B. Franck, D. Gantz, F. Hüper*, Angew. Chem. *84*, 432 (1972); Angew. Chem. Int. Ed. Engl. *11*, 420 (1972).
[74] *B. Frydman, R. B. Frydman*, Acc. Chem. Res. *8*, 201 (1975).
[75] *A. I. Scott, K. S. Ho, M. Kajiwara, T. Takahashi*, J. Am. Chem. Soc. *98*, 1589 (1976).
[76] *A. R. Battersby*, Experientia *34*, 1 (1978).
[77] *B. Franck, G. Fels, G. Ufer*, Angew. Chem. *89*, 677 (1977); Angew. Chem. Int. Ed. Engl. *16*, 652 (1977).
[78] *L. Velluz, J. Ralls, G. Nominé*, Angew. Chem. *77*, 185 (1965); Angew. Chem. Int. Ed. Engl. *4*, 181 (1965).
[79] *G. H. Cookson, C. Rimington*, Biochem. J. *57*, 476 (1954).
[80] *D. Mauzerall*, J. Am. Chem. Soc. *82*, 2605 (1960).
[81] *B. Franck, A. Rowold, Ch. Wegner, H.-G. Eckert*, Philos. Trans. R. Soc. London Ser. *B 273*, 181 (1976).
[82] *B. Franck, Ch. Wegner*, Angew. Chem. *87*, 419 (1975); Angew. Chem. Int. Ed. Engl. *14*, 423 (1975); *R. Steinkamp*, Dissertation, Universität Münster 1978.
[83] *F. Grubenbecher*, Dissertation, Universität Münster 1978.
[84] *G. Sawitzki, H.-G. von Schnering*, Angew. Chem. *88*, 616 (1976); Angew. Chem. Int. Ed. Engl. *15*, 552 (1976).
[85] *S. L. Miller*, Science *117*, 528 (1953).
[86] *K. Dose, H. Rauchfuss:* Chemische Evolution und der Ursprung lebender Systeme. Wissenschaftliche Verlagsgesellschaft, Stuttgart 1975, p. 87.
[87] *B. Franck*, Chem. Ber. *93*, 446 (1960).
[88] *E. Pfeil, H. Rückert*, Justus Liebigs Ann. Chem. *641*, 121 (1961).
[89] *A. A. Akhrem, Y. A. Titov:* Total Synthesis of Steroids. Israel Program for Scientific Translations, Jerusalem 1969, p. 8.

Photochemical Reactions of Surfactant Molecules in Condensed Monolayer Assemblies—Environmental Control and Modification of Reactivity[**]

By David G. Whitten[*]

An investigation of the effects of a controlled microenvironment on reactivity has been carried out by the synthesis and study in organized monolayers of surfactant molecules containing photochemically reactive chromophores. Reactions where substantial environmental effects have been observed include the *cis-trans* isomerization of olefins, ketone photoeliminations, ligand substitution processes, excimer and photodimer formation, and photoredox reactions. Both reactions occurring within the organized assemblies as well as interfacial phenomena have been investigated. Results obtained in these studies suggest possible extensions and applications for the development of new catalyst systems, biological models and controlled syntheses.

1. Introduction

The phenomenon of monolayer film formation at an air-water interface has been known and studied for a long time. Such films are formed when molecules containing a hydrophilic group, for example a carboxyl group, and a sufficiently long hydrophobic chain are brought onto the surface of water; these molecules are referred to as surface active (or as surfactants). Techniques for the study and manipulation of such films were developed by *Pockels*[1], *Blodgett*[2,3], and *Langmuir*[3] and later extended by numerous other investigators. *Langmuir* found in 1917 that films spread on water could be transferred to solid supports[4]; later studies developed and refined the techniques for depositing several consecutive film layers. In recent years the techniques for the preparation and study of monolayers have been greatly elaborated and at the same time simplified, largely due to the elegant investigations of *Kuhn et al.*[5–10]. The possibilities for preparing assemblies of a known and controlled molecular architecture have been developed and used to investigate a wide range of phenomena ranging from electronic energy transfer and polymerization to protein-membrane interactions and photographic sensitization[5].

A number of investigations have dealt with chemical reactions occurring within monolayer films or assemblies or occurring between a reactant contained in a monolayer and another present in an adjacent phase. Reactions investigated in some early studies include hydrolysis reactions[11,12], oxidations[13], and polymerizations[14]. In a number of investigations the occurrence of specific reactions has indicated that considerable but frequently retarded penetration of monolayers by various reagents from adjacent bulk phases can occur[15]. These observations as well as other evidence emphasize the intermediacy of the properties of compressed layers between those of liquids and solids. Thus the spacing indicated by surface pressure-area relationships in many condensed monolayers is regular and close to that occurring in highly ordered hydrocarbon crystals, yet the same monolayers can be penetrated by relatively large organic reagents such as α-naphthol[5,15].

Our interest in examining a variety of chemical processes and photoreactions in monolayers was stimulated by the attractive possibility of having reactive molecules present in a specific orientation and in a known and controlled microenvironment. The close resemblance of monolayer films and assemblies to biological membranes further suggested that phenomena occurring in monolayers might in some cases provide reasonable models for processes occurring within membranes or at membrane-solution interfaces. In our investigations of reactions occurring in monolayer films and assemblies and at monolayer interfaces, we have examined a variety of processes and in many cases we have been able to make comparisons between reactivity in solution, the solid state, monolayers and other organized media. Our results indicate that the microenvironment of a molecule after incorporation in a monolayer film or assembly can produce striking effects on reactivity that can be explained in terms of concentration and orientation effects, hydrophilic-hydrophobic relationships, restricted diffusion and packing phenomena. While most of the reactions examined to date have been carried out on an extremely small scale, the rather pronounced effects observed would justify the future development of practical applications.

2. Unimolecular Reactions in Monolayers

2.1. Photoisomerization of Olefins

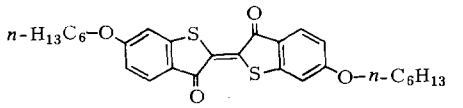
One of the most widely studied of all photoreactions is the *cis-trans* isomerization of olefins[16]. Although this reaction generally does not occur in crystalline solids it occurs readily in fluid solution. In most cases isomerization occurs *via* rapid relaxation of *cis* or *trans* excited states to a twisted intermediate which can decay to ground states of both isomers. In viscous solutions photoisomerization is sometimes retarded and in certain cases selective restriction of the isomerization in one of the two directions occurs[16,17]. For example, in the much investigated stilbenes, it has been observed that an increase in viscosity of the medium retards the *trans* to *cis* process selectively while allowing the reverse process to pro-

[*] Professor Dr. D. G. Whitten
Department of Chemistry
University of North Carolina
Chapel Hill, North Carolina 27514 (USA)

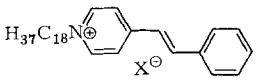
[**] Photochemical Reactions in Organized Monolayer Assemblies, Part 12.—Part 11: *P. R. Worsham, D. W. Eaker, D. G. Whitten*, J. Am. Chem. Soc. *100*, 7091 (1978).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/06 06-0440 $ 02.50/0

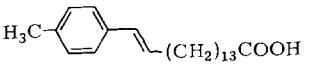
ceed[17]. This viscosity effect has been ascribed to an increase in molecular volume along the path of the *trans* to *cis* process. Such an effect might be expected to play a major role in highly condensed monolayer systems, and for this reason we have examined the behavior of olefins *(1)*—*(3)*, all of which can be incorporated into monolayer films and assemblies but in rather different environments[18-21].



(1)



(2)



(3)

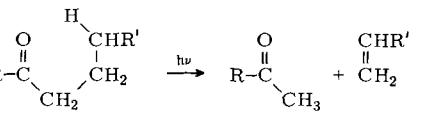
All three olefins (as well as their non-surfactant analogs) undergo facile *cis-trans* photoisomerization in both directions in solution. For *(1)* and *(2)* selective wavelength irradiation of solutions enables preparation of monolayer films and assemblies rich in one or the other isomer. For *(3)* only the photobehavior of the *trans* isomer has been investigated[21]. The photoisomerization behavior of *(1)* in films and assemblies has been the most extensively investigated[18]. The thioindigo chromophore absorbs strongly in the visible region and the spectra of the two isomers in assemblies are only slightly altered from those in solution. From measurements of the absorption spectrum with polarized light, in analogy to results obtained by Kuhn *et. al.*[5] with structurally related cyanine dyes, we conclude that the chromophore of *(1)* lies at or near the hydrophilic interface parallel to the surface in films and assemblies. On irradiation of films or assemblies containing *cis-(1)* a rapid and irreversible conversion to *trans-(1)* is observed. In contrast films or assemblies containing *trans-(1)* were found to be photostable and no conversion to the *cis* isomer or other photoreaction was detected even on relatively long term irradiation. A study of the pressure-area isotherms of spread films of *cis-* and *trans-(1)* on the water surface indicates that a greater cross sectional area per molecule is required for the *cis* isomer and that a significant reduction in pressure occurs when films of *cis-(1)* are irradiated and undergo conversion into *trans-(1)*. Thus there appears to be a very reasonable parallel between the behavior of *(1)* in the films and assemblies and the viscosity effects previously observed with olefins such as the stilbenes[17]. A similar behavior has been observed for the stilbazole derivative *(2)* in films and assemblies. This positively charged analog of stilbene evidently also resides at a site at or near the hydrophilic interface. Irradiation of *cis-(2)* in monolayer assemblies results in rapid and irreversible formation of the *trans* isomer. The *trans* isomer does not form *cis-(2)* on irradiation in the assemblies; however, in this case the *trans* isomer undergoes photoreaction to form other products (cf. Section 3.2)[19,20]. That a restriction to increased molecular volume caused by tight packing plays the major role in inhibiting the *trans* to *cis* process in *(1)* and *(2)* rather than simple orientation effects is indicated by the finding that *(2)* undergoes efficient isomerization in both directions *(trans* $\rightleftharpoons$ *cis, cis* $\rightleftharpoons$ *trans)* as its chief photoreaction upon incorporation into cationic micelles.

The surfactant styrene *(3)* also readily forms monolayer films and assemblies[21]; however, for this compound the olefinic chromophore lies at the end of a hydrocarbon chain in a highly hydrophobic environment. The behavior of *(3)* in films and assemblies closely resembles that of *(2)*. Irradiation of *trans-(3)* leads rapidly and cleanly to a photoproduct, but no isomerization to the *cis*-isomer occurs[21]. A pressure-area study of *trans-(3)* suggests that highly compressed films and assemblies are formed which can not easily expand to accomodate the bulkier *cis* isomer.

The similar behavior of the three rather different olefinic systems described here would indicate that partial inhibition of isomerization could be a fairly general phenomenon in highly condensed assemblies owing to the effective high pressures caused by close packing of the paraffin chains and hydrophilic (head) groups.

2.2. Photoreactions of Ketones in Monolayers

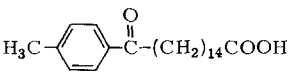
We have recently investigated another intramolecular photoreaction in monolayers which should be extremely sensitive to the environment: the Norrish type II photoelimination of ketones [eq. (a)]. This reaction, which occurs with moderate quantum efficiency, is the dominant photoreaction of most aliphatic and aromatic ketones possessing abstractable γ-hydrogens in solution[22,23]. The reaction proceeds *via*



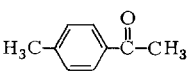
(a)

γ-hydrogen abstraction in a cyclic six-membered transition state followed by cleavage of the diradical to form an enol of the methyl ketone and an olefin. The reaction has been examined in micelles[24] and in several polymer systems[25,26]. Studies on polymers have shown that the rates of reaction and efficiencies are relatively high in polyethylene and vinyl ketone copolymers above the glass transition point[26]. At low temperatures below the glass transition point and in some crystalline solids very little reaction *via* the type II process is observed because the rigidity of the medium makes it difficult to achieve the proper geometry for reaction to occur[26].

In our investigations of the type II process [eq. (a)] in monolayers we used the oxo acid *(4)*, which was expected to form films and assemblies with the ketone in a somewhat ordered hydrophobic region. It was found that *(4)* does in fact form good films and assemblies in 1:1 mixtures with arachidic acid[27]. In compressed films formed from these mix-



(4)

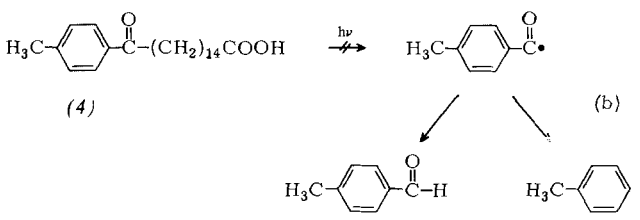


(5)

tures the area per molecule of *(4)* is 20 Å^2; this corresponds closely to the cross sectional area of a paraffin chain. Irradiation of *(4)* in benzene solution gives the expected methyl ketone *(5)* as the chief volatile product with a quantum efficiency (ϕ) of 0.2. In contrast irradiation of *(4)* in assemblies leads to disappearance of the ketone chromophore (as meas-

ured by spectral changes in the ultraviolet or infrared) with a quantum efficiency of 0.06[27]. However, the methyl ketone *(5)* is only a minor product formed in low yield. Thus, the quantum yield for the type II elimination ranges from 0.0001–0.03 (depending on assembly architecture), down considerably from the value in solution. The low quantum efficiency for the type II elimination in monolayer assemblies can be attributed to a perpendicular (zig-zag) arrangement of the paraffin chains which cannot be easily distorted to allow the cyclic transition state necessary for γ-hydrogen abstraction to be attained.

The contrast between the extremely low quantum yield for the reaction of *(4)* in the type II process [eq. (a)] and the moderate quantum yield for the disappearance of *(4)* suggests that other photochemical reactions occur. One such process which might be anticipated is the photoelimination of type I (α-cleavage) [eq. (b)]. This would be expected to result in chain scission of *(4)*, leading to either or both *p*-methylbenzaldehyde and toluene. However, analysis of the volatile products obtained on photolysis of *(4)* in the assemblies



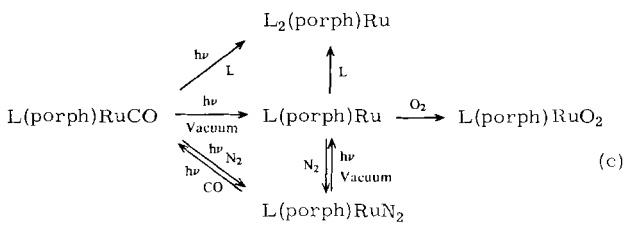
reveals that neither product is formed in detectable yield. The lack of type I cleavage products [eq. (b)] is perhaps surprising but also reasonable if the monolayer environment prevents diffusion of free radicals formed by α-cleavage such that only recombination occurs. The disappearance of *(4)* must therefore be accounted for by other reactions; a reasonable possibility is intermolecular hydrogen abstraction from a paraffin chain in close proximity to the carbonyl group. Such a process could lead to net photoreduction of the keto group or to a cross-linking reaction. We are currently examining the non-volatile products in order to determine precisely the major reaction path.

We are also examining reactions of the oxo acid *(4)* as a structural probe in other organized media and in modified monolayer assemblies. In anionic sodium dodecyl sulfate (SDS) micelles we find that *(4)* undergoes Norrish type II photoelimination to give the methyl ketone *(5)* as the only volatile product. The quantum yield for the process in SDS micelles is 0.8, four times the value obtained in hydrocarbon solution. This value is comparable to those obtained for non-surfactant ketones solubilized in cationic micelles[24]; in these studies it was inferred that the increase in quantum efficiency in micelles was consistent with location of the ketone chromophore in a relatively polar environment, since the Norrish II photoelimination in solution increases markedly in alcohols or other polar solvents[22,23]. A reasonable inference from the present results is that for *(4)* in SDS micelles the polymethylene chain is coiled back on itself so that both ends (carbonyl and carboxy group) may lie near the micellar surface. The high value obtained for the photoelimination of *(4)* in SDS micelles ($\Phi_{II} = 0.8$) emphasizes the contrast in order and rigidity or microviscosity between monolayers and micelles. Thus, even though both media are formed by self-organization of amphipathic molecules, the one structure closely resembles a crystalline solid in many of its properties while the other is essentially solution-like.

2.3. Ligand Exchange Processes in Metalloporphyrin Complexes

Previous indications that the microenvironment provided by deposited monolayer assemblies is intermediate between a crystalline solid and a viscous solution suggested that ligand exchange processes would be a particularly attractive class of reactions to study in these media. Both thermal and photochemical ligand exchange reactions have been observed for a wide variety of transition metal complexes; while the former may involve both association and dissociation processes, photochemical reactions almost invariably involve ejection of a ligand to generate an intermediary, highly reactive coordinatively unsaturated metal center. In solution such intermediates are usually very short-lived; the reactive complex is normally consumed rapidly by reaction with ligating solvent or solute molecules or by recapture of the ejected fragment. We hoped that ligand photoejection in organized monolayer assemblies might permit the isolation and selective reaction of the reactive complexes thus formed. Our investigations in this area have centered around ligand exchange processes occurring with metalloporphyrin complexes.

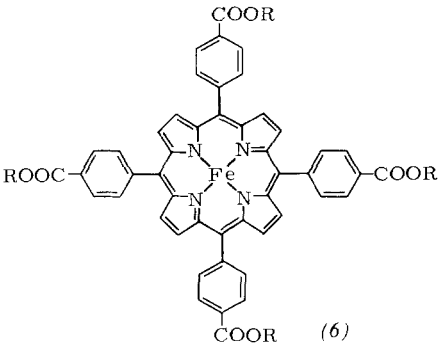
The photoejection of bound CO from iron(II) porphyrin complexes such as carboxyhemoglobin and carboxymyoglobin as well as simpler synthetic complexes has been observed in numerous investigations[28,29]; more recent work has shown that photoejection processes involving other ligands as well as other metals can occur in porphyrin complexes[30-33]. We have investigated the photoejection of CO from ruthenium(II) and osmium(II) porphyrin complexes in solution[30]. In these investigations the overall reaction observed was replacement of the departing CO by a new ligand. The CO-free metalloporphyrin which is formed in the photoejection cannot be isolated in solution even though it can be detected by flash photolysis. In our studies with surfactant metalloporphyrins in monolayer assemblies we found that the carbonylruthenium(II) complex of the dioctadecyl ester of mesoporphyrin IX (porph) forms good monolayer assemblies in which the porphyrin is photochemically active[34]. The complex can be introduced into assemblies as either the aquo-CO or pyridine-CO complex; both complexes exhibit similar photochemical behavior. Irradiation of dry monolayer assemblies containing these complexes, L(porph)RuCO (where L is pyridine or water), *in vacuo* leads to isolation of the CO-free complex. This complex, L(porph)Ru, is extremely reactive on exposure to air, nitrogen, oxygen, pyridine or CO, but it is fairly stable in a highly evacuated cell. The reactions we have observed to date are summarized in Scheme (c)[34]. The absence of ligating molecules in the dry



(c)

and evacuated monolayer environment permits isolation of the otherwise unobtainable L(porph)Ru and thus its exploitation for the directed synthesis of novel nitrogen and oxygen complexes[34]. It is interesting to note that, subsequent to these investigations, solution studies on the photolysis of similar carbonylruthenium(II) porphyrin complexes in weakly ligating solvents such as acetonitrile have led to the production of labile oxygen complexes having spectra similar to those of the oxygen complexes L(porph)RuO_2 isolated in the monolayers[35]. Here a labile L_2(porph)Ru species is evidenced as intermediate in the formation of the oxygen complex.

We have also examined ligand exchange processes with surfactant iron porphyrins in monolayer assemblies[36]. Assemblies are generally prepared by introducing the air-stable iron(III) complex into the monolayer film and reducing the complex after it has been incorporated into a multilayer assembly. We have found that the iron(III) porphyrins in monolayer assemblies can be reduced to the corresponding iron(II) complex by two rather different procedures. Exposure of dry, evacuated assemblies to the reducing ligand piperidine leads to quantitative reduction to the iron(II) complex. With the surfactant iron(II) porphyrin *(6)*, R = cholestanyl [cf. *(18b)*], we find that exposure to oxygen or carbon monoxide in the monolayer assemblies leads to the formation of substituted iron(II) complexes and not to the corresponding iron(III) complex. Both the oxygen- as well as the carbonyl-complex regenerate the unsubstituted iron(II) complex on evacuation of the assembly[36]. We have also found that reduction of iron(III) porphyrins can occur through addition of other ligand-reducing agent systems. Addition of NO to evacuated assemblies results in formation of an NO complex having a characteristic iron(II) NO^+ spectrum. This complex can be decomposed by addition of methanol to give the iron(II) complex [eq. (d)][36].



(6)

$$(porph)Fe^{II}NO^{\oplus}Cl^{\ominus} + CH_3OH \rightarrow (porph)Fe^{II} + CH_3ONO + HCl \quad (d)$$

Reactions of iron(II) complexes prepared in assemblies by this method are currently under investigation.

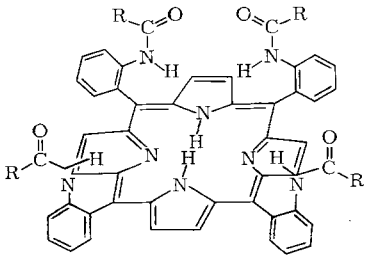
3. Bimolecular Reactions in Monolayer Films and Assemblies

3.1. Dimer Formation and Aggregation

Investigations with surfactant dyes and other compounds with strongly absorbing chromophores have indicated that considerable aggregation occurs in monolayer films and assemblies[5-7]. This can frequently be observed both in pure and in mixed monolayers and can involve both inter- and intra-layer interactions. The aggregation can most easily be established by comparison of the absorption and emission spectra of the molecules under investigation in dilute solution and in the condensed monolayer assemblies. Aggregation can result as a consequence of several factors, depending upon the system under investigation and the techniques used to form the monolayer assembly[37]. In many cases studies of isotherms obtained from separate and mixed monolayers indicate that the latter are not homogeneous but consist of domains or patches of separate monolayers[38,39]. While in certain cases separate phases may result from differences in solubility of the components in the spreading solvent, in other systems the occurrence of separate phases may be due to nonmixing or nonideality in the spread film[39]. Such factors are evidently much more severe in organized media than in conventional solutions; it has recently been shown, for example, that in micelles formed from mixtures of fluorocarbon and hydrocarbon surfactants there is a nearly complete segregation into distinct phases of the individual components[40]. Even where the components of mixed monolayers are completely miscible in the spread film, in cases where both components are present in anywhere near equimolar amounts the effective local concentrations obtained in the films can be quite high. Thus, the films and assemblies frequently provide a means for obtaining concentrations much higher than in solution, such that dimer formation or aggregation is conceivable even if there is only relatively weak attraction between the molecules. The tight packing of components in condensed monolayers may also lead to an interlocking or association of groups which might not associate in solution, particularly if facilitated by the spatial arrangements in the component surfactants. Examples where such factors have been demonstrated as being important include the packing of surfactant cyanine dyes into Scheibe aggregates[5-7] and the interlocking functional units consisting of an azobenzene dye oriented perpendicular to a cyanine dye which have recently been prepared by *Polymeropoulos, Möbius* and *Kuhn*[41].

Our work in this area has demonstrated the importance of dimerization and aggregation for several different surfactant molecules in monolayer films and multilayer assemblies. Some of our first investigations involved a study of monolayers formed from various porphyrins and their metal complexes. In solution studies we were able to show that porphyrins and their zinc complexes form dimers at low temperatures in moderately dilute (10^{-6} M) hydrocarbon solutions[42]. When the same porphyrin chromophore is incorporated into a surfactant molecule we find in several cases that the resulting monolayer assembly formed by transfer of several film layers from water gives a temperature-independent absorption spectrum nearly identical to that of the dimer obtained in solution at low temperatures[42]. Such dimers, which are formed by contact of the chromophores of neighboring layers can easily be distinguished from the dimers formed within a layer in which dye layers are separated by intercalated fatty acid layers. Hence, for several surfactant porphyrins the dimerization, *i. e.* association of two chromophores, is a purely intralayer phenomenon such that identical spectra are obtained both from multilayers in contact and

those in which "inert" arachidate "spacer layers" separate the layers containing porphyrin. However with certain porphyrins, most notably those of the "picket fence" type such as *(7)*, the dimers obtained in multilayers are exclusively or predominantly interlayer as determined by the "spacer layer" technique[43]. The fact that *(7)* and some closely related "picket fence" porphyrins form interlayer dimers indicates that the porphyrin must lie at the hydrophilic interface in a rather well-defined site. We are currently attempting to take advantage of this property to construct assemblies of controlled architecture in which two different metal complexes are in close proximity with each another.



(7), R = $C_{15}H_{31}$

The tendency of porphyrins to associate in monolayer films and assemblies led to interesting but troublesome results in our attempts to study iron porphyrins in assemblies[44]. Since iron(II) porphyrins are not air-stable in solution, it was anticipated that assemblies should be constructed from the corresponding iron(III) complexes which could then be reduced by various reagents. As outlined in Section 2.3, for certain complexes this procedure has proven feasible. However, for several surface-active iron porphyrins it was found that spreading of films from the chloroiron(III) porphyrin led to immediate and irreversible formation of the corresponding μ-oxo compounds [eq.(e)][44]. This reaction which can be viewed as a simple three-step substitution process [eqs (f)—(h)], occurs in solution, but only at high pH... and then rather slowly[45-47]. In contrast, we found that in the monolayer films the reaction is complete and irreversible even where the subphase is strongly acidic (down to pH = 2)[44]. The results can be fairly easily interpreted by

$$2\,(\text{porph})\text{FeCl} + 2\,\text{OH}^{\ominus} \rightarrow (\text{porph})\text{FeOFe}(\text{porph}) + \text{H}_2\text{O} + 2\,\text{Cl}^{\ominus} \quad \text{(e)}$$

$$(\text{porph})\text{FeCl} + \text{OH}^{\ominus} \rightarrow (\text{porph})\text{FeOH} + \text{Cl}^{\ominus} \quad \text{(f)}$$

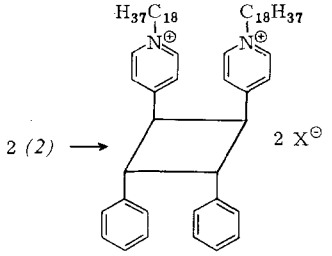
$$(\text{porph})\text{FeOH} + \text{OH}^{\ominus} \rightarrow (\text{porph})\text{FeO}^{\ominus} + \text{H}_2\text{O} \quad \text{(g)}$$

$$(\text{porph})\text{FeO}^{\ominus} + (\text{porph})\text{FeCl} \rightarrow (\text{porph})\text{FeOFe}(\text{porph}) + \text{Cl}^{\ominus} \quad \text{(h)}$$

assuming that reaction (h) is highly favored in the dimers (or aggregates) formed in the spread film while steps leading to decomposition of the μ-oxo dimer should be rendered slower and more difficult. The net effect of the microenvironment provided by the monolayer film in this case is to produce a rather pronounced alteration of both rate processes and equilibria.

3.2. Excimer and Photodimer Formation

The *trans* isomers of olefins *(2)* and *(3)* can be incorporated into monolayer films and assemblies in which the usual solution photoreaction, *trans* to *cis* isomerization, does not occur. For the stilbazole derivative *(2)* it was found that the absorption spectrum in the assemblies is nearly identical to that obtained for dilute acetonitrile solutions of *(2)*[20] (see Section 2.1). Consequently, there is little indication that complex formation in the ground state is important. Compound *(2)* fluoresces strongly both in solution and in monolayer assemblies; however, the fluorescence in the assemblies is shifted about 50 nm to longer wavelength as compared to acetonitrile solutions. Although *(2)* does not undergo *trans*→*cis* isomerization in assemblies upon irradiation, it undergoes a rapid photobleaching which was shown to be due to dimer formation[19,20]. A similar red-shifted fluorescence and rapid photobleaching was also observed for crystals of *(2)*, X = *p*-chlorobenzenesulfonate or *p*-bromobenzenesulfonate. For these crystals it was found that the dimers were of the cyclobutane-type *(8)*, formed from parallel addition of two molecules of *(2)*[19]. The formation of the photodimers in crystalline *(3)* and in monolayers appears to be closely related—though there are some notable differences. In all cases the occurrence of dimerization is accompanied by a red-shift in the fluorescence. Consequently, it can be inferred that the red-shifted fluorescence is due to an excimer, which is probably an intermediate in the formation of *(8)* [eqs. (i)—(l)].



(8)

$$(2) \xrightarrow{h\nu} (2)^* \quad \text{(i)}$$

$$(2)^* + (2) \rightarrow [(2)\ldots(2)]^* \quad \text{(j)}$$

$$[(2)\ldots(2)]^* \rightarrow (2) + (2) + h\nu \quad \text{(k)}$$

$$[(2)\ldots(2)]^* \rightarrow (8) \quad \text{(l)}$$

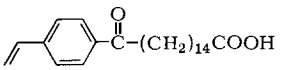
While excimer formation is frequently observed in solution as a diffusion process, excimer formation in crystals and monolayer assemblies of *(2)* must involve pre-formed units in which relatively little molecular motion occurs following excitation.

Interestingly, no excimer fluorescence has been detected for *(2)* or similar stilbazole quaternary salts in solution, although photodimerization to give a number of cyclobutane dimers of different stereochemistry than *(8)* has been observed[20,48]. As pointed out above, excimer fluorescence and photodimer formation are coupled in crystals of *(2)*; while both processes are observed for some anions, other anions yield crystals that are photostable and show only monomer fluorescence. For monolayers of *(2)* the photobehavior is independent of the anion used (this may simply reflect rapid exchange with the anions in the aqueous phase); however, a strong dependence upon assembly architecture has been observed. Thus, when *(2)* is diluted with increasing amounts of an inert surfactant such as tripalmitine or arachidic acid, a reduction in both the rate and extent of the photoreaction is observed[19]. This is, of course, reasonable in view of the need for "pre-formed" dimer sites to afford the possibility of reaction. Furthermore, it was found that both the rate and extent

of photoreaction are reduced when assemblies are constructed with the layers containing *(2)* separated by inert "spacer layers" of tripalmitine or arachidate[19]. The two observations indicate that for *(2)* in monolayers the dimerizable sites can be formed both within single layers and between adjacent layers. Although it has not yet been verified, it may be anticipated that interlayer dimerization would produce a dimer having a different stereochemistry from that of *(8)*.

The fact that excimer fluorescence and photodimer formation for *(2)* are observed in solid crystals and monolayers but not in concentrated solutions suggests that the tight packing in the former phases may play a major role in this phenomenon. *Schmidt et al.* have made extensive investigations of solid-state photoaddition and photodimerization reactions in which it has been shown that properly aligned monomer units must be within a distance of *ca.* 4.2 Å of one another[49]; this is the typical interchain spacing determined for ordered hydrocarbons to permit reactions[50]. When photoactive crystals of *(2)* (X=*p*-chlorobenzenesulfonate) are heated it is found that reversible loss of excimer fluorescence occurs at temperatures considerably below the melting point[20]. One possible explanation for this would be a "melting" of the hydrocarbon chains with a corresponding release of the chromophores from close proximity to one another. It is frequently observed that phospholipids and similar substances undergo phase transitions below their melting points; the hydrocarbon chains become more disordered and liquid-like with an increase in the interchain separation[50]. Self-organization alone of hydrophilic and hydrophobic regions in an organized assembly is not sufficient for excimer formation in the olefin *(2)*. This is indicated by the fact that no photodimerization or excimer formation is observed when *(2)* is incorporated into cationic cetyltrimethylammonium bromide (CTAB) micelles[20]. Appreciable concentrations of *(2)* in micellar CTAB can be obtained, indicating that there are several molecules/micelle as well as *(2)*:CTAB ratios corresponding to the *(2)*:surfactant ratios in monolayer assemblies where both excimer fluorescence and photodimerization are observed. For these micelles, however, only monomer fluorescence and relatively efficient *trans→cis* photoisomerization of *(2)* are observed[20].

We have recently investigated photochemical and thermal reactions of the surfactant styrene derivatives *(3)* and *(9)* in different media including the solid state, monolayer films, deposited monolayer assemblies, micelles and solution[21].



(9)

Like the oxo acids *(4)* these compounds possess a potentially reactive chromophore in what would be anticipated to be a highly hydrophobic site in organized media. Both *(3)* and *(9)* form good films which can be easily manipulated and transferred to yield deposited monolayer assemblies. The styrene *(3)* exhibits especially favorable properties, forming good films from the pure compound which yield compressed monolayers very similar to those of saturated fatty acids such as arachidate. The area per molecule *(3)* in a monomolecular film is 19 Å^2 for a surface pressure of 20 dyn/cm[21]. The UV absorption spectrum of monolayers of *(3)* is altered considerably as compared to the solution spectrum (cf. Fig. 1); thus in this case—in contrast to the surfactant *(2)*—there is evidently

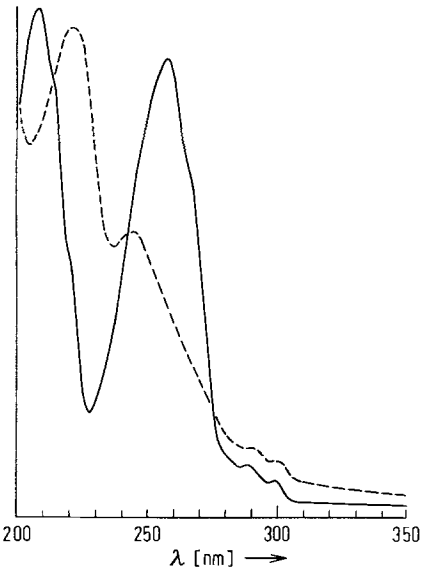


Fig. 1. Comparison of absorption spectra of styrene *(3)* in hexane solution (——) and in quartz supported multilayers (---).

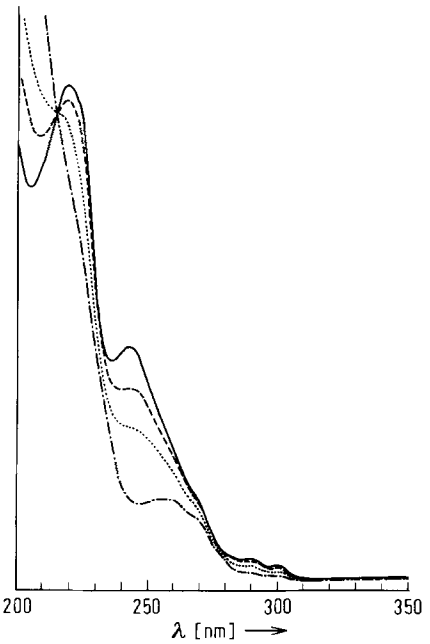
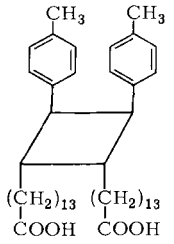


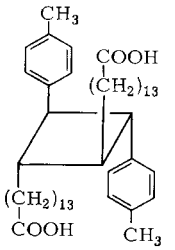
Fig. 2. Spectra of styrene *(3)* in quartz supported multilayers. (——), and after 5 min (---), 15 min (····) and 60 min (·–·) irradiation.

considerable interaction between the chromophores, even in the ground state. On irradiation of assemblies containing *(3)* at wavelengths between 254—300 nm there is a rapid bleaching of the styrene absorption (cf. Fig. 2). Good isosbestic points are obtained throughout the reaction, suggesting that only a single reaction is taking place. A similar bleaching occurs when films of *(3)* are irradiated at an air-water interface. The bleaching is due to formation of a photodimer similar to that obtained from *(2)* in crystals and monolayer assemblies. The product could be isolated by preparative scale irradiation of large slides containing several styrene multilayers or by recovery of material from several films spread and irra-

diated at an air-water interface. The product was found to consist of a single product having NMR, IR and mass spectral data in accord with those expected for a cyclobutane structure as in *(10)* or *(11)*.



(10)



(11)

Irradiation of *(3)* in solution, in SDS micelles, and in crystals also leads to the formation of dimeric products which are evidently cyclobutane derivatives[21]. However, preliminary indications are that products having different stereochemistry are formed in the solid state and in SDS micelles. The reactions in solution and micelles also appear to produce more than one product. Although we have not yet obtained conclusive evidence, it appears that the product formed from *(3)* in the monolayers is the *trans-syn-trans* dimer *(10)* resulting from the parallel alignment of the chromophore in the monolayer[21]. The fact that only a single product is formed in relatively high quantum yield ($\phi = 0.14$) affords reasonable confirmation of the extended regular structure of the hydrocarbon chain expected for the compressed monolayer. The results obtained in this case seem quite analogous to the "topological control" observed in the solid-state photochemical dimerization and addition reactions investigated by *Schmidt, Cohen et al.*[49,51,52].

Although the scale for the reactions in monolayer films or assemblies is obviously somewhat limited, the results obtained with *(3)* suggest a number of exciting possibilities for obtaining regio- and stereospecific control of reactions by the construction and use of especially tailored surfactants. A particular advantage illustrated by the reactions of both *(2)* and *(3)* is that hydrophobic-hydrophilic interactions and the close packing of the hydrocarbon chains dictate the structure of the films and assemblies in a predictable fashion. Thus, it appears that reactions in monolayers offer many of the same possibilities obtainable in the solid state by "crystal engineering" with the possible advantage that monolayer structure may be somewhat easier to predict and control.

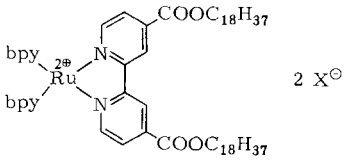
3.3. Photoinduced Electron Transfer Reactions in Monolayer Assemblies

Photoinduced electron transfer reactions of transition metal complexes, dyes and other substances having relatively low excitation energies have been the subject of extensive investigation during recent years. It has been found that excited states of metal complexes, for example, can be quenched by electron donors or electron acceptors in redox processes that can involve efficient conversion of light energy into chemical energy in the form of energy-rich products. Both the initial photoreactions and subsequent "dark" processes have been well-characterized for several systems[53-57]. In most cases, the quenching-energy conversion processes [eqs. (m) and (o)] are followed by energy-wasting back reactions which regenerate ground states of the starting species [eqs. (n) and (p)]. The obvious potential utility of reactions of this type for energy conversion and storage has led to several investigations in which means have been sought to capture or utilize the high energy redox products or otherwise avert the back reactions[58-63]. Our own work in this area has included extensive investigations in solution as well as in monolayer assemblies.

$$MC^{n\oplus *} + Ox \rightarrow MC^{(n+1)\oplus} + Ox^{red} \quad (m)$$
$$MC^{(n+1)\oplus} + Ox^{red} \rightarrow MC^{n\oplus} + Ox \quad (n)$$
$$MC^{n\oplus *} + Red \rightarrow MC^{(n-1)\oplus} + Red^{ox} \quad (o)$$
$$MC^{(n-1)\oplus} + Red^{ox} \rightarrow MC^{n\oplus} + Red \quad (p)$$

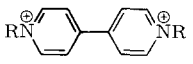
$MC^{n\oplus *}$ = excited metal complex, Ox = oxidant, Ox^{red} = reduced oxidant, Red = reductant, Red^{ox} = oxidized reductant.

One of the most widely used metal complexes in studies of electron transfer reactions has been tris(2,2′-bipyridyl)ruthenium(II), ($Ru(bpy)_3^{2+}$). This complex is strongly luminescent in fluid solution and reasonably photostable; hence, the quenching of its luminescence by electron donors and acceptors has proven to be a convenient means for studying these reactions. Our interest in studying electron transfer quenching processes in monolayer assemblies led us to prepare the hydrophobic surfactant complex *(12)*. This complex



(12)

was found to form monolayer films which could be transferred to solid supports[64]. We found that dry assemblies containing *(12)* exhibited intense luminescence similar to that of $Ru(bpy)_3^{2+}$ in solution. Since its luminescence is strongly quenched by electron acceptors such as the dication paraquat *(13a)*, we decided to investigate quenching of the luminescence of *(12)* in monolayer assemblies with the surfactant counterpart of paraquat, *(13b)*. Assemblies were constructed

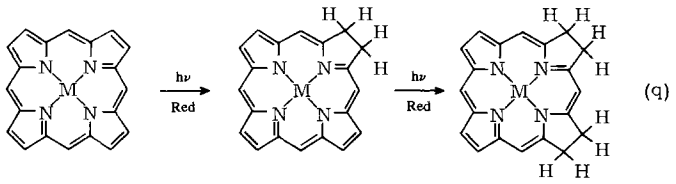


(13a), R = CH_3
(13b), R = $C_{18}H_{37}$

with *(12)* and *(13b)* in the same layer and with *(12)* and *(13b)* in adjacent layers having hydrophilic-hydrophilic contact. In both cases significant quenching of the luminescence of *(12)* was observed[65]. Separation of layers containing *(13b)* from those containing *(12)* by two or more layers of cadmium arachidate generally resulted in no quenching of the luminescence—as might be expected for an electron transfer process requiring near-contact of donor and acceptor. In cases where there was quenching of the luminescence of *(12)* no permanent bleaching was observed, at least on short term irradiation[65]. This suggests that oxidative electron transfer in the assemblies is followed in this case by rapid reverse electron transfer [cf. eq. (n)] analogous to the solution behavior. Sub-

sequent to our investigations more extensive studies on electron transfer quenching in monolayers have been reported[66]. In these investigations it has been found that quenching of the luminescence of several cyanine dyes occurs over statistical spacings of up to $R = 75$ Å in contrast to the average quenching distance between *(12)* and *(13b)* of 10 Å. These very interesting results indicate a correlation between the distance and the ionization energy of the excited state of the electron donor[66].

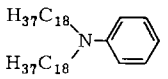
One case where electron transfer quenching of an excited state leads to formation of permanent products, albeit rather inefficiently, is the photoreduction of metalloporphyrins by various reducing agents. It has been found, for example, in solution that a number of metal porphyrin complexes *(14)* including those of tin(IV), germanium(IV), zinc(II), platinum(II) and palladium(II) can be photoreduced sequentially to chlorin (dihydroporphyrin) *(15)* and tetrahydroporphyrin *(16)* products [eq. (q)] with reducing agents (Red) such as stannous chloride, ascorbic acid and tertiary amines[67-70].



(q)

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

The reduction of palladium(II) porphyrins with tertiary amines has been extensively investigated; evidently the initial step involves electron transfer from the amine to the excited porphyrin[71]. Depending upon the medium, subsequent steps may involve proton transfers, secondary electron transfer steps and free radical processes. In an effort to determine whether such a sequence of reactions can occur in monolayer assemblies we have examined reactions of the palladium(II) complexes of surfactant porphyrins *(6)* and *(7)* with the sur-



(17)

factant tertiary amine *(14)*[71]. In very recent experiments we have found that both dry assemblies and assemblies immersed in water undergo partial conversion as outlined in eq. (q) when the amine *(17)* and palladium porphyrin are present in a 1:1 ratio in the same layer with an excess of arachidate host. We have also observed similar reactivity for assemblies in which *(17)* and palladium porphyrin are present in adjacent layers with hydrophilic-hydrophilic contact[71]. In both cases only partial conversion has been observed. Fairly rapid conversion occurs on initial irradiation, resulting even in formation of some tetrahydroporphyrin *(16)*, but prolonged irradiation results in little additional conversion. Evidently here, as with the dimerization phenomena observed with *(2)*, there are some sites capable of reaction while others are non-reactive; once the "reactive sites" are exhausted no further reaction can occur. We are currently exploring different combinations of porphyrin reductant and host surfactant to define what constitutes a reactive or an unreactive site.

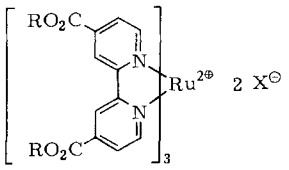
4. Interfacial Phenomena: Monolayer Solution and Monolayer-Gas Reactions

Recently, considerable interest has centered around interfacial processes in which an immobilized reactant or catalyst interacts with a reagent present in a contacting solution or vapor phase. The relative ease of constructing monolayer assemblies on various supports would suggest that this might be an area where monolayers could offer considerable utility both for mechanistic studies as well as practical applications. Our initial interest in this area centered around the possibility of carrying out heterogeneous light-induced electron transfer processes involving an immobilized light absorbing complex and potential oxidants or reductants in solution. The first system planned for investigation involved monolayer assemblies containing the ruthenium complex *(12)* and aqueous solutions of various electron acceptors. Initial experiments with assemblies containing an outer hydrophobic layer of *(12)* revealed that the strong luminescence observed from the dry assemblies was almost completely quenched upon immersion of these assemblies in water[64]. The absorption spectrum of *(12)* in the assemblies was little altered by this process and we found that gentle heating in a vacuum restored the luminescence to nearly its original intensity[64,65]. In contrast we found that the luminescence of *(12)* in organic solvents was virtually unaffected by addition of considerable amounts of water, aqueous acid or aqueous base.

The observation that water quenched the luminescence of monolayer assembly-bound *(12)* suggested the possibility that a photoreaction involving *(12)* and water could be occurring. Initial experiments on the irradiation of monolayer assemblies of the surfactant ruthenium complex *(12)* in the presence of water led to the production of hydrogen in an apparent light-induced cleavage of water by the monolayer-bound complex[64]. Although slides containing monolayers formed from the initial preparation of *(12)* repeatedly gave sustained gas evolution upon irradiation, irradiation of assemblies formed from subsequent preparations of the complex under identical conditions has not produced comparable results[65,66,72]. It is now clear that light-induced water cleavage does not occur with pure *(12)* in monolayer assemblies; the underlying reason behind the initial results remains as yet an unsolved mystery. The original preparation of *(12)* was found to contain several impurities including other surfactant ruthenium(II) complexes and it seems likely that the net process of water cleavage in the layers may require at least two different complexes. Attempts to prepare useful systems with the complex *(12)* in assemblies have been somewhat disappointing because of the extreme sensitivity of its film properties to impurities—especially anions—and to its rapid degradation on contact with water[65,66]. Although different samples of carefully purified complex have been thoroughly investigated in several different laboratories, there still remain significant discrepancies regarding its photobehavior in monolayer films and assemblies[65,66,72].

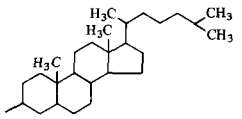
The instability of *(12)* in monolayers in the presence of water led us to focus our studies on interfacial electron transfer processes in monolayers on other metal complexes; however, our work with *(12)* initiated numerous other studies on structurally related hydrophobic ruthenium(II) complexes in solution[63,73,74]. We have found that the photochemical reac-

tivity of these complexes having the general structure *(18)* is significantly different from that of the parent complex $Ru(bipy)_3^{2+}$. This renders them potentially useful in energy storage applications and at the same time provides some insight into how the original preparation may have functioned. We have prepared and studied a series of complexes *(18)* in which the parent complex $Ru(bpy)_3^{2+}$ is surrounded by hydrophobic groups ranging in size from isopropylcarbonyl in *(18a)* to cholestanyloxycarbonyl in *(18b)*[73]. All of these



(18a), R = $-CH(CH_3)_2$

(18b), R =



complexes are insoluble in water but can be readily studied in a variety of organic solvents. The presence of the electron-withdrawing carboxyester groups on the bipyridine ligands shifts the redox potentials of the complexes to more anodic values as compared to that of $Ru(bipy)_3^{2+}$. Figure 3 compares the redox potentials in the ground state and in the excited state. An interesting consequence of the shifted redox poten-

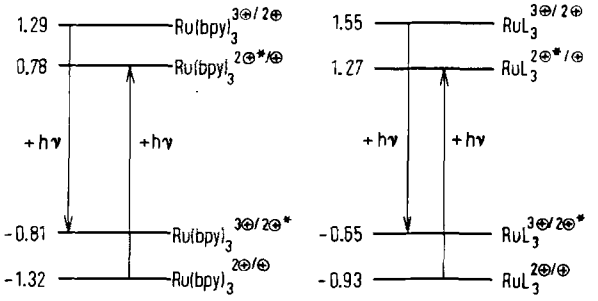


Fig. 3. Formal redox relationships for ground and excited states of ruthenium(II) complexes: left: $Ru(bipy)_3$, right: hydrophobic complexes *(18)*. Energy in volts referred to SCE.

$$RuL_3^{2\oplus *} + RuL_3^{2\oplus} \rightarrow RuL_3^{3\oplus} + RuL_3^{\oplus} \quad (r)$$

$$RuL_3^{2\oplus *} + RuL_3'^{2\oplus} \rightarrow RuL_3^{3\oplus} + RuL_3'^{\oplus} \quad (s)$$

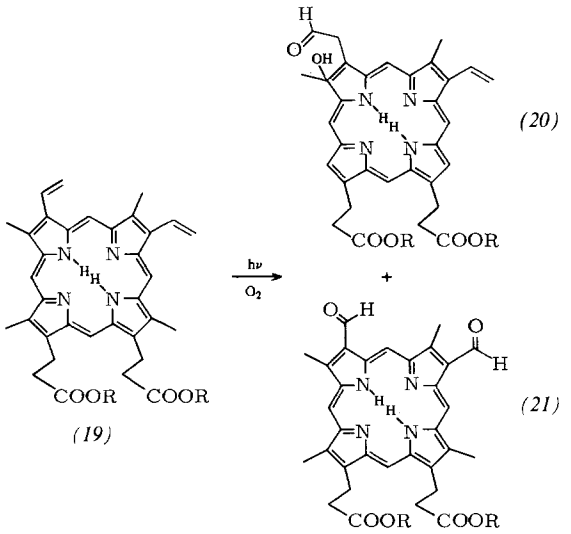
tials for the hydrophobic complexes is that while both $Ru(bipy)_3^{2+}$ and the various hydrophobic complexes should be stable towards self-quenching electron transfer processes [cf. eq. (r)], a quenching process with one of the hydrophobic complexes *(18)* as an electron acceptor and $Ru(bipy)_3^{2+}$ as a donor should be energetically favored [cf. eq. (s)]. Although we have not yet obtained evidence for the reaction according to eq. (s), we have found evidence that efficient light induced electron transfer processes involving the complex *(18)* can result in irreversible reactions for both oxidative[74] and reductive quenching[63,73,74]. Although it is beyond the scope of this paper to report in detail on reactions of hydrophobic complexes *(18)* in solution, it is worth noting that the hydrophobic groups produce significant effects on the course of excited state electron transfer processes and subsequent events. Thus both excited state quenching and reverse electron transfer processes involving *(18a)* and *(18b)* are slowed down considerably in several cases as compared to those in the case of $Ru(bipy)_3^{2+}$. The bulky groups evidently retard approach by several reagents—especially cationic species—such that while both efficient but slower oxidative [cf. eq. (m)] and reductive [cf. eq. (o)] quenching processes occur, the back-transfer of electrons is rendered sufficiently slow to permit other processes to compete[73,74]. Thus considerable energy can be stored in the form of one or both of the high energy products produced in eqs. (m) and (o).

Returning to interfacial processes occurring in monolayer assemblies we have recently examined reactions of monolayer-bound porphyrins with potential reducing agents present in a contacting aqueous solution[71]. As with the results reported in Section 3.3, most of our studies in this area have involved palladium(II) complexes of the surfactant porphyrins *(6)* and *(7)* (see Section 3.3). We have found that irradiation of multilayer assemblies containing the palladium porphyrins in contact with aqueous solutions of *N,N*-dimethylaniline or triethylamine can result in reduction of the porphyrin as outlined in eq. (q). The reaction has been examined using assemblies having different architecture. It has been found that a photoreduction takes place both in multilayer assemblies of porphyrins *(6)* or *(7)* as well as in systems containing only a single outer hydrophilic or hydrophobic layer; however, reaction is considerably more rapid when assemblies containing only 1—4 outer monolayers of palladiumporphyrin are irradiated[71]. The fact that both porphyrins react at comparable rates is interesting since porphyrin *(6)* is believed to lie in a relatively more hydrophobic environment than *(7)*, which lies at the hydrophilic interface. It seems reasonable that in this case the moderately polar amines can penetrate both hydrophobic and hydrophilic portions of the monolayer assembly. Such penetration most likely involves a temporary "dissolving" of microscopic portions of the assembly; in agreement with this it is found that addition of excess amine to the contacting aqueous solution can result in removal of the mutlilayer from the support. The occurrence of considerable reaction in multilayers without removal of porphyrin would indicate that penetration through several layers can occur.

In contrast to the lack of discrimination between reactivity of porphyrins at hydrophilic *vs* hydrophobic sites in the case of amine-mediated photoreduction, there is a pronounced site-dependence upon the interfacial incorporation of metal ions from aqueous solutions contacted with monolayer-bound surfactant porphyrins. Thus, while all the surfactant porphyrins examined readily incorporate Cu^{2+} in solution, we find the microenvironment provided by the monolayer produces major effects in both spread films and multilayer assemblies[43]. Films or assemblies containing porphyrins such as *(7)*, which evidently reside in a highly hydrophilic site, are rapidly metalated by aqueous Cu^{2+}. In contrast *(6)* and other porphyrins which are located in more hydrophobic regions are totally inert towards Cu^{2+} incorporation in films and assemblies. The different rates of Cu^{2+} incorporation in *(7)* can also be correlated with the relative hydrophilicity of the site[43]. We have found that monolayer-incorporated porphyrin *(7)* incorporates several other divalent metal ions from aqueous solution, but the relative ease of metal ion incorporation differs substantially from that observed in homogeneous solution[43]. Thus while the rate of incorporation of metal ion for a number of porphyrins in solution decreases along the series $Cu^{2+} > Zn^{2+} > Co^{2+} > Ni^{2+} \gg Mg^{2+}$[75],

we find that *(6)* incorporates Mg^{2+}, Co^{2+}, Ni^{2+} and Mn^{2+} from aqueous solutions but not Zn^{2+} or Fe^{3+}. The failure of zinc and iron to metalate in contrast with the facile incorporation of magnesium is especially striking. We are currently studying interfacial metalation phenomena with other more hydrophobic metalating reagents, but it is clear from the foregoing results that the microenvironment provided by the monolayer assembly can produce striking effects on reactivity, particularly when there is limited or selective penetration of one of the reagents from the solution.

In other studies of reactions involving surfactant porphyrins at an assembly-air or assembly-water interface we have likewise observed differences from the behavior of the same reagents in solution. One example where a substantial difference has been observed is the photooxidation of the protoporphyrin derivatives *(19)*[76]. In solution the major oxidation product obtained from irradiation of protoporphyrin IX esters in the presence of oxygen is the hydroxyaldehyde *(20)* (and its isomer where the other vinyl group has reacted)[77].



(19) *(20)* *(21)*

In contrast, irradiation of protoporphyrin esters in micelles, monolayer films or dry monolayer assemblies leads to production of the diformyl derivative *(21)* as the major product[77]. The ratio of the products *(21)*/*(20)* increases on going from micelles to spread films to condensed monolayer assemblies. Although formation of both *(20)* and *(21)* can be rationalized in terms of well-established singlet oxygen addition paths, it is clear that the path leading to *(20)* sould be favored in the absence of special effects. Although it is not possible to specify the precise cause of the change in product distribution for this reaction it appears once again that the microenvironment plays a major role in the organized media, either in controlling access of the incoming oxygen or in favoring or disfavoring formation of a reaction intermediate.

5. Summary

The results summarized in this review of reactions occurring in organized monolayer assemblies indicate that the particular microenvironment provided by the assemblies can often produce major changes in behavior compared to in solution and even other organized media. In view of recent interests in processes occurring in organized media it is particularly instructive to compare and contrast reactivity in monolayers with that occurring in micelles, bilayers, lipid vesicles and microemulsions. While the above examples include some cases where similar effects on reactivity are obtained in different media, there are more often striking differences between monolayers and the other media which can largely be attributed to differences in packing and the degree of molecular organization. Thus in many cases the particular environment produced by a monolayer assembly affords the opportunity for a specific and unique reaction. The examples discussed in this article include some reactive systems where the role of the microenvironment can be quite clearly defined as well as others where precise structure-reactivity relationships remain to be determined. The number of reactions investigated thus far represent only a beginning and it is clear that as more reactions are studied the role of the microenvironment will become sharply defined.

One of the most important future uses of monolayer assemblies will probably be the construction of increasingly more complex functional units in which reactions are mediated through cooperative interaction of the individual components. In this way it should be possible to build model systems of increasing complexity which hopefully will approach the structure and reactivity of biological systems. A number of simple systems such as mixed metal complexes of specific structure appear capable of realization as extensions of some of the present experiments. Certainly an interesting area for future study will be interfacial reactions involving interaction of such functional units with mobile substrates. The relative ease of construction of monolayer assemblies of different molecular architecture suggests that extended studies of interfacial reactions should be useful for the design and development of catalysts. Whether catalyst systems based on monolayers can be developed for practical purposes remains to be seen; certainly the fragility of the layers and the small amounts of material contained in the assemblies provide formidable problems.

The rather striking examples of topological control obtained in the photodimerization reactions suggests that considerable control and prediction of regio- and stereochemistry can be obtained in assemblies, in analogy to the "crystal engineering" proposed for solid state processes. In fact, in many ways the monolayer systems should be perhaps simpler to design and easier to construct than crystal-based systems. The major limitation on synthetic processes employing monolayer films and assemblies is the extremely limited scale of reaction possible with present techniques and equipment.

I am indebted to my co-workers, present and past, at the University of North Carolina, who carried out most of the experiments described in this article and who provided valuable insights into their interpretation. I am also indebted to Professor H. Kuhn and Dr. D. Möbius at the Max Planck Institut für biophysikalische Chemie in Göttingen for valuable discussion and advice in several aspects of this work and to the Alexander-von-Humboldt-Stiftung for a Senior U. S. Scientist Award (1975) which permitted extended collaboration with the Göttingen group.

Received: May 16, 1978 [A 273 IE]
German version: Angew. Chem. *91*, 472 (1979)

[1] *A. Pockels*, Nature *43*, 437 (1891).
[2] *K. B. Blodgett*, Phys. Rev. *55*, 391 (1939).
[3] *K. B. Blodgett, I. Langmuir*, Phys. Rev. *51*, 964 (1937).
[4] *I. Langmuir*, J. Am. Chem. Soc. *39*, 1848 (1917).
[5] *H. Kuhn, D. Möbius, H. Bücher* in *A. Weissburger, B. Rossiter:* Physical Methods of Chemistry. Vol. 1, Part 3b. Wiley, New York 1972, p. 577.
[6] *H. Kuhn, D. Möbius*, Angew. Chem. *83*, 672 (1971); Angew. Chem. Int. Ed. Engl. *10*, 620 (1971).
[7] *H. Kuhn*, Pure Appl. Chem. *27*, 421 (1971).
[8] *M. M. Zwick, H. Kuhn*, Z. Naturforsch. *A 17a*, 411 (1962).
[9] *K. H. Drexhage, M. M. Zwick, H. Kuhn*, Ber. Bunsenges. Phys. Chem. *67*, 62 (1963).
[10] *H. Bucher, K. H. Drexhage, M. Fleck, H. Kuhn, D. Möbius, D. Molzahn, K. Rollig, F. P. Schafer, J. Sondermann, W. Sperling, P. Tillmann, J. Wiegand*, Mol. Crys. *2*, 199 (1967).
[11] *N. K. Adam*, Proc. R. Soc. London *A 140*, 223 (1933).
[12] *R. J. Fosbinder, E. K. Rideal*, Proc. R. Soc. London *A 143*, 61 (1933).
[13] *A. R. Gilby, A. E. Alexander*, Aust. J. Chem. *9*, 347 (1956).
[14] *G. Gee, E. K. Rideal*, Proc. Roy. Soc. London *A 153*, 116 (1935).
[15] *G. L. Gaines, Jr.:* Insoluble Monolayers at Liquid-gas Interfaces. Wiley Interscience, New York 1966, p. 308.
[16] For a review see *J. Saltiel et al.*, Org. Photochem. *3*, 1 (1973).
[17] *D. Gegiou, K. A. Muszkat, E. Fischer*, J. Am. Chem. Soc. *90*, 12 (1968).
[18] *D. G. Whitten*, J. Am. Chem. Soc. *96*, 594 (1974).
[19] *F. H. Quina, D. G. Whitten*, J. Am. Chem. Soc. *97*, 1602 (1975).
[20] *F. H. Quina, D. G. Whitten*, J. Am. Chem. Soc. *99*, 877 (1977).
[21] *P. R. Worsham, D. G. Whitten*, unpublished results.
[22] For a review see *P. J. Wagner*, Acc. Chem. Res. *4*, 168 (1971), and references therein.
[23] *P. J. Wagner*, Pure Appl. Chem. *49*, 259 (1977).
[24] *N. J. Turro, K-C Liu, M-F Chow*, Photochem. Photobiol. *26*, 413 (1977).
[25] *G. H. Hartley, J. E. Chow, Macromolecules 1*, 165; 413 (1977).
[26] *J. E. Guillet*, Pure Appl. Chem. *49*, 249 (1977).
[27] *P. R. Worsham, D. W. Eakers, D. G. Whitten*, J. Am. Chem. Soc. *100*, 7091 (1978).
[28] *O. H. Gibson, S. Ainsworth*, Nature *180*, 1416 (1957).
[29] *E. Antonini, M. Brunori* in: Hemoglobin and Myoglobin and their Reactions with Ligands. North Holland, Amsterdam 1971.
[30] *F. R. Hopf, T. P. O'Brien, W. R. Scheidt, D. G. Whitten*, J. Am. Chem. Soc. *97*, 277 (1975).
[31] *J. C. W. Chien*, J. Am. Chem. Soc. *91*, 2166 (1969).
[32] *B. C. Chow, I. A. Cohen*, Bioinorg. Chem. *1*, 57 (1971).
[33] *B. M. Hoffman, O. H. Gibson*, Proc. Nat. Acad. Sci. USA *75*, 21 (1978).
[34] *F. R. Hopf, D. G. Whitten*, J. Am. Chem. Soc. *98*, 7422 (1976).
[35] *N. Farrell, D. H. Dolphin, B. R. James*, J. Am. Chem. Soc. *100*, 324 (1978).
[36] *F. R. Hopf, R. H. Schmehl*, unpublished results.
[37] *D. Möbius*, in press (1978).
[38] *H. Bücher, O. V. Elsner, D. Möbius, P. Tillmann, J. Wiegand*, Z. Phys. Chem. N. F. *65*, 152 (1969).
[39] *G. L. Gaines, Jr.:* Insoluble Monolayers at Liquid-gas Interfaces. Wiley Interscience, New York 1971, Chapt. 6.
[40] *P. Mukerjee, A. Y. S. Yang*, J. Phys. Chem. *80*, 1388 (1976).
[41] *E. E. Polymeropoulos, D. Möbius, H. Kuhn*, J. Chem. Phys., in press.
[42] *K. A. Zachariasse, D. G. Whitten*, Chem. Phys. Lett. *22*, 527 (1973).
[43] *R. H. Schmehl, D. G. Whitten*, Chem. Phys. Lett. *58*, 549 (1978).
[44] *F. R. Hopf, D. Möbius, D. G. Whitten*, J. Am. Chem. Soc. *98*, 1584 (1976).
[45] *I. A. Cohen*, J. Am. Chem. Soc. *91*, 1980 (1969).
[46] *M. A. Torrens, D. K. Straub, L. M. Epstein*, J. Am. Chem. Soc. *94*, 4160 (1972).
[47] *A. B. Hoffman, D. M. Collins, V. M. Day, E. B. Fleischer, T. S. Srivastava, T. L. Hoard*, J. Am. Chem. Soc. *94*, 3620 (1972).
[48] *F. H. Quina, P. Richmond*, unpublished results.
[49] *G. M. T. Schmidt*, Pure Appl. Chem. *27*, 641 (1971), and references therein.
[50] *C. Tanford:* The Hydrophobic Effect. Wiley, New York 1973, p. 112.
[51] *M. D. Cohen*, Angew. Chem. *87*, 439 (1975); Angew. Chem. Int. Ed. Engl. *14*, 386 (1975).
[52] *A. Elgavi, B. S. Green, G. M. T. Schmidt*, J. Am. Chem. Soc. *95*, 2058 (1973).
[53] *H. D. Gafney, A. W. Adamson*, J. Am. Chem. Soc. *94*, 8238 (1972).
[54] *C. R. Bock, T. J. Meyer, D. G. Whitten*, J. Am. Chem. Soc. *96*, 4710 (1974).
[55] *C. R. Bock, T. J. Meyer, D. G. Whitten*, J. Am. Chem. Soc. *97*, 2909 (1975).
[56] *G. Navon, N. Sutin*, Inorg. Chem. *13*, 2159 (1974).
[57] *G. S. Lawrence, V. Balzani*, Inorg. Chem. *13*, 2976 (1974).
[58] *C. T. Lin, N. Sutin*, J. Phys. Chem. *80*, 97 (1976).
[59] *V. Balzani, L. Moggi, N. F. Manfrin, F. Dolletto, M. Gleria*, Science *189*, 852 (1975).
[60] *R. Scheerer, M. Grätzel*, J. Am. Chem. Soc. *99*, 865 (1977).
[61] *M. Maestri, M. Grätzel*, Ber. Bunsenges. Phys. Chem. *81*, 504 (1977).
[62] *D. Meisel, M. S. Matheson, J. Rabani*, J. Am. Chem. Soc. *100*, 117 (1978).
[63] *P. J. DeLaive, J. T. Lee, H. W. Sprintschnik, H. Abruna, T. J. Meyer, D. G. Whitten*, J. Am. Chem. Soc. *99*, 7094 (1977).
[64] *G. Sprintschnik, H. W. Sprintschnik, P. P. Kirsch, D. G. Whitten*, J. Am. Chem. Soc. *98*, 2337 (1976).
[65] *G. Sprintschnik, H. W. Sprintschnik, P. P. Kirsch, D. G. Whitten*, J. Am. Chem. Soc. *99*, 4947 (1977).
[66] *K. P. Seefeld, D. Möbius, H. Kuhn*, Helv. Chem. Acta *60*, 2608 (1977).
[67] *G. R. Seely, M. Calvin*, J. Chem. Phys. *23*, 1968 (1955).
[68] *J. H. Fuhrhop, T. Lumbantobin*, Tetrahedron Lett. *1970*, 2815.
[69] *D. G. Whitten, J. C. Yau, F. A. Carroll*, J. Am. Chem. Soc. *93*, 2291 (1971).
[70] *Y. Harel, J. Manassen*, J. Am. Chem. Soc. *99*, 5817 (1977).
[71] *J. Mercer-Smith, D. G. Whitten*, unpublished results.
[72] *G. L. Gaines, Jr., P. E. Behnken, S. J. Valenty*, J. Am. Chem. Soc. *100*, 6549 (1978).
[73] *P. J. DeLaive, J. T. Lee, H. W. Sprintschnik, H. Abruña, T. J. Meyer, D. G. Whitten*, Adv. Chem. Ser., *168*, 28 (1978).
[74] *P. J. DeLaive, C. Giannotti, D. G. Whitten*, J. Am. Chem. Soc. *100*, 7413 (1978).
[75] *P. Hambright* in *K. M. Smith:* Porphyrins and Metalloporphyrins. Elsevier, Amsterdam 1975, p. 233.
[76] *B. E. Horsey, D. G. Whitten*, J. Am. Chem. Soc. *100*, 1293 (1978).
[77] *H. H. Inhoffen, H. Brockmann, K. B. Bliesener*, Justus Liebigs Ann. Chem. *730*, 173 (1969).

The Chemistry of Isolated Cations

By Richard D. Bowen, Dudley H. Williams, and Helmut Schwarz[*]

Organic ions decompose in the field-free regions of a mass spectrometer after a relatively well-defined lifetime ($t \approx 10^{-5}$ s). This lifetime is very long compared with the time-scale of molecular bond vibrations and consequently the excess internal energy ("non fixed" energy) present in the transition state for dissociation is comparable with that found in solution experiments. In general, only the energetically most favorable decay routes are able to compete. Moreover, information concerning kinetic energy release (T) accompanying unimolecular decomposition may be obtained from a consideration of the metastable peak for the process; these extremely valuable data are inaccessible to solution experiments because of the effects of collisions. The chemistry of ions may therefore be investigated conveniently by generating the ions of interest in a mass spectrometer and analyzing the reactions which occur in metastable transitions.

1. Introduction

Mass spectrometry has found a wide variety of applications in analytical and organic chemistry. Most of the earlier work performed by organic mass spectroscopists was centered on the fragmentation patterns of ionized organic molecules. The mass spectrometer thus became a powerful tool for structure elucidation[1–5]. The observation of metastable peaks, which were known to arise from the dissociation of ions after acceleration[6], was regarded in some quarters as a nuisance. These metastable peaks sometimes obscure daughter ion peaks and occasionally cause counting problems. However, it later became apparent that because these peaks correspond to an actual dissociation, occurring under relatively well-defined conditions, they contain valuable information concerning the reactions of ions in the gas phase [7–9]. Indeed, it is now evident that an ideal method for investigating the chemistry of isolated cations is to generate the ions in question in a mass spectrometer and document the reactions which occur in the field-free regions[10]. Certain techniques, which may be applied, parallel some of those available to early solution organic chemists; for example, the extents to which various decompositions occur, isotope labeling, and energetic data. On the other hand, further information may be acquired for which there are no counterparts in solution chemistry; for instance, the observation of kinetic energy release accompanying a given dissociation.

In this article, the more important theoretical principles of the approach are discussed and some instructive examples are presented to illustrate the application of the method to study the chemistry of isolated organic cations.

2. Theoretical Principles

2.1. The Mass Spectrometer Time Scale

Figure 1 shows a schematic representation of a conventional mass spectrometer in which ions are transmitted by the electrostatic analyzer (ESA) before entering the magnetic analyzer (MA). The time required for an ion to reach the second field-free region of such an instrument depends on many parameters; however, this time is usually of the order of 10^{-5} s. The frequency of molecular vibrations is approximately 10^{13} to 10^{14} s^{-1}; hence, an ion which decomposes in the second field-free region will have undergone some 10^8—10^9 vibrations. Consequently, there will have been ample time for the available internal energy to fluctuate throughout the ionized molecule, which in turn will have had sufficient time to attain essentially all energetically accessible reacting configurations. Furthermore, because the lifetime of the ion is so long compared to the time scale of bond vibrations, only ions with just enough energy to undergo decomposition will dissociate in the second field-free region. Any ion with a large excess internal energy above that needed to promote dissociation will normally decompose before arriving at the second field-free region. Thus, the decomposition of *metastable* ions in the second field-free region occurs with relatively small excess internal energy ε^+ in the transition state[8a]. Moreover, since there is enough time for essentially all energetically accessible reacting configurations to be sampled, only the lowest energy processes are observed[11]. Precisely analogous arguments apply for ions which dissociate in the first field-free region, or to the decomposition of ions in the field-free regions of mass spectrometers with geometries different from that depicted in Figure 1 (for instance, "reversed geometry" instruments where ions traverse the magnetic analyzer before reaching the electrostatic analyzer).

The observation of primary deuterium isotope effects in the decomposition of many ^{2}H-labeled ions reveals that en-

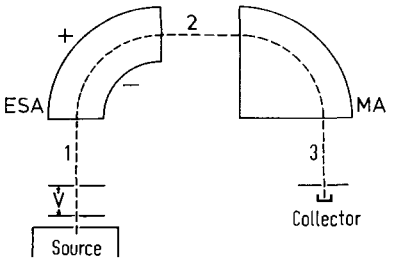


Fig. 1. Schematic representation of a double focusing mass spectrometer in which ions pass through the electrostatic analyzer (ESA) before entering the magnetic analyzer (MA). The numbers 1 to 3 refer to the field-free regions.

[*] Dr. R. D. Bowen, Dr. D. H. Williams
University Chemical Laboratory
Lensfield Road, Cambridge CB2 1EW (England)
Prof. Dr. H. Schwarz
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

ergy is indeed the dominant parameter in determining the occurrence or non-occurrence of a given decay route. For instance, the dissociation of all the metastable $CH_nD_{4-n}^{+\cdot}$ ($n=0$—4) ions have been reported[12]; exclusive $H^{\cdot}$ elimination is observed in each case, apart from $CD_4^{+\cdot}$ which is unique in losing $D^{\cdot}$. Large isotope effects are also encountered in the decomposition of other small hydrocarbon ions[13–15]; $CH_3CD_3^{+\cdot}$ eliminates $H^{\cdot}$ and $D^{\cdot}$ in a ratio of *ca.* 600:1[13].

2.2. Kinetic Energy Release (T)

Consider a general reaction, $A^+ \rightarrow B^+ + C$; suppose there is a reverse activation energy, E_r, which is composed of a translational component, E_t, and a vibrational and/or rotational component, E_i (Fig. 2). When A^+ decomposes into B^+ and

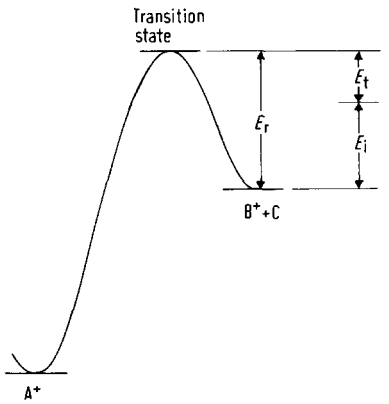


Fig. 2. Energy diagram for dissociation of A^+ into B^+ and C; the associated reverse activation energy, E_r, has a translational component E_t and an internal energy component E_i.

C in solution, collisions between the product molecules and other molecules (chiefly those of the solvent) result in the assimilation of the total energy released (E_r) into the overall Maxwell-Boltzmann energy distribution. It is therefore impossible to differentiate between the translational and vibrational/rotational component of any reverse activation energy owing to the effects of collisions. In contrast, in the absence of collisions (that is, in the gas phase and at low pressures), the occurrence of any translational component in the reverse activation energy will be evidenced by the product molecules B^+ and C repelling each other.

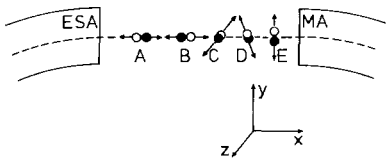


Fig. 3. Dissociation of metastable ions in the second field-free region of a mass spectrometer having the same basic geometry as that depicted in Fig. 1. "Closed" circles denote the daughter ion produced and "open" circles represent the neutral eliminated. A—E, see text.

Figure 3 shows the dissociation of a metastable ion of unit charge and mass m_1 in the second field-free region of a mass spectrometer having the same basic geometry as that depicted in Figure 1. (Similar arguments apply to decompositions taking place in the first field-free region or in the field-free regions of mass spectrometers with other geometries.) A daughter ion of mass m_2 ("closed" circles), together with a neutral species of mass $m_1 - m_2$ ("open" circles), is produced.

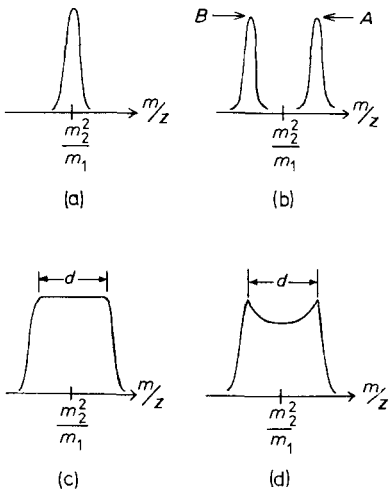


Fig. 4. Second field-free region metastable peaks corresponding to dissociation of ions shown in Fig. 3: a) with no large and specific kinetic energy release; b) with a large and specific kinetic energy release (only components for extreme orientations A and B are given); c) with a large and specific kinetic energy release (overall peak shape); d) with a large and specific kinetic energy release (overall peak shape with discrimination against "C" type ions owing to the finite length of the slits).

If there is no translational contribution to any reverse activation energy ($E_t=0$), there will be little or no kinetic energy release accompanying dissociation. Irrespective of the orientation (A, B, C, D, E, *etc.*) in which decomposition actually occurs, the daughter ion and neutral drift apart and a relatively narrow gaussian metastable peak results, which appears in the normal mass spectrum at an m/z value of m_2^2/m_1[6] (Fig. 4a). Suppose, however, that a relatively large and specific kinetic energy, T, is released upon dissociation. Decompositions occurring in orientation A (Fig. 3) give rise to daughter ions with slightly increased momentum, relative to that if no kinetic energy were released, because the ions thus formed are "pushed along the beam" (x direction). Consequently, these ions possess more momentum than normal ions and are deflected slightly less readily by the magnetic analyzer and so appear at an m/z value marginally higher than m_2^2/m_1. Conversely, dissociations occurring in orientation B result in the ions formed being "pushed back along the beam"; hence; they are deflected slightly more readily by the magnetic analyzer and so appear at an m/z value marginally lower than m_2^2/m_1 (Fig. 4b). Dissociations from intermediate orientations (for example C, D, and E in Fig. 3) also take place, thus giving rise to an "exploding sphere" of ions. The result is a flat-topped metastable peak (Fig. 4c). Mathematical analysis of the problem leads to a simple relationship between the width of the peak d and the kinetic energy release T[16,17]. In some cases, ions which dissociate in an orientation such as C (Fig. 3) are deflected so extensively by the momentum release that they are unable to pass through the slits (which are aligned in length along the z direction). This discrimination, against the transmission of daughter ions formed from decompositions occurring from orientations such as C, arises because of the finite length of the

slits[17] and results in a dish-topped metastable peak as shown in Figure 4d. However, the main point is that a flat-topped or dish-topped metastable peak indicates that a relatively large and discrete kinetic energy T is released upon dissociation. In contrast, a gaussian peak (Fig. 4a) reveals that decomposition takes place without releasing a large and relatively specific quantity of kinetic energy. Nevertheless, a value for the average kinetic energy release, T^{av}, may be computed from the width at half-height of a gaussian metastable peak[18]. This average kinetic energy release is sensitive to the excess internal energy (ε^*) present in the transition state for the dissociation step[8]; the greater the kinetic energy release, the greater the excess energy in the reaction coordinate.

Thus, it is apparent that the shapes of metastable peaks contain valuable information concerning the nature of the kinetic energy release which accompanies unimolecular dissociation of gaseous ions. The metastable peaks themselves comprise a "direct picture" of what happens when decomposition occurs. This is a unique advantage of conducting the experiments in the absence of interactions with other molecules.

2.3. Competing Reactions

Just as early organic chemists obtained structural information by degrading the compound of interest, so the actual dissociations undergone by organic ions in the gas-phase may be used to make deductions about the structure of the ion in question. Moreover, when ions undergo more than one dissociation, the approximate relative abundances of these decomposition channels may be easily obtained from the sizes of the corresponding metastable peaks. It may generally be assumed that these decay routes are available to each ion and that there is direct competition between the various channels on an energetic basis. This model takes no account of the possibility of the occurrence of isolated electronic states which could in principle interfere by preventing the competition between all possible dissociations or by giving rise to fast reactions. There are definite examples of the interference of isolated electronic states[8b,19]; however, these appear to be the exception rather than the rule. In the absence of such interference, the extent to which the competing decompositions occur may be used to determine the relative heights of the energy barriers towards interconversion and dissociation of two or more isomeric structures. Three general cases may be envisaged; these are shown in Figure 5.

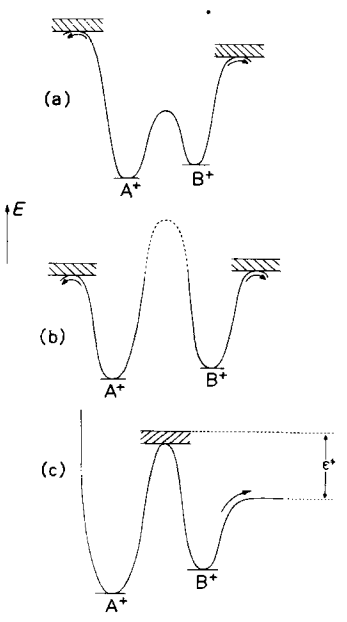


Fig. 5. Potential energy profiles corresponding to a) *complete* interconversion of A^+ and B^+ prior to dissociation; b) *no* interconversion of A^+ and B^+ prior to dissociation; and c) rate-determining isomerization of A^+ to B^+ prior to dissociation (arrows signify dissociation).

In Figure 5a the energy needed to cause dissociation of either ion, A^+ or B^+, is greater than that required to promote interconversion of the two isomers. Consequently, these ions undergo rapid and reversible isomerization *prior* to decomposition, from a common structure or mixture of structures, through the same transition states. An important historical example is the behavior of the carbenium ion, $C_6H_{13}^+$ [eq. (a)]. Irrespective of whether the incipient cation in the precursor has a primary, secondary, or tertiary structure, elimination of C_2H_4 and C_3H_6 is always observed in the same ratio (*ca.* 1:1.6)[11]. Other members of the $C_nH_{2n+1}^+$ homologous series of ions behave similarly[20] as do many other carbenium ions of varying degrees of unsaturation (for example $C_nH_{2n-1}^+$[21,22] and $C_nH_{2n-3}^+$[21,23,24]).

prim., sec., or tert. $C_6H_{13}X$

$$\downarrow \longrightarrow C_4H_9^{\oplus} + C_2H_4\ (\approx 40\%)$$
$$C_6H_{13}^{\oplus} \qquad\qquad (a)$$
$$\longrightarrow C_3H_7^{\oplus} + C_3H_6\ (\approx 60\%)$$

The potential energy profile of Figure 5b represents the opposite situation; here the energy needed to decompose either A^+ or B^+ is *less* than that required to bring about interconversion. In this case, A^+ and B^+ undergo different dissociations, through different transition states, in preference to equilibrating with each other. There are many examples of this behavior; a system of early importance is $C_2H_5O^+$, where two distinct classes of ions are observed[25]. Those of the first class are derived from precursors of general formula CH_3OCH_2X and presumably have the structure $CH_3\overset{+}{O}{=}CH_2$. These ions undergo essentially exclusive loss of CH_4. In contrast, the second group of $C_2H_5O^+$ ions loses C_2H_2 and CH_4 in an approximately constant ratio (1.9:1). These ions, which are formed from precursors containing a carbon-carbon bond (for instance CH_3CHXOH or XCH_2CH_2OH), probably comprise an interconverting mixture of $CH_3CH{=}\overset{+}{O}H$ and $\overline{CH_2CH_2}OH^+$. The overall potential energy diagram is extremely instructive (see Section 3.1).

The third possibility, that of Figure 5c, corresponds to a situation in which dissociation is energetically more favorable than isomerization for one ion, B^+, but not for the other, A^+. Thus, B^+ decomposes in preference to rearranging to A^+; however, starting from A^+, the lowest energy decay channel is isomerization to B^+[26]. The ion B^+, formed in this way, contains more internal energy than is needed to promote dissociation which therefore occurs relatively rapidly, with excess internal energy (ε^*) in the transition state for the final step. This excess energy may be partitioned in part as translation, hence causing an increase in the kinetic energy release associated with dissociation. Therefore, if A^+

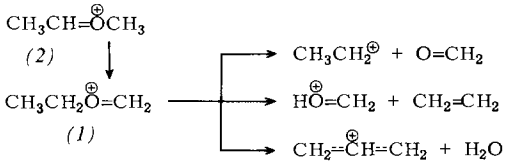
and B^+ undergo any common decompositions, the kinetic energy release should be greater starting from A^+ than from B^+. The excess energy $\varepsilon^{\ddagger}$, present in the transition states when rearranged ions of original structure A^+ decompose, also causes a discrimination against any decay route of B^+ which has a stringent geometric requirement. This is because the rate-determining step (RDS) in decomposition of A^+ is rearrangement to B^+; after the rearrangement, energy ceases to be the dominant parameter in determining the occurrence of possible dissociation channels. Instead, the controlling factor is how fast a particular dissociation may occur given the amount of excess energy available. Consequently, since simple-bond cleavages may generally proceed *via* less ordered transition states than rearrangement processes, especially when the latter must involve a cyclic geometry, these reactions are likely to be favored starting from A^+. In contrast, energy remains the most important consideration for dissociation of ions generated originally as B^+. These ions do not therefore exhibit the discrimination against dissociation routes involving considerable rearrangements; indeed, such rearrangements are expected to occur to a considerable extent provided they are the lowest energy decay channels.

An example of this behavior is furnished by the isomeric $C_3H_7O^+$ ions *(1)* and *(2)* (Scheme 1)[26]. Starting from *(1)*, elimination of H_2O is the main reaction, accompanied by a small amount of C_2H_4 loss. These are the energetically most favorable decay channels; it is significant that H_2O loss is the dominant process, even though it must involve extensive rearrangement, because it has the lowest overall activation energy (Table 1). Loss of CH_2O from *(1)* is not observed, even though it may occur *via* simple cleavage of the C—O single bond, because it requires too much energy and is preempted by H_2O and C_2H_4 elimination.

Table 1. Relative abundances, average kinetic energy T^{av}, and thermochemical data for dissociation of isomeric $C_3H_7O^+$ ions *(1)* and *(2)*.

Products and ΔH_f [kcal mol^{-1}]		$\sum\Delta H_f$ [kcal mol^{-1}]	Abundance [a]		T^{av}[b] [kcal mol^{-1}]		Transition state energy [c] [kcal mol^{-1}]	
			(1)	*(2)*	*(1)*	*(2)*	*(1)*	*(2)*
$CH_2{\cdot}\dot{C}H{-}CH_2 + H_2O$								
226 [27]	− 58 [28]	168	95	2	1.0	1.6	176	208
$CH_2{\cdot}\dot{O}H$	$+C_2H_4$							
170 [29]	12 [28]	182	5	86	0.4	1.3	181	208
$CH_3\dot{C}H_2$	$+CH_2O$							
219 [30]	− 28 [28]	191	0	12	—	—	—	212

[a] Measured by metastable peak area for dissociations occurring in the second field-free region and normalized to a total of 100 units [26]. [b] Measured from first field-free region metastable peak widths [26]. [c] Obtained from appearance potential measurements on metastable ions dissociating in the first field-free region [26].



Scheme 1

In contrast, starting from *(2)*, H_2O loss becomes only a very minor process; the main dissociation is now C_2H_4 loss and, moreover, CH_2O is also eliminated to a significant extent. This suggests that *(2)* undergoes rate-determining rearrangement to *(1)* which then dissociates relatively rapidly. Consequently, there is discrimination against H_2O loss which requires extensive rearrangement after the rate-determining step; C_2H_4 and CH_2O losses, which may proceed without much rearrangement, are therefore the main dissociations of *(2)* because they can occur faster. Further evidence in favor of this rate-determining rearrangement stems from the kinetic energy release associated with H_2O and C_2H_4 losses from *(1)* and *(2)*. In each case, a greater average kinetic energy accompanies decomposition of *(2)* (Table 1); this is consistent with *(2)* dissociating through the same transition states as *(1)* but with a greater excess energy. Finally the measured activation energies for H_2O and C_2H_4 losses from *(1)* are different; as expected from the preferential elimination of H_2O from *(1)*, this process has the lower transition state energy (Table 1). In contrast, starting from *(2)*, H_2O and C_2H_4 eliminations require the same energy, which now reflects only the height of the energy barrier towards rearrangement to *(1)*. Furthermore, this energy is greater than that needed to dissociate *(2)* and is more than enough to cause CH_2O loss which is no longer precluded for energetic reasons.

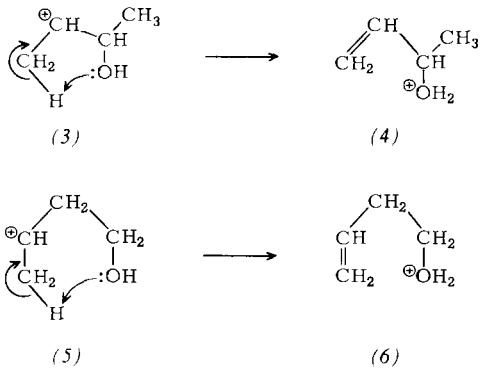
The above examples serve to give a brief illustration of how the unimolecular reactions of isolated organic ions may be interpreted in terms of a potential energy profile approach[10]. The three basic types of potential energy profiles (Fig. 5) described above may be combined to produce more complex energy profiles. Before giving examples of these more sophisticated energy diagrams (Section 3), it is instructive to examine some of the other methods which are available to investigate the structures and reactivities of organic ions in the gas phase.

2.4. Energetics

The use of energetic data and energy measurements in constructing potential energy profiles is in many ways self-evident; some of these uses may be seen from the analysis of the two $C_3H_7O^+$ isomers, *(1)* and *(2)*, discussed above. When accurate values for the heats of formation of all relevant species are known, these data may be used, in conjunction with the organic chemist's concept of reaction mechanism, to produce a complete energy level diagram for the system. This procedure frequently explains the reactions of previously investigated ions and is often of predictive use[10, 20, 22, 24, 31–35].

However, it is comparatively rare that reliable thermochemical data are available for all the species of interest; in such cases appearance potential measurements may be made, or, alternatively, recourse may be made to quantum mechanical calculations or estimation techniques. The disadvantage of the former is that, unless specialized mass spectrometers are employed, it may result in unreliable results owing to systematic errors in analyzing the data[36,37]. Nevertheless, it ought to be possible to detect large differences in transition state energies in this way. The problem with calculated or estimated heats of formation is that these values may easily be in error and, moreover, it is preferable to use experimental values whenever possible. Notwithstanding this, when the data are inaccessible to experimental methods, calculated[38] or estimated values must be used; the latter are often obtained from results for lower homologues by means of a group equivalent approach[39], or from isodesmic[40] substitutions[40,41].

It is frequently also necessary to estimate the energy required to cause an isomerization to occur. For example, the occurrence of 1,2-hydride or alkyl shifts is commonly postulated in the reactions of organic ions. Solution NMR experiments show that these reactions usually occur with activation energies close to the enthalpy differences involved[42]; quantum mechanical calculations suggest that a similar situation prevails in the gas phase[38]. Hence, it is reasonable to assume that these symmetry-allowed[43] rearrangements may occur without significant energy barriers other than those associated with the inherent difference in stability of the ions concerned. In contrast, 1,3-hydride shifts occurring in even electron cations [in a four-electron system, *e. g. (2)→(1)*] appear in some cases to involve very large energy barriers[26]; presumably these energy barriers originate from the symmetry-forbidden nature of the reactions. An intermediate position is occupied by hydrogen transfer occurring through five and six-membered ring transition states (Scheme 2). An activation energy of *ca.* 10 kcal mol^{-1} is required to cause the rearrangement *(3)→(4)*; however, *(5)→(6)* has an essentially negligible activation energy[34]. Similar conclusions may be reached in analogous[35] or homologous systems[33].



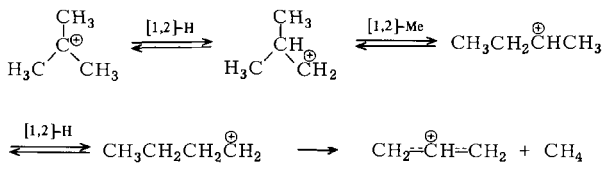
Scheme 2

Fortunately, the range of ions for which accurate heats of formation are available is increasing. Reliable values are known for numerous hydrocarbon cations and radical cations[27,28b,30,44-48], and a selection of oxonium ions $C_nH_{2n+1}O^+$[29,49]. More recently, proton affinity measurements have provided a wealth of new information; this method, which generates gaseous ions under equilibrium conditions, is relatively accurate and potentially very extensive in scope[50-54].

2.5. Isotope Labeling

There are two main uses of stable isotopes in elucidating the reactions undergone by organic ions in the gas phase.

a) The loss of identity of labeled ions may furnish information as to which atoms in the ions may become equivalent, *via* reversible rearrangement processes, prior to decomposition. Suppose two ions may interconvert *via* a series of 1,2-hydride shifts; if all the hydrogen atoms in the molecule are able to participate in these shifts at some stage, then the rapid interconversion of the two ions leads to loss of identity of all the hydrogen atoms. When dissociation eventually takes place, any of the hydrogen atoms may therefore be eliminated even through the actual decomposition channel may involve the selection of a hydrogen atom attached to a specific site. This effect is common and is sometimes referred to as "scrambling" or "randomization" of the label. These expressions are potentially misleading because they may be construed to mean that the chemistry of the system is not understood. Moreover, the observation of random selection of atoms from labeled ions is occasionally taken to mean that the decomposition pathway must involve a symmetrical intermediate in which all the relevant atoms are equivalent. This is not necessarily the case; in some systems it is the equilibration of isomeric structures which leads to loss of identity of atoms in labeled species. Consider the case of the isomeric cations $C_4H_9^+$; these may be considered to interconvert *via* the series of 1,2-hydride and methyl shifts shown in Scheme 3. The heats of formation of each of the four "classical" isomers are known and dissociation to allyl cation and CH_4 requires more energy than interconversion. Hence, these ions are expected to equilibrate prior to decomposition. This is confirmed by experiment: irrespective of the precursor used to generate $C_4H_9^+$, CH_4 loss and a constant minor percentage of C_2H_4 loss are observed[55a]. Furthermore, the interconversion of the four isomers permits the hydrogen and carbon atoms to sample each possible site in each structure. Therefore the observed random elimination of methane[55] from ^2H- and ^{13}C-labeled analogues of $C_4H_9^+$ may be explained without postulating the existence of any symmetrical intermediate.



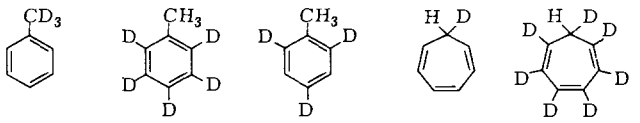
Scheme 3

There are many examples of this behavior[56-60]; the important point is that labeling may be used to discover which atoms in a given ion are able to exchange sites *via* isomerization processes that precede decomposition.

b) The observation of isotope effects in the decomposition of labeled ions may yield information concerning which bond (or which kind of bond) is broken in the rate-determin-

ing step. Thus, the large isotope effects which occur in hydrogen radical loss from some small hydrocarbon ions mentioned previously indicate that the cleavage of a C—H (or C—D) bond is indeed the rate-determining step for dissociation[12–15].

These isotope effects are frequently encountered in the unimolecular chemistry of organic ions in the gas phase; often an isotope effect is superimposed upon statistical selection of some (or all) of the atoms needed to make up the neutral which is eliminated. For example, the competition between $H^{\cdot}$ and $D^{\cdot}$ loss from the molecular ions of the ^{2}H-labeled toluenes, *(7)*—*(9)*, may be interpreted in terms of loss of any of the original H or D atoms together with an isotope effect of 2.8:1[61] or 3.5:1[62] favoring $H^{\cdot}$ loss. (The slight discrepancy between the magnitude of the isotope effects found in the two studies may be ascribed to a slight difference in ion lifetimes and hence average internal energies[62].) Similar behavior is observed for the radical cations of the ^{2}H-labeled cycloheptatrienes *(10)* and *(11)*[61]; this is consistent with interconversion of ionized toluene and cycloheptatriene prior to decomposition.



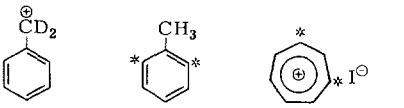
(7) *(8)* *(9)* *(10)* *(11)*

2.6. Collisional Activation (CA) and Ion Cyclotron Resonance (ICR)

These two techniques facilitate the detection of any ion structure which exists in a significant potential energy well. Collisional activation (CA) is the more commonly employed and has now become a routine method for investigating the structures of isolated non-decomposing ions[63]. A detailed discussion of CA is beyond the scope of this article; however, the basis of the method is to allow accelerated ions of low internal energy, which have not dissociated even after some 10^8 vibrations, to collide with an "inert" gas. These inelastic collisions cause excitation of the ions which acquire sufficient internal energy to undergo relatively fast dissociations. Since there is not usually enough time for extensive interconversion of isomeric ions to occur after collision, if two ions formed from different precursors exhibit the same CA spectra then they must have interconverted before collision ("fingerprint" criterion). Conversely, when isomeric ions have different CA spectra, this indicates that there is a fairly substantial energy barrier towards their interconversion. A difference in the CA spectra of two ions does not however preclude the equilibration of these ions at energies appropriate to slow unimolecular decompositions. This is because the energy barriers towards isomerization of the two ions may be less than those for dissociation but nevertheless sufficiently large to cause appreciable differences in the CA spectra.

Consider, for instance, the long-standing "benzyl *versus* tropylium" controversy; several $C_7H_7^+$ species with different CA spectra are observed[64]. The observation that $C_7H_5D_2^+$ ions of nominal structure *(12)* eliminate CD_2 in CA spectroscopy proves that such low energy ions do not collapse to tropylium structures.

Moreover, ICR experiments reveal the existence of two distinct $C_7H_7^+$ populations (presumably benzyl and tropylium cations) which exhibit different behavior in their ion/molecule reactions in the gas phase[65]. These data constitute strong evidence that both benzyl and tropylium cations exist in significant potential energy wells in the gas phase.



(12) *(13)*, * = ^{13}C *(14)*, * = ^{13}C

Notwithstanding this, higher energy ions, which decompose in the ion source or field-free regions, appear to interconvert between benzyl and tropylium structures before dissociation takes place[66–69]. For example, the molecular ion of [2,6-$^{13}C_2$]-toluene *(13)* fragments to form some unlabeled $C_5H_5^+$ and some $^{13}C_2H_2$. This cannot be interpreted in terms of dissociation of ionized *(13)* without prior rearrangement, nor by collapse to a tropylium-like structure which then decomposes without further isomerization. Similar behavior is observed for the cation of the tropylium salt *(14)*[68].

2.7. Predictive Capacity

Some of the more important methods which may be applied to study the chemistry of isolated organic ions are discussed above. The data furnished by these experimental methods may be used to construct a potential energy profile over which the ions under investigation may be considered to react. These potential energy profiles may frequently be used to explain the reactions of organic ions (having lifetimes $\geq 10^{-5}$ s) in the gas phase. In some instances, apparently inexplicable behavior may be easily understood in terms of this model[33,34]. Furthermore, when the necessary thermochemical information is available, it is possible to predict successfully the reactions undergone by previously uninvestigated ions[20,22,24,33,35]; these predictions are potentially extensive in scope. The test of all scientific theories lies in their capacity to formulate predictions in cases for which no results are known. In this respect, the potential energy profile approach has proved remarkably successful.

A few cogent examples of the application of the approach to rationalize or predict the slow reactions of gaseous ions are given below.

3. Examples of Potential Energy Profiles

3.1. The Ions $C_2H_5O^+$

The relative abundances of competing slow dissociations of isomeric $C_2H_5O^+$ ions and the kinetic energy release associated with these reactions are given in Table 2.

It is clear from the data of Table 2 that at least two distinct populations of ions, which do not interconvert appreciably at energies appropriate to slow reactions, are being formed. First, precursors of general formula CH_3OCH_2X produce $C_2H_5O^+$ ions (presumably with the $CH_3\dot{O}H{=}CH_2$ structure) which exclusively undergo CH_4 loss. In contrast, ions generated from other precursors (these ions are probably an inter-

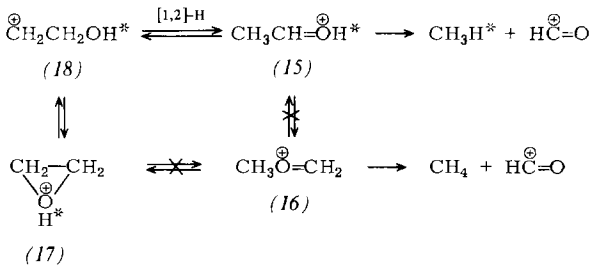
Table 2. Observed decompositions of some $C_2H_5O^+$ ions (data from ref. [25]).

Precursor	Ratio of C_2H_2 loss to CH_4 loss	T values for CH_4 loss [kcal mol^{-1}]
CH_3OCH_2X	0.01:1	<3 [a]
$HOCH_2CH_2X$	(1.8±0.2):1	11.5±0.9 [b]
CH_3CHXOH	(1.9±0.1):1	10.1±0.5 [b]

[a] Gaussian metastable peak, see Fig. 5a. [b] Dish-topped metastable peak, see Fig. 5d.

converting mixture of $CH_3\overset{\oplus}{C}H{=}\dot{O}H$ and $\overset{\oplus}{C}H_2CH_2\dot{O}H$) lose C_2H_2 and CH_4 in the ratio of approximately 1.9:1. Moreover, CH_4 loss from the two classes of ions is evidenced by metastable peaks of completely different shapes. Elimination of CH_4 from $CH_3\dot{O}{=}CH_2$ gives rise to a gaussian metastable peak whereas the other type of ions lose CH_4 with a large and relatively specific kinetic energy release as shown by the dish-topped metastable peak for this process[25]. Furthermore, the measured transition state energies for the two separate CH_4 loss channels, although only approximate, are widely different[70]. Finally, ^{2}H-labeling studies reveal that CH_4 loss from $CH_3\dot{O}{=}CH_2$ proceeds with random selection of any of the original five hydrogen atoms[26,70]. In contrast, CH_4 loss from ions generated as $CH_3CH{=}\dot{O}H$ involves specific elimination of the hydrogen atom originally bound to oxygen, which does not lose its identity to a significant extent, together with any three of the four carbon-bound hydrogen atoms[58,60].

These data constitute conclusive evidence that $CH_3\dot{O}{=}CH_2$ reacts over a potential energy profile which is distinct from that over which $CH_3CH{=}\overset{\oplus}{O}H$ and $\overset{\oplus}{C}H_2CH_2\dot{O}H$ interconvert and dissociate. The potential energy profile of Figure 6 may be constructed using known[28,29,49,71,72] and estimated[41] heats of formation. The observed interconversion of $CH_3CH{=}\overset{\oplus}{O}H$ *(15)* and $\overset{\oplus}{C}H_2CH_2\dot{O}H$ *(17)* prior to dissociation may be understood because these ions may isomerize, *via* $^+CH_2CH_2OH$, at a lower energy than is needed to cause decomposition. Scheme 4 also explains why all the carbon-bound hydrogen atoms and both carbon atoms of *(15)* become equivalent prior to CH_4 loss[58–60] whereas the hydrogen atom attached to oxygen retains its identity[70]. Rapid interconversion of *(15)* and *(17)*, *via (18)*, results in random distribution of carbon-bound hydrogen atoms and both carbon atoms but allows the hydrogen atom bound to oxygen to remain distinct.



Scheme 4

However, rearrangement of *(15)* or *(17)* to *(16)*, or *vice versa*, requires more energy than elimination of CH_4; this is because some very high energy species, such as the diradical $\dot{C}H_2\dot{O}H\dot{C}H_2$, must be involved. Consequently, *(16)* dissociates over a separate potential energy profile from *(15)* and *(17)*. Moreover, C_2H_2 loss can plausibly occur only from

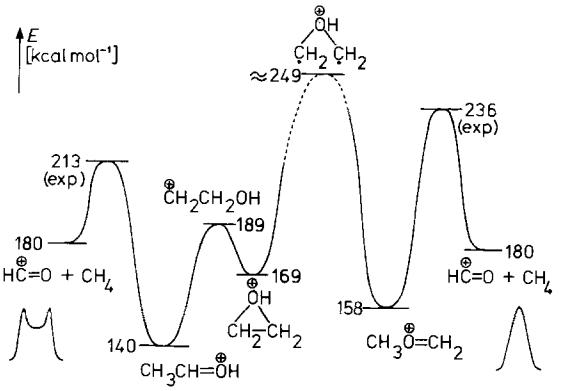


Fig. 6. Potential energy profile for CH_4 loss from the $C_2H_5O^+$ isomers $CH_3CH{=}\dot{O}H$ *(15)* and $CH_3\dot{O}{=}CH_2$ *(16)*; metastable peaks associated with dissociation of *(15)* and *(16)*.

some structure of $C_2H_5O^+$ in which the two carbon atoms are directly linked, such as $CH_2{=}CH\dot{O}H_2$. This type of ion is really only accessible *via (15)*, *(17)*, or *(18)*; hence, the non-occurrence of C_2H_2 loss from *(16)* may be rationalized because this ion prefers to eliminate CH_4[70].

3.2. The Ions $C_4H_9O^+$

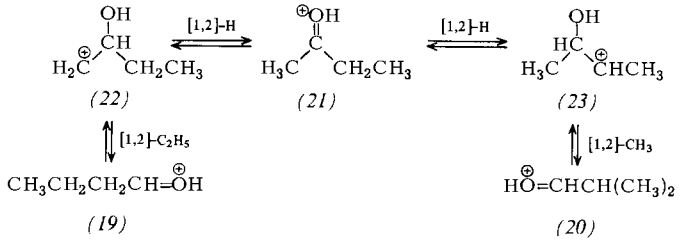
It is also instructive to consider the behavior of three isomers of $C_4H_9O^+$, which is a higher homologue of $C_2H_5O^+$. Relevant data concerning the decomposition of these ions, which are all protonated aldehydes or ketones, are given in Table 3.

Table 3. Observed decompositions of some isomers of $C_4H_9O^+$ *(19)*—*(21)* (data from ref. [73]).

Ion		Neutral lost [a] H_2O	C_2H_4	CH_2O
$CH_3CH_2CH_2CH{=}\dot{O}H$	*(19)*	99	1	0
$(CH_3)_2CHCH{=}\dot{O}H$	*(20)*	90	3	7
$CH_3CH_2(CH_3)C{=}\dot{O}H$	*(21)*	89	3	8

[a] Abundances normalized to a total of 100 units.

The data shown in Table 3 reveal that *(20)* and *(21)* interconvert prior to dissociation but *(19)* reacts over a separate potential energy profile. This conclusion is further strengthened by a consideration of the kinetic energy release which accompanies dissociation, the energy required to promote decomposition, and the results of ^{2}H-labeling[34,73]. It seems rather strange at first sight that protonated butanone *(21)* should interconvert with protonated isobutyraldehyde *(20)* but not with protonated *n*-butyraldehyde *(19)* prior to decomposition. However, when the mechanism whereby *(19)*, *(20)*, and *(21)* may interconvert is considered (Scheme 5) this apparent anomaly may be readily explained.



Scheme 5

Clearly *(20)* and *(21)* may interconvert *via* the *secondary* carbenium ion *(23)*; in contrast, *(21)* may only rearrange to *(19) via* the *primary* carbenium ion *(22)*. Starting from *(21)*, rearrangement to *(20)* is therefore energetically more favorable than isomerization to *(19)*; the relevant potential energy profile, constructed using known[53] or estimated[41] heats of formation, is depicted in Figure 7[34]. Analysis of the potential energy profiles over which *(19)*, *(20)*, and *(21)* may actually dissociate, reveals that decomposition of *(20)* and *(21)* requires more energy than interconversion of the two but less energy than rearrangement to *(19)*. Hence, *(20)* and *(21)* equilibrate prior to dissociation but do not rearrange to *(19)*. Starting from *(19)*, decomposition is energetically more favorable than isomerization to *(20)* and *(21)*; therefore, *(19)* dissociates without rearranging to *(20)* or *(21)*. Similar behavior is observed for the nitrogen analogues of *(19)*, *(20)*, and *(21)*[35].

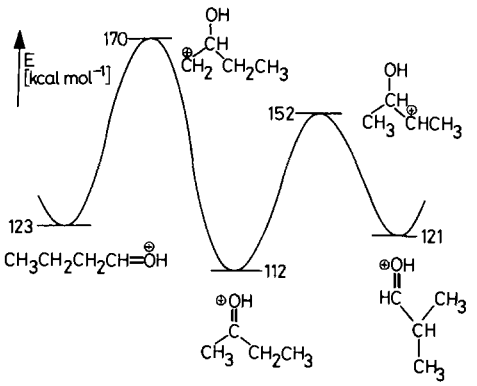
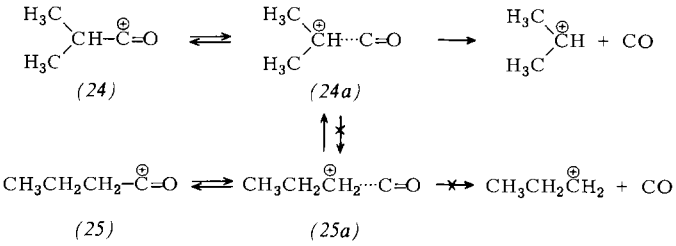


Fig. 7. Potential energy profile for isomerization of the $C_4H_9O^+$ isomers $CH_3CH_2CH_2CH{=}\dot{O}H$ *(19)*, $CH_3CH_2(CH_3)C{=}\dot{O}H$ *(21)*, and $(CH_3)_2CHCH{=}\dot{O}H$ *(20)*.

3.3. Carbenium Ion Rearrangements

The rearrangement of carbenium ions has often intrigued organic chemists. In most simple cases, small hydrocarbon ions undergo facile isomerizations before decomposition occurs in the gas phase[20-24,55-57]. It would clearly be of interest if these isomerizations could be observed *directly*. In the gas phase, this may be done by generating the ion of interest bound to a suitable leaving group which effectively serves to protect the ion from rearrangement until dissociation actually begins to take place. A convenient leaving group is CO and the case where this group is attached to the two isomeric propyl cations is considered in Scheme 6.

Starting from *(24)*, simple bond breaking may proceed to the energetically most favorable products, $i\text{-}C_3H_7^+$ and CO, without rearrangement. This reaction channel may plausibly involve a negligible reverse activation energy and thus *(24)* → products is probably continuously endothermic. The metastable peak for this dissociation is very narrow correspond-



Scheme 6

ing to an average kinetic energy release of only 0.2 kcal mol^{-1}[74]. On the other hand, the corresponding process in *(25)* results in the formation of the energetically unfavorable *n*-propyl cation. Although such a reaction would probably proceed without appreciable reverse activation energy, it can be pre-empted by isomerization of the incipient *n*-propyl cation and subsequent formation of $i\text{-}C_3H_7^+$ and CO. This rearrangement of the incipient *n*-propyl cation to the thermochemically more stable isopropyl cation [*(25a)*→*(24a)*] releases approximately 18 kcal mol^{-1} of potential energy[30] which then causes rapid dissociation to form $i\text{-}C_3H_7^+$ and CO. The corresponding metastable peak is broadened owing to the conversion of part of the liberated potential energy into kinetic energy release accompanying CO loss[26,74]. The average kinetic energy released when *(25)* eliminates CO is 2.0 kcal mol^{-1}, essentially an order of magnitude greater than that accompanying CO loss from *(24)*. The metastable peaks for these processes are depicted in Figure 8; the broad peak for CO loss from *(25)* may be taken as diagnostic evidence that the incipient carbenium ion undergoes an exo-

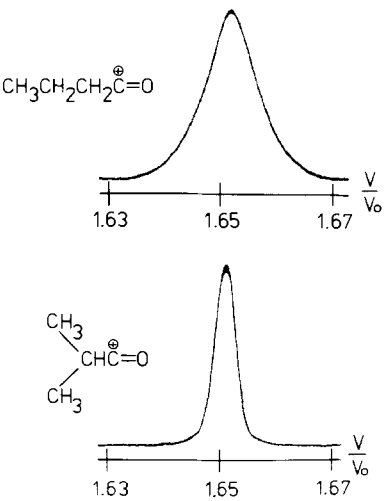


Fig. 8. First field-free region metastable peaks for CO elimination from $CH_3CH_2CH_2^+CO$ *(25)* and $(CH_3)_2CH^+CO$ *(24)*. The abscissae are in units of V/V_0 where V_0 is the accelerating voltage employed to transmit the main beam and V is the corresponding voltage required to transmit $C_3H_7^+$ ions formed in the first field-free region.

thermic isomerization before CO loss occurs. Indeed, appearance potential measurements establish that CO loss from *(25)* requires less energy than that needed to produce an *n*-propyl cation together with CO. Similar effects are observed when CO is lost from higher homologues of *(24)* and *(25)*; in

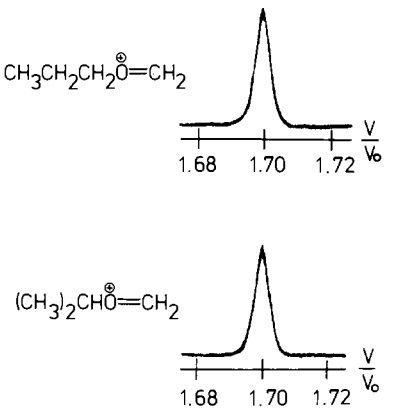


Fig. 9. First field-free region metastable peaks for CH_2O elimination from $CH_3CH_2CH_2\dot{O}{=}CH_2$ *(27)* and $(CH_3)_2CH\dot{O}{=}CH_2$ *(26)* (the abscissae have a similar significance to those in Fig. 8).

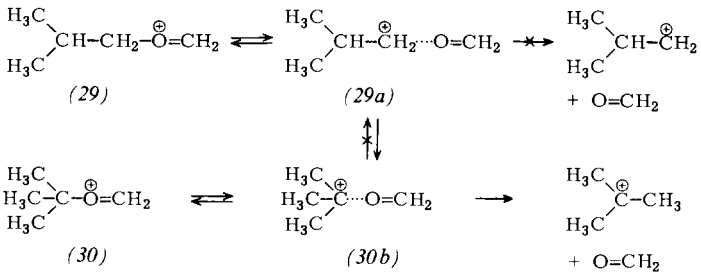
general, incipient primary carbenium ions rearrange to thermochemically more stable isomers prior to dissociation, as evidenced by the broader metastable peaks for these processes. This behavior also occurs when leaving groups other than CO are employed, for example loss of Br• from ionized alkyl halides[74]. It is usually found that any incipient cation which would not be expected to exist in a potential energy well undergoes rearrangement to a more stable structure (or structures)[74,75]. In contrast, narrow peaks, thus indicating the absence of rearrangement in the potential cation, are generally found for cases where the relevant cation ought to be in a potential energy well (that is, tertiary and most secondary alkyl carbenium ions). The kinetic energy release accompanying dissociation of cations bound to suitable leaving groups may therefore be used to investigate which of a set of isomeric ions exist in potential energy wells. This method is frequently a useful complementary probe to CA spectroscopy[75].

When the CO leaving group in *(24)* and *(25)* is replaced by CH_2O, however, identical metastable peaks are observed starting from either $C_4H_9O^+$ ion with *n*- or isopropyl groups [*(27)* and *(26)*, respectively] (Fig. 9). These data, together with conclusions from more detailed investigations of *(26)* and *(27)*[73,76], show that reversible rearrangement of the incipient $C_3H_7^+$ ion may occur prior to CH_2O loss (Scheme 7). In particular, energy measurements reveal that CH_2O loss from *(26)* and *(27)* requires essentially the same energy in each case and this energy corresponds almost exactly to that expected if *i*-$C_3H_7^+$ and CH_2O were the products[76].

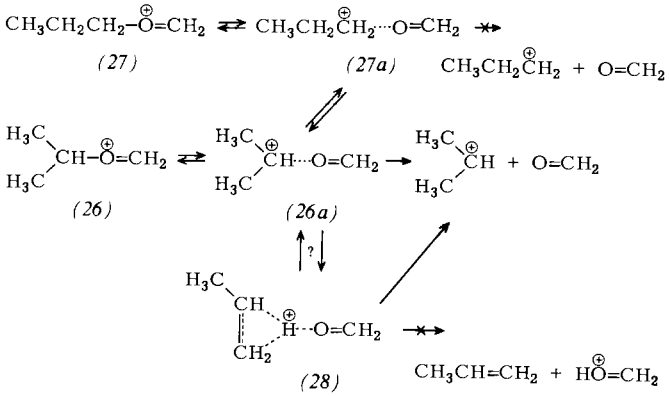
The most likely explanation of this striking change in behavior, relative to *(24)* and *(25)* where rate-determining rearrangements are observed, is that *(26a)* and *(27a)* are stabilized by a sizeable ion-dipole interaction[77]. The magnitude of this stabilization can theoretically be as great as 18 kcal mol^{-1} even when the C···O bonds of *(26a)* and *(27a)* are sufficiently stretched (to a length of 3 Å) that the covalent bonds are essentially broken. Experimental evidence is also available which supports an ion-dipole stabilization of similar size in higher homologues of *(26a)* and *(27a)*[78]. This stabilization of *(26a)* and *(27a)* is greater than (or equal to) the energy released when a primary carbenium ion isomerizes to a secondary carbenium ion. Hence, when *(27)* rearranges to *(26a)*, *via (27a)*, the combination of isopropyl cation and CH_2O is still sufficiently stable to avoid rapid dissociation. Interconversion of *(26)* and *(27)* may thus occur prior to CH_2O loss.

The ion dipole stabilization of *(26a)* and *(27a)* arises because CH_2O has a fairly large permanent electric dipole[79]. In contrast, CO and Br• have negligible or zero electric dipoles; hence, rate-determining rearrangements of the incipient *n*-propyl cation occurs in these cases[74].

However, the rearrangement of an incipient primary carbenium ion to a tertiary isomer would release approximately 32 kcal mol^{-1}[30]. This should be more than enough to overcome the attractive ion-dipole interaction, thus resulting in a relatively large kinetic energy release. This is found to be the case for incipient butyl cations having tertiary and iso structures (Scheme 8). As expected, the metastable peak for CH_2O loss from *(29)* is much broader than that starting from *(30)* (Fig. 10).



Scheme 8



Scheme 7

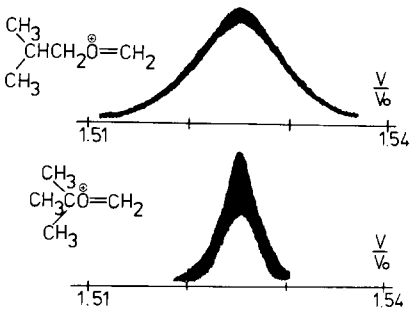


Fig. 10. First field-free region metastable peaks for CH_2O elimination from $(CH_3)_2CHCH_2\dot{O}{=}CH_2$ *(29)* and $(CH_3)_3C\dot{O}{=}CH_2$ *(30)* (the abscissae have a similar significance to those in Fig. 8).

A final point in connection with the isomerization and dissociation of *(26)* and *(27)* and homologous ions is that rearrangement of *(26a)* or *(27a)* to *(28)* might take place. This species is effectively a complex in which C_3H_6 and CH_2O are bound to a common proton. Breakdown of *(28)* may then occur so that the neutral having the greater proton affinity keeps the proton. This mechanism may be used to explain, or predict successfully, the decomposition of numerous oxonium ions, related to *(26)* or *(27)*, *via* loss of olefins or carbonyl compounds. [In *(28)*, this corresponds to the formation of $i\text{-}C_3H_7^+/CH_2O$ rather than $CH_3CH{=}CH_2/H\overset{+}{O}{=}CH_2$[77].]

3.4. The Concept of a Hierarchy of Reactions in Homologous Ions

When the dissociations undergone by members of a homologous series of ions are compared, it is frequently found that the decay routes observed for lower members of the series are pre-empted by energetically more favorable processes for higher ions. Thus, for example, H_2 loss is a common decomposition channel for many small hydrocarbon ions; however, a significant amount of H_2 loss is rarely observed for larger homologous ions[20-24,31]. This effect arises because, as more CH_2 residues are inserted into the first member of the series, new dissociation pathways are opened up which require less energy. An example of this behavior is given in Table 4 which lists the energies required to cause decomposition of the first four members of the homologous series of protonated aldehydes, $C_nH_{2n+1}O^+$. The first member of the series, protonated formaldehyde, eliminates H_2 with an activation energy of 80 kcal mol^{-1}. However, energetically less demanding pathways are available for the next homologue, protonated acetaldehyde, which does not eliminate a significant amount of H_2 in slow reactions. These processes, loss of CH_4 and C_2H_2, are themselves pre-empted for protonated propionaldehyde which requires much less energy to eliminate H_2O and C_2H_4 than is needed to dissociate the lower homologues. Another substantial drop in the activation energy needed to cause the most facile dissociation is found in progressing to protonated *n*-butyraldehyde. It may be noted in passing that H_2O loss from protonated *n*-butyraldehyde is a different process from H_2O loss from protonated propionaldehyde because it is characterized by a different kinetic energy release[34,81].

Table 4. Activation energies for dissociation of some $C_nH_{2n+1}O^+$ ions.

Ion	Neutral lost	Act. energy [kcal mol^{-1}]
$CH_2{=}\dot{O}H$	H_2	80 [80]
$CH_3CH{=}\dot{O}H$ *(15)*	CH_4	73 [70]
	C_2H_2	73 [70]
$CH_3CH_2CH{=}\dot{O}H$	H_2O	42 [81]
	C_2H_4	48 [81]
$CH_3CH_2CH_2CH{=}\dot{O}H$ *(19)*	H_2O	27 [34]

4. Conclusion

The theoretical principles and examples of potential energy profiles discussed above serve to illustrate how the slow unimolecular reactions ($k \approx 10^5\ s^{-1}$) of gaseous organic ions may be investigated using a mass spectrometer. A major advantage associated with conducting the experiments in the absence of collisions is that information concerning the kinetic energy release accompanying dissociation is directly accessible from the shape of the corresponding metastable peak. *These metastable peaks constitute a "direct picture" of what happens when decomposition takes place.* In common with solution chemistry, the rate-determining step in dissociation is not always the final step but may be a slow prior isomerization which is then followed by relatively rapid decomposition. In such cases, a broadening of the metastable peak is observed; numerous examples of this behavior have been reported recently and it would appear to be a fairly general phenomenon[26,33 35,70,74 78,81,82].

The precise definition of those structures of carbenium ions (in solution) which are associated with potential energy minima has been a vexing and controversial problem[83]. In the gas phase, the study of the kinetic energy release associated with carbenium ion formation can give important information about the shape of the potential energy profile; morever, in many cases it is possible to detect whether cation formation is associated with the participation of bonding electrons which may be somewhat remote from the site of the [carbon]—[leaving group] bond. The nature of such participation processes may be uncovered, since the structure of the carbocation which is finally formed is established by collision-induced decomposition of the cation.

A further important feature of the method is that it deals with the energies, the reactions, and the transition state properties of isolated ions. It is precisely such experimental properties which are required for comparison with those molecular properties which are derived by "computer chemistry"[84]. Additionally, comparison of the properties and chemistry of isolated cations with those associated with the corresponding cations in condensed phases will allow a clearer understanding of solvation effects[85]. Finally, if the energetics of unimolecular decompositions can be clearly defined then, in those cases where the principle of microscopic reversibility is applicable, an understanding of the energetics of the reverse bimolecular process has been established.

It appears that in the future the technique will help in answering fundamental questions about one of chemistry's most basic problems—the unimolecular reactions undergone by isolated molecules.

R. D. B. thanks Sidney Sussex College Cambridge for a Research Fellowship, D. H. W. thanks the S.R.C. (U.K.) for financial support and H. S. gratefully acknowledges financial support from the Deutsche Forschungsgemeinschaft (project Schw 221/4) and the Fonds der Chemischen Industrie and the receipt of a Fellow Commonership from Churchill College, Cambridge (1977/78).

Received: October 19, 1978 [A 274 IE]
German version: Angew. Chem. *91*, 484 (1979)

[1] *J. H. Beynon:* Mass Spectrometry and its Applications to Organic Chemistry. Elsevier, Amsterdam 1960.
[2] a) *K. Biemann:* Mass Spectrometry. McGraw-Hill, New York 1962; b) *G. Spiteller:* Massenspektrometrische Strukturanalyse Organischer Verbindungen. Verlag Chemie, Weinheim 1966.
[3] *H. Budzikiewicz, C. Djerassi, D. H. Williams:* Interpretation of Mass Spectra of Organic Compounds. Holden-Day, San Francisco 1964.
[4] *H. Budzikiewicz, C. Djerassi, D. H. Williams:* Mass Spectrometry of Organic Compounds. Holden-Day, San Francisco 1967.

[5] a) *J. H. Beynon, R. A. Saunders, A. E. Williams:* The Mass Spectra of Organic Molecules. Elsevier, Amsterdam 1968; b) *J. Seibl:* Massenspektrometrie. Akademische Verlagsgesellschaft, Frankfurt 1970.

[6] *J. A. Hipple, R. E. Fox, E. V. Condon,* Phys. Rev. *69*, 347 (1946).

[7] *D. H. Williams, I. Howe:* Principles of Organic Mass Spectrometry. McGraw-Hill, New York 1972.

[8] a) *R. G. Cooks, J. H. Beynon, R. M. Caprioli, G. R. Lester:* Metastable Ions. Elsevier, Amsterdam 1973; b) *K. Levsen:* Fundamental Aspects of Organic Mass Spectrometry. Verlag Chemie, Weinheim 1978.

[9] Specialist Periodical Reports: Mass Spectrometry. Vol. 1—4. The Chemical Society, London 1971—1977.

[10] *D. H. Williams,* Acc. Chem. Res. *10*, 280 (1977).

[11] *H. M. Rosenstock, V. H. Dibeler, F. N. Harllee,* J. Chem. Phys. *40*, 591 (1964).

[12] *L. P. Hills, M. L. Vestal, J. H. Futrell,* J. Chem. Phys. *54*, 3834 (1971).

[13] *U. Lohle, Ch. Ottinger,* J. Chem. Phys. *51*, 3097 (1969).

[14] *M. L. Vestal, J. H. Futrell,* J. Chem. Phys. *52*, 978 (1970).

[15] *C. Lifshitz, L. Sternberg,* Int. J. Mass Spectrom. Ion Phys. *2*, 303 (1969).

[16] *J. H. Beynon, R. A. Saunders, A. E. Williams,* Z. Naturforsch. *A 20*, 180 (1965).

[17] *J. H. Beynon, A. E. Fontaine,* Z. Naturforsch. *A 22*, 334 (1967), and references cited therein.

[18] *D. T. Terwilliger, J. H. Beynon, R. G. Cooks,* Proc. Roy. Soc. London Ser. *A 341*, 135 (1974).

[19] *I. G. Simm, C. J. Danby, J. H. D. Eland,* J. Chem. Soc. Chem. Commun. *1973*, 832.

[20] *R. D. Bowen, D. H. Williams,* J. Chem. Soc. Perkin Trans. II *1976*, 1479.

[21] *M. A. Shaw, R. Westwood, D. H. Williams,* J. Chem. Soc. *B 1970*, 1529.

[22] *B. J. Stapleton, R. D. Bowen, D. H. Williams,* Tetrahedron *34*, 259 (1978).

[23] *A. J. Dale, W. D. Weringa, D. H. Williams,* Org. Mass Spectrom. *6*, 501 (1972).

[24] *R. D. Bowen, B. J. Stapleton, D. H. Williams,* Org. Mass Spectrom. *13*, 330 (1978).

[25] *T. W. Shannon, F. W. McLafferty,* J. Am. Chem. Soc. *88*, 5021 (1966).

[26] *G. Hvistendahl, D. H. Williams,* J. Am. Chem. Soc. *97*, 3097 (1975).

[27] *F. P. Lossing,* Can. J. Chem. *49*, 357 (1971).

[28] a) *J. L. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl, F. H. Field:* Ionization Potentials, Appearance Potentials, and Heats of Formation of Gaseous Positive Ions. National Bureau of Standards, Washington, D.C., 1969; b) *H. M. Rosenstock, K. Draxl, B. W. Steiner, J. T. Herron,* J. Phys. Chem. Ref. Data *6*, Suppl. 1 (1977).

[29] *K. M. A. Refaey, W. A. Chupka,* J. Chem. Phys. *48*, 5205 (1968).

[30] *F. P. Lossing, G. P. Semeluk,* Can. J. Chem. *48*, 955 (1970).

[31] *R. D. Bowen, D. H. Williams,* Org. Mass Spectrom. *12*, 453 (1977).

[32] *D. H. Williams, R. D. Bowen,* J. Am. Chem. Soc. *99*, 3192 (1977).

[33] *R. D. Bowen, J. R. Kalman, D. H. Williams,* J. Am. Chem. Soc. *99*, 5481 (1977).

[34] *R. D. Bowen, D. H. Williams,* J. Chem. Soc. Perkin Trans. II *1978*, 68.

[35] *R. D. Bowen, D. H. Williams,* J. Chem. Soc. Perkin Trans. II *1978*, 1064.

[36] *J. H. Beynon, R. G. Cooks, K. R. Jennings, A. J. Ferrer-Correia,* Int. J. Mass Spectrom. Ion Phys. *18*, 87 (1975).

[37] *H. M. Rosenstock,* Int. J. Mass Spectrom. Ion Phys. *20*, 139 (1976).

[38] See, *e. g., L. Radom, J. A. Pople, V. Buss, P. v. R. Schleyer,* J. Am. Chem. Soc. *94*, 311 (1972).

[39] See ref. [28a], appendix 1 and 2; see also *J. L. Franklin,* Ind. Eng. Chem. *41*, 1070 (1949); J. Chem. Phys. *21*, 2029 (1953).

[40] *L. Radom, J. A. Pople, P. v. R. Schleyer,* J. Am. Chem. Soc. *94*, 5935 (1972).

[41] *R. D. Bowen, D. H. Williams,* Org. Mass Spectrom. *12*, 475 (1977).

[42] *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions. Wiley, New York 1968–1973; especially Vol. 4, Chap. 33.

[43] *R. B. Woodward, R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

[44] *F. P. Lossing,* Can. J. Chem. *50*, 3973 (1972).

[45] *F. P. Lossing, J. C. Traeger,* J. Am. Chem. Soc. *97*, 1579 (1975).

[46] *F. P. Lossing, J. C. Traeger,* Int. J. Mass Spectrom. Ion Phys. *19*, 9 (1976).

[47] *F. P. Lossing, A. Maccoll,* Can. J. Chem. *54*, 990 (1976).

[48] *K. Watanabe, T. Nakayama, J. Mottl,* J. Quant. Spectrosc. Radiat. Transfer *2*, 369 (1962).

[49] *F. P. Lossing,* J. Am. Chem. Soc. *99*, 7526 (1977).

[50] *J. L. Beauchamp, M. C. Caserio,* J. Am. Chem. Soc. *94*, 2638 (1972).

[51] *D. H. Aue, H. M. Webb, M. T. Bowers,* J. Am. Chem. Soc. *97*, 4137 (1975).

[52] *D. H. Aue, W. R. Davidson, M. T. Bowers,* J. Am. Chem. Soc. *98*, 6700 (1976).

[53] a) *J. L. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver, Jr., J. L. Beauchamp, R. W. Taft,* J. Am. Chem. Soc. *99*, 5417 (1977); b) *P. Kebarle,* Annu. Rev. Phys. Chem. *28*, 445 (1977); c) *J. J. Solomon, F. M. Field,* J. Am. Chem. Soc. *97*, 2625 (1975); *98*, 1567 (1976).

[54] a) *J. L. Beauchamp,* Annu. Rev. Phys. Chem. *22*, 527 (1971); b) *T. A. Lehman, M. M. Bursey:* Ion Cyclotron Resonance Spectrometry. Wiley Interscience, New York 1976.

[55] a) *B. Davis, D. H. Williams, A. N. H. Yeo,* J. Chem. Soc. *B 1970*, 81; b) *R. Liardon, T. Gäumann,* Helv. Chim. Acta *54*, 1968 (1971); c) *H. W. Leung, C. W. Tsang, A. G. Harrison,* Org. Mass Spectrom. *11*, 664 (1976).

[56] *W. A. Bryce, P. Kebarle,* Can. J. Chem. *34*, 1249 (1956).

[57] *G. G. Meisels, J. Y. Park, B. G. Geissner,* J. Am. Chem. Soc. *91*, 1555 (1969).

[58] *D. van Raalte, A. G. Harrison,* Can. J. Chem. *41*, 3118 (1963).

[59] *A. G. Harrison, B. G. Keyes,* J. Am. Chem. Soc. *90*, 5046 (1968).

[60] *B. G. Keyes, A. G. Harrison,* Org. Mass Spectrom. *9*, 221 (1974).

[61] *I. Howe, F. W. McLafferty,* J. Am. Chem. Soc. *93*, 99 (1971).

[62] *J. H. Beynon, J. E. Corn, W. E. Baitinger, R. M. Caprioli, R. A. Benkeser,* Org. Mass Spectrom. *3*, 1371 (1970).

[63] Reviews: a) *K. Levsen, H. Schwarz,* Angew. Chem. *88*, 589 (1976); Angew. Chem. Int. Ed. Engl. *15*, 509 (1976); b) *R. G. Cooks:* Collision Spectroscopy. Plenum Press, New York 1978; c) *F. W. McLafferty* in *M. L. Gross:* High Performance Mass Spectrometry: Chemical Applications. ACS Symp. Ser. *70*. American Chemical Soc., Washington, D.C., 1978.

[64] *J. Winkler, F. W. McLafferty,* J. Am. Chem. Soc. *95*, 7533 (1973); *F. W. McLafferty, J. Winkler, ibid. 96*, 5182 (1974).

[65] a) *R. C. Dunbar,* J. Am. Chem. Soc. *97*, 1382 (1975); b) *J. L. M. Abbond, W. J. Hehre, R. W. Taft, ibid. 98*, 6072 (1976); c) *J. A. A. Jackson, S. G. Lias, P. Ausloos, ibid. 99*, 7515 (1977).

[66] a) *H. M. Grubb, S. Meyerson* in *F. W. McLafferty:* Mass Spectrometry of Organic Ions. Academic Press, New York 1963, p. 453; b) *J. T. Bursey, M. M. Bursey, D. G. I. Kingston,* Chem. Rev. *73*, 191 (1973).

[67] *K. L. Rinehart, Jr., A. C. Buchholz, G. E. van Lear, H. L. Cantrill,* J. Am. Chem. Soc. *90*, 2983 (1968).

[68] *A. Siegel,* J. Am. Chem. Soc. *96*, 1251 (1974).

[69] *R. A. Davidson, P. S. Skell,* J. Am. Chem. Soc. *95*, 6843 (1973).

[70] *R. D. Bowen, D. H. Williams, G. Hvistendahl,* J. Am. Chem. Soc. *99*, 7509 (1977).

[71] *B. H. Solka, M. E. Russell,* J. Chem. Phys. *78*, 1268 (1974).

[72] *M. A. Haney, J. L. Franklin,* Trans. Faraday Soc. *65*, 1794 (1969).

[73] *T. J. Mead, D. H. Williams,* J. Chem. Soc. Perkin Trans. II *1972*, 876.

[74] *D. H. Williams, J. Stapleton, R. D. Bowen,* Tetrahedron Lett. *1978*, 2919.

[75] a) *R. D. Bowen, D. H. Williams, H. Schwarz, C. Wesdemiotis,* J. Am. Chem. Soc., in press; b) J. Chem. Soc. Chem. Commun., *1979*, 261; c) *W. Franke, C. Wesdemiotis, H. Schwarz,* to be published.

[76] *R. D. Bowen, D. H. Williams,* J. Am. Chem. Soc. *99*, 6822 (1977).

[77] *R. D. Bowen, B. J. Stapleton, D. H. Williams,* J. Chem. Soc. Chem. Commun. *1978*, 24.

[78] *R. D. Bowen, D. H. Williams,* Int. J. Mass Spectrom. Ion Phys., *29*, 47 (1979).

[79] *D. R. Lide, A. A. Maryott:* Selected Values of Electric Dipole Moments for Molecules in the Gas Phase. NSRDS-NBS 10, Washington, D.C., 1967.

[80] *D. H. Williams, G. Hvistendahl,* J. Am. Chem. Soc. *96*, 6753 (1974).

[81] *G. Hvistendahl, R. D. Bowen, D. H. Williams,* J. Chem. Soc. Chem. Commun. *1976*, 294.

[82] a) *H. Schwarz, D. H. Williams, C. Wesdemiotis,* J. Am. Chem. Soc., *100*, 7052 (1978); b) *A. Weisz, A. Mandelbaum,* J. Chem. Soc. Chem. Commun. *1978*, 521; c) *H. Schwarz, C. Wesdemiotis,* Angew. Chem. *90*, 724 (1978); Angew. Chem. Int. Ed. Engl. *17*, 678 (1978); d) Org. Mass Spectrom., *14*, 25 (1979); e) *B. J. Stapleton, R. D. Bowen, D. H. Williams,* J. Chem. Soc., Perkin Trans. II, in press; f) *R. D. Bowen, D. H. Williams,* J. Chem. Res. (S), *1978*, 483.

[83] See, *e. g., H. C. Brown:* The Non-Classical Ion Problem. Plenum Press, New York 1973.

[84] See, *e. g., P. v. R. Schleyer,* Nachr. Chem. Tech. Lab. *24*, 571 (1976).

[85] *E. M. Arnett,* Acc. Chem. Res. 6, 404 (1973); b) *P. Kebarle, W. R. Davidson, J. Sunner, S. Meza-Hajer,* Pure Appl. Chem. *51*, 63 (1979).

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.

An Easily Prepared, Air-Stable Compound with a Triple Metal-to-Metal (MoMo) Bond[**]

By *Avi Bino* and *F. Albert Cotton*[*]

Since double, triple, and quadruple metal-to-metal bonds were first recognized, in 1963, 1966, and 1964, respectively, hundreds of compounds containing such bonds have been reported and scores of them have been structurally characterized by X-ray crystallography. Nonetheless it appears that many chemists tend to think of compounds containing such bonds, especially the triple and quadruple ones, as constituting chemical *exotica*. Nothing, of course, could be farther from the truth, as many such compounds are actually among the most easily prepared and stable ones formed by the elements in question. However, some such compounds, especially those with Mo≡Mo and W≡W bonds[1], are indeed highly reactive or thermally unstable and some contain relatively uncommon ligands, such as R_2N—, RO— or Me_3SiCH_2—.

This communication reports a striking example of how easy it can be to prepare an air-stable, thermally stable compound containing an Mo≡Mo triple bond.

The compound $Cs_2[Mo_2(HPO_4)_4(H_2O)_2]$ is prepared by first dissolving $K_4Mo_2Cl_8 \cdot 2H_2O$[2] in 2 M H_3PO_4. The resulting solution is then allowed to mix slowly, by diffusion through a glass frit, with a solution of CsCl in 2 M H_3PO_4. Over a period of a week a beautifully crystalline, purple solid is precipitated. All these operations are conducted at *ca.* 25 °C in vessels open to the laboratory atmosphere. The compound appears to be stable indefinitely in ordinary laboratory air.

Figure 1 shows the result of routine X-ray crystallography[3]. The structure of the $[Mo_2(HPO_4)_4(H_2O)_2]^{2-}$ unit is reminiscent of that found for $[Mo_2(SO_4)_4(H_2O)_2]^{3-}$ and also for $Mo_2(SO_4)_4^{4-}$[4], but there are significant differences in detail. One of the most interesting differences is the long MoMo distance [2.223(2) Å, as compared to 2.164(2) Å and 2.111(1) Å in the two sulfato species, respectively] which tells us quite clearly that we are dealing with a triple bond between the molybdenum atoms. The loss of one δ electron in the sulfato system increased the MoMo distance by 0.053 Å;

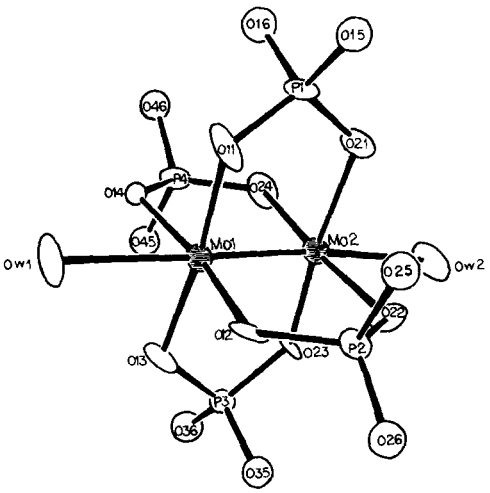


Fig. 1. Structure of the $[Mo_2(HPO_4)_4(H_2O)_2]^{2-}$ ion in crystal.

if we assume that the phosphato system can be compared directly with the sulfato ones, a further increase of 0.053 Å upon loss of the second δ electron would give a predicted triple bond distance of 2.164 + 0.053 = 2.217 Å in excellent agreement with the observed value. The Mo≡Mo distance found here is also close to those found in a variety of other molecules such as $Mo_2Cl_2(NMe_2)_4$ (2.201(2) Å) and $Mo_2(OC_4H_9)_4(O_2COC_4H_9)_2$ (2.241(1) Å)[1].

The hydrogen atoms of the HPO_4 groups were not found directly, but their locations are clearly indicated by the P—O bond lengths, O—P—O angles, and the hydrogen bonding. The eight P—O bonds to coordinated oxygen atoms (*endo* oxygens) range from 1.51 to 1.56 Å, with a mean of 1.54 ± 0.015 Å. The P—*exo*-O distances clearly fall into two sets. On each phosphato unit there is one such bond with a length of 1.48 ± 0.01 Å and another with a length of 1.56 ± 0.02 Å. The former can be assigned to P=O and the latter to P—OH. Moreover, each O atom of the P—OH groups is hydrogen bonded to an O atom of a P=O group of an adjacent molecule, with O···O distances of 2.48 to 2.53 Å, and P=O···HO angles of 113 to 120°.

The water molecules are quite loosely bound to Mo at distances of 2.46(1) Å and 2.53(1) Å and each of them also forms one strong (2.70 Å or 2.78 Å) and one weak (*ca.* 2.90 Å) hydrogen bond to phosphate oxygen atoms of adjacent molecules.

Since the $[Mo_2(HPO_4)_4(H_2O)_2]^{2-}$ unit is not subject to any crystallographic symmetry element and the existence of only a triple bond imposes no barrier to internal rotation, it is pertinent to examine the rotational conformation. The four torsional angles (dihedral angles between OMoMo′ and MoMo′O planes) that should be equal to zero for the ideal eclipsed structure have values of 0.5°, 1.6°, 2.1°, and 2.1°; the structure is thus essentially eclipsed, presumably because this conformation is favored by the ligands.

This substance belongs to the still rare but growing class of compounds containing simple triple M≡M bonds[5] in an environment of four-fold ligation of each metal atom. These include $La_4Re_2O_{10}$[6] as well as several molecules that result

[*] Prof. Dr. F. A. Cotton, Dr. A. Bino
Department of Chemistry
Texas A & M University
College Station, Texas 77843 (USA)

[**] This work was supported by The Robert A. Welch Foundation (Grant No. A-494).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0462 $ 02.50/0

from addition of donors to Mo_2L_6[7a] or W_2L_6[7b] molecules. $Cs_2[Mo_2(HPO_4)_4(H_2O)_2]$ is unique, however, in the simplicity and ease with which it can be prepared and in its chemical stability. It is also the first definite example of phosphato bridging of a bonded pair of metal atoms. In view of the possibility of adjusting the overall charge by changing the degree of protonation of the *exo* oxygen atoms, phosphato-bridged species may prove to be numerous and diverse.

Received: January 29, 1979 [Z 213 IE]
German version: Angew. Chem. *91*, 496 (1979)

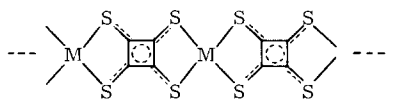
CAS Registry numbers:
$Cs_2[Mo_2(HPO_4)_4(H_2O)_2]$, 70281-26-4; $K_4Mo_2Cl_8 \cdot 2H_2O$, 22239-46-9

[1] *M. H. Chisholm, F. A. Cotton*, Act. Chem. Res. *11*, 356 (1978).
[2] *J. V. Brencic, F. A. Cotton*, Inorg. Chem. *8*, 7 (1969); *9*, 351 (1970).
[3] Crystal data: space group $P2_1/c$; $a = 8.751(3)$ Å, $b = 11.217(3)$ Å, $c = 17.938(4)$ Å, $\beta = 90.92(2)°$, $V = 1761(1)$ Å^3, $Z = 4$; 1515 independent reflections with $I > 3\sigma(I)$; $R_1 = 0.051$, $R_2 = 0.079$. [Enraf-Nonius Structure Determination package at the Molecular Structure Corporation, College Station, Texas.]
[4] *F. A. Cotton, B. A. Frenz, E. Pedersen, T. R. Webb*, Inorg. Chem. *14*, 391 (1975).
[5] It must be kept in mind that there are two principal types of MM triple bonds: 1) those with no δ bond ($\sigma^2\pi^4$) and 2) those in which there is cancellation of the δ bond by electrons occupying the δ* orbital ($\sigma^2\pi^4\delta^2\delta^{*2}$). We refer to the former as *simple* triple bonds and only they are considered in our present discussion.
[6] *K. Waltersson*, Acta Crystallogr. *B 32*, 1485 (1976).
[7] a) *M. H. Chisholm, F. A. Cotton, M. W. Extine, W. W. Reichert*, J. Am. Chem. Soc. *100*, 153, 1727 (1978). b) *M. H. Chisholm, F. A. Cotton, P. E. Fanwick*, unpublished work on $W_2(OCHMe_2)_6py_2$.

Transition Metal Complexes with the Tetrathiosquarate Dianion as Bridging Bischelate Ligand

By *Franz Götzfried, Wolfgang Beck, Anton Lerf*, and *Angelika Sebald*[*]

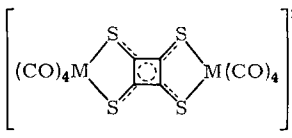
Organometallic compounds having chain structures are of interest as potential one-dimensional electrical conductors[1]. Tetrathiosquarate dianion $C_4S_4^{2-}$[2] appears to be especially suitable for the production of such *catena* complexes on account of its high symmetry (D_{4h}) and readily polarizable S atoms.



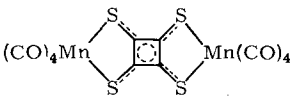
Anionic thio ligands often act as bridging ligands[3], and d^8 metal ions such as Ni^{II} are known to form polymeric complexes with, *e. g.*, ethylene tetrathiolate[4].

Whereas squaric acid[5a] and its dianion $C_4O_4^{2-}$[5b] do not occur as *O,O*-chelate ligands in transition metal complexes[5c], the dithiosquaric dianion $C_4O_2S_2^{2-}$ can form *S,S*-chelate complexes[5d]. We have now found that the dianion of tetrathiosquaric acid forms numerous compounds having bischelate structure with transition metals.

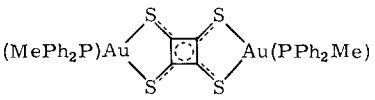
Thus the highly air-sensitive compounds *(1)* are formed by reaction of hexacarbonyl-6A metals with the potassium salt



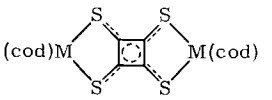
(1a), M = Cr
(1b), M = Mo
(1c), M = W
} Ph_4As– salts, violet



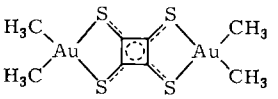
(2), red



(3), orange



(4a), M = Rh, red-brown
(4b), M = Ir, brown



(5), red

$C_4S_4K_2 \cdot H_2O$[2] in diglyme at 120 °C and subsequent precipitation with Ph_4AsCl; the neutral complexes *(2)*—*(5)* are obtained from the corresponding halometal derivatives by stirring for several hours with the thioligand at 20 °C in tetrahydrofuran (THF).

The IR, NMR, and mass spectra are in agreement with the expected structures:

(1a): ν(CO) = 1985 m, 1887 s, 1861 vs, 1820 s cm^{-1}; *(1b)*: ν(CO) = 1998 m, 1894 s, 1863 s, 1822 s cm^{-1}; *(1c)*: ν(CO) = 1992 m, 1886 s, 1861 s, 1825 m cm^{-1} (in THF); ^{13}C-NMR (in D_6-DMSO, int. TMS): δCO, C_4S_4 = 171.27 (s), 176.85 (s), 179.21 (s); *(2)*: ν(CO) = 2093 m, 2023 s, 2002 s, 1956 s cm^{-1} (solid in Nujol); *(3)*: ^{1}H-NMR (in $CDCl_3$, int. TMS): $\delta CH_3 = 2.17$ (d, $J_{PH} = 10$ Hz); *(5)*: ^{1}H-NMR (in $CDCl_3$, int. TMS): $\delta CH_3 = 1.17$ (s); MS (70 eV): $m/e = 630$ (M^+), correct isotope pattern

The characteristic intense C···C···S stretching vibration is always observed at higher wave numbers (max. 1305 cm^{-1}) in the complexes *(1)*—*(5)* than for the free ligand ($\nu_{C\cdots C\cdots S} = 1235$ cm^{-1}); the broad band is often split into several intense sharp bands.

Complex *(5)* can be irreversibly reduced in two steps (at −0.75 and −1.52) by voltammetry[6]. The reduction of squaric acid derivatives is particularly interesting, because it must ultimately lead to substituted cyclobutadienes! In contrast to $C_4O_4^{2-}$[7], the $C_4S_4^{2-}$ dianion can be smoothly reduced polarographically[8] in two one-electron steps (half-wave potentials: −1.53 V and −1.79 V) in aqueous solution to the tetraanion $C_4S_4^{4-}$.

Reaction of aqueous solutions of $NiCl_2$ or Na_2PdCl_4 with $K_2C_4S_4$ affords diamagnetic products

$Ni_{25}(C_4S_4)_{26}K_2 \cdot xH_2O$ ($x \approx 8$) *(6)*, dark-red
$Pd_{10}(C_4S_4)_9Cl_4K_2 \cdot xH_2O$ *(7)*, brownish black

The composition of these lustrous compounds is in agreement with a chain structure, the chain terminals being saturated with tetrathiosquarato ligands in *(6)* and by chloro ligands in *(7)*. K_2PtCl_4 or $(PhCN)_2PtCl_2$ react with $K_2C_4S_4$ to give blackish green complexes *(8)* containing Pt and C_4S_4 in the ratio of 1:1 and also varying amounts of K, O, Cl, and H, depending upon the reaction conditions.

[*] Prof. Dr. W. Beck, Dipl.-Chem. F. Götzfried, A. Sebald
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Dr. A. Lerf
Institut für Tieftemperaturforschung
Hochschulgelände, D-8046 Garching (Germany)

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

In addition to the bands at 1250 cm^{-1}, the IR spectrum of *(7)* and *(8)* contain weak ν(CO) absorptions at 1720 and 1740 cm^{-1}, which are attributable to partial replacement of S by O (ν(Ni—S) of *(6)*: 338, 267 cm^{-1}).

The electrical conductivity of the compressed powders *(6)*—*(8)* are comparable with corresponding values for neutral or anionic "metal dithiolenes"[1]; the resistance of the powders shows the same temperature dependence as semiconductors.

Polymer	Electrical conductivity at 20 °C δ [Ω^{-1} cm^{-1}]
(6)	5×10^{-4}
(7)	3×10^{-7}
(8)	6×10^{-7}

Given a parallel arrangement of the chains in *(6)*—*(8)*, interactions could occur between the metal atoms of neighboring chains which suggest electron delocalization perpendicular to the chain direction. A similar structure was recently suggested for a Ni^{II}-tetrathionaphthalene complex with semiconductor properties[9].

Received: February 15, 1979 [Z 216 IE]
German version: Angew. Chem. *91*, 499 (1979)

CAS Registry numbers:
(1), 70247-53-9; *(1b)*, 702247-55-1; *(1c)*, 70247-57-3; *(2)*, 70247-58-4; *(3)*, 70247-59-5; *(4a)*, 70247-60-8; *(4b)*, 70247-61-9; *(5)*, 70281-08-2; *(6)*, 70355-35-0; *(7)*, 70281-09-3; $NiCl_2$, 7718-54-9; Na_2PdCl_4, 13820-53-6; K_2PtCl_4, 10025-99-7; $(PhCN)_2PtCl_2$, 15617-19-3

[1] *J. S. Miller, A. J. Epstein*, Prog. Inorg. Chem. *20*, 1 (1976).
[2] *R. Allmann, T. Debaerdemaeker, K. Mann, R. Matusch, R. Schmiedel, G. Seitz*, Chem. Ber. *109*, 2208 (1976).
[3] *W. Hieber, M. Gscheidmeier*, Chem. Ber. *99*, 2312 (1966); *E. Lindner, R. Grimmer*, J. Organomet. Chem. *25*, 493 (1970); *H. Laufen, B. Meyn, K. G. Steinhäuser, D. Vogel, R. Kramolowsky, ibid. 112*, C34 (1976); *H. Weber, R. Mattes*, Chem. Ber. *112*, 95 (1979).
[4] *R. R. Schumaker, E. M. Engler*, J. Am. Chem. Soc. *99*, 5521 (1977); *H. Poleschner, W. John, G. Kempe, E. Hoyer, E. Fanghänel*, Z. Chem. *18*, 345 (1978).
[5] a) *W. Beck, F. Götzfried, M. W. Chen*, Chem. Ber. *111*, 3719 (1978); b) *M. Habenschuss, B. C. Gerstein*, J. Chem. Phys. *61*, 852 (1974); *J. A. C. van Ooijen, J. Reedijk*, Abstr. Pap. XVIII. Int. Conf. Coord. Chem., Prague 1978, p. 95; *A. Weiss, E. Riegler*, personal communication; c) cf., however, *R. West, H. J. Niu*, J. Am. Chem. Soc. *85*, 2589 (1963); *G. J. Long*, Inorg. Chem. *17*, 2702 (1978); *J. T. Wrobleski, D. B. Brown, ibid. 17*, 2959 (1978); d) *D. Coucouvanis, D. G. Holah, F. J. Hollander, ibid. 14*, 2657 (1975).
[6] PAR™ Model 170 Electrochemistry System; 10^{-3} M solution of *(5)* in 0.1 M $(n\text{-}C_4H_9)_4N^+ClO_4^-$ in CH_2Cl_2; Pt sheet as working electrode, reference electrode: Ag/AgCl in CH_3CN. We are indebted to Prof. *H. Nöth* and Dr. *R. Schwerthöfer* for the electrochemical measurements.
[7] *E. V. Patton, R. West*, J. Phys. Chem. *77*, 2652 (1973).
[8] 10^{-3} M solution of $C_4S_4K_2$ in 0.1 M $NaClO_4$; dropping Hg electrode, reference electrode: standard calomel electrode.
[9] *B. K. Teo, F. Wudl, J. J. Hauser, A. Kruger*, J. Am. Chem. Soc. *99*, 4862 (1977).

$Ag_{10}Si_4O_{13}$—The First Tetrasilicate[**]

By *Martin Jansen* and *Hans-Lothar Keller*[*]

On surveying the silicate structures discovered so far, the absence of a smooth transition from single chains ($^1_\infty SiO_3^{2-}$) to layers ($^2_\infty Si_2O_5^{2-}$) is noted[1]. A similar situation is encountered in the concatenation of individual (SiO_4^{4-}) tetrahedra to give chain-type anions: ortho- and disilicates are common, but trisilicates are much rarer. We have now succeeded in the first synthesis and characterization of a tetrasilicate.

$Ag_{10}Si_4O_{13}$ was obtained by reaction of the binary components Ag_2O and SiO_2 (low-temperature quartz) under oxygen pressure as a homogeneous, vermilion, moisture-insensitive powder [$P(O_2) = 2$—4.5 kbar, $T = 500$—600 °C, $t = 1$—3 d]. None of the neighboring phases $Ag_6Si_2O_7$ (I)[2] and $Ag_6Si_2O_7$ (II)[3] having a slightly higher silver content was detectable in the product. Crystals could be grown starting from the binary oxides in a silver nitrate melt by a previously described method[4] using an oxygen pressure of *ca.* 4.5 kbar at 600 °C.

$Ag_{10}Si_4O_{13}$ forms triclinic crystals, space group $P\bar{1}$[5]. The Si—O distances in the tetrasilicate anion (Fig. 1) vary between 158.9 and 168.3 pm, with average values of 161.6 pm for terminal and 165.0 pm for bridging bonds; the three Si—O—Si angles are 146.5, 137.7, 128.4°.

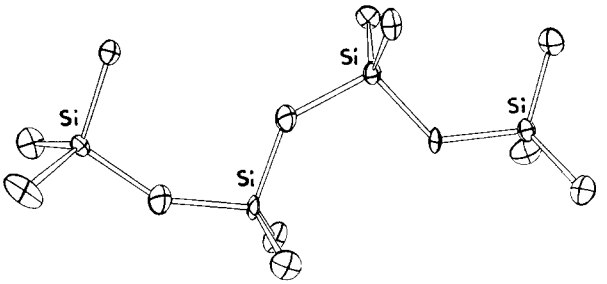


Fig. 1. Structure of the $Si_4O_{13}^{10-}$ anion in the silver salt.

The apparent preference for certain kinds of silicate anions could be attributable to the fact that most of the known structures are those of minerals formed under conditions in which the variety of available cations was limited by geochemical selection. Thus, it cannot be ruled out that synthetic approaches may lead to further unusual silicates, as in the case of the present silver silicate.

Received: February 19, 1979 [Z 217 IE]
German version: Angew. Chem. *91*, 500 (1979)

[1] *F. Liebau* in *K. H. Wedepohl*: Handbook of Geochemistry, Vol. *II/3*, 14 A 1. Springer-Verlag, Berlin 1972; *L. G. Mallinson, J. L. Hutchison, D. A. Jefferson, J. M. Thomas*, J. Chem. Soc. Chem. Commun. *1977*, 910; cf. also Nachr. Chem. Tech. Lab. *26*, 293 (1978).
[2] *M. Jansen*, Acta Crystallogr. *B 33*, 3584 (1977).
[3] *M. Jansen*, Habilitationsschrift, Universität Giessen 1978.
[4] *H.-L. Keller*, Dissertation, Universität Giessen 1973.
[5] $a = 1135.6$, $b = 913.1$, $c = 803.8$ pm, $\alpha = 100.32$, $\beta = 98.62$, $\gamma = 112.83°$; $Z = 2$. 2296 observed intensities (diffractometer data); solution by Patterson and Fourier methods, full matrix LSQ; $R = 0.049$.

Chemical Synthesis of Human Blood Group B Antigenic Determinant: Type 2 Tetrasaccharide[**]

By *Marie-Louise Milat* and *Pierre Sinaÿ*[*]

The "imidate procedure"[1] introduced by our group has recently enabled, *inter alia*, a high-yield synthesis of the trisaccharide *(1)*[2], which is considered as the antigenic determinant of the human blood group B in the AB0 system. We

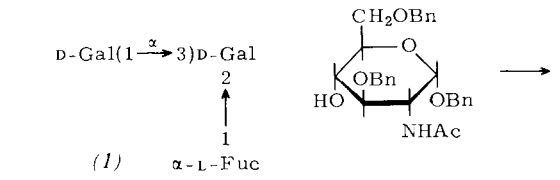
[*] Dr. habil. M. Jansen
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Lahn-Giessen (Germany)
Dr. H.-L. Keller
Institut für Anorganische Chemie der Universität
Olshausenstrasse 40—60, D-2300 Kiel (Germany)

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

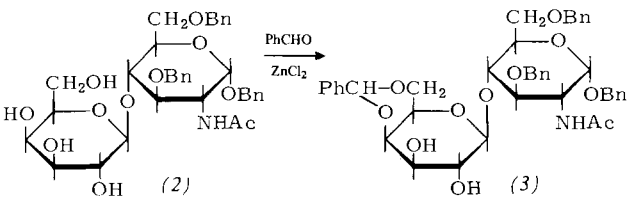
[*] Prof. Dr. P. Sinaÿ, M. L. Milat
Laboratoire de Biochimie Structurale, E.R.A. 739
U.E.R. de Sciences Fondamentales et Appliquées
F-45045 Orléans Cédex (France)

[**] Synthesis of blood-group substances, Part 10.—Part 9: [2].

have now succeeded in synthesizing the corresponding terminal tetrasaccharide *(10)* of type 2.

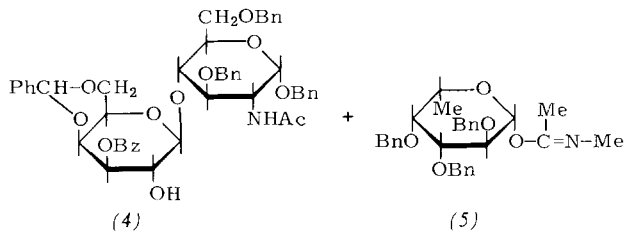


(1)

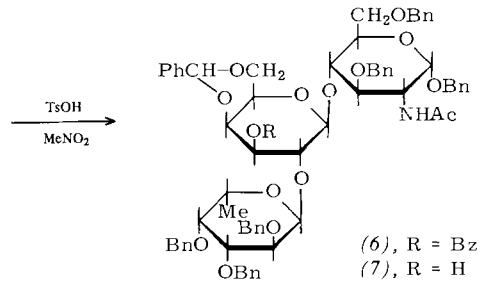


(2) *(3)*

As a key starting material we used the readily accessible[3] benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside which, on condensation with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide ($HgBr_2$, dichloromethane, molecular sieve 4 Å[4]) and subsequent deacetylation (MeONa in methanol), afforded the disaccharide *(2)*. Reaction of *(2)* with benzaldehyde in the presence of zinc chloride gave the benzylidene compound *(3)*, which was then selectively benzoylated[5] (*N*-benzoylimidazole in dichloroethane) to the derivative *(4)*. 1-*O*-[1-(Methylimino)ethyl]-2,3,4-tri-*O*-benzyl-β-L-fucopyranoside *(5)*[6] was condensed (*p*-toluenesulfonic acid/nitromethane) with *(4)* to provide, after debenzoylation (MeONa in methanol), the protected trisaccharide *(7)*. The structure of *(7)* was confirmed by complete deblocking (catalytic hydrogenolysis; Pd/C in pure acetic acid) to the known[7] trisaccharide of type 2. Further proof of the structure was provided by the NMR spectrum of the benzoate *(6)*.



(4) *(5)*



(6), R = Bz
(7), R = H

The expected protected tetrasaccharide *(9)* was obtained by reaction of 1-*O*-[1-(methylimino)ethyl]-2,3,4,6-tetra-*O*-benzyl-β-D-galactopyranoside *(8)*[2] with *(7)*. The tetrasaccharide chain *(10)* of the blood group substance B (type 2) is finally generated by hydrogenolytic cleavage of *(9)* with Pd/C in glacial acetic acid. This tetrasaccharide has been isolated from the alkaline degradation products of a human blood-group B substance[8]. Physical data of some of the compounds are listed in Table 1.

Table 1. Physical data of the compounds *(2)*—*(4)*, *(6)*, *(7)*, *(9)* and *(10)*.

	Yield [%]	M. p. [°C]	$[\alpha]_D^{20}$ [°]	(*c*, solvent)
(2)	77	155	+ 85	0.9 H_2O
(3)	92	175	+ 76.5	1.1 $CHCl_3$
(4)	91	179	+ 119	1.2 $CHCl_3$
(6)			+ 36.7	1.66 $CHCl_3$
(7)	89		+ 13.6	1 $CHCl_3$
(9)	90		+ 34	1.4 $CHCl_3$
(10) [a]	90		+ 14.1	0.36 H_2O

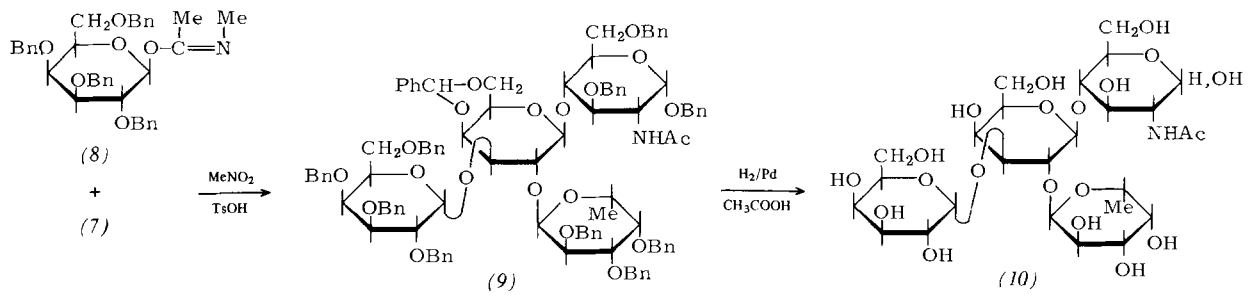
[a] $[\alpha]_D^{22} = +12°$ ($c = 0.5$, H_2O) [8].

A synthesis of the homologous type 1 tetrasaccharide has recently been reported[9].

Received: February 19, 1979 [Z 221 IE]
German version: Angew. Chem. *91*, 501 (1979)

CAS Registry numbers:
(2), 70209-54-0; *(3)*, 70209-55-1; *(4)*, 70209-56-2; *(5)*, 70267-04-8; *(6)*, 70209-52-3; *(7)*, 70209-58-4; *(8)*, 70267-71-9; *(9)*, 70209-59-5; *(10)*, 70267-05-9; benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside, 55287-49-5; 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide, 512-09-8

[1] *J.-R. Pougny, J.-C. Jacquinet, M. Nassr, D. Duchet, M.-L. Milat, P. Sinaÿ*, J. Am. Chem. Soc. *99*, 6762 (1977).
[2] *J.-C. Jacquinet, P. Sinaÿ*, Tetrahedron *35*, 365 (1979).
[3] *J.-C. Jacquinet, J.-M. Petit, P. Sinaÿ*, Carbohydr. Res. *38*, 305 (1974).
[4] *J.-C. Jacquinet, J.-R. Pougny, D. Duchet, P. Sinaÿ*, 2nd Joint Conference CIC-ACS, Montreal 1977, CARB 44.
[5] *G. J. F. Chittenden*, Carbohydr. Res. *16*, 495 (1971).
[6] *J.-C. Jacquinet, P. Sinaÿ*, J. Chem. Soc. Perkin Trans. I *1979*, 319.
[7] *J.-C. Jacquinet, P. Sinaÿ*, Tetrahedron *32*, 1693 (1976).
[8] *T. J. Painter, W. M. Watkins, W. T. J. Morgan*, Nature *206*, 594 (1965).
[9] *H. Paulsen, Č. Kolář*, Angew. Chem. *90*, 823 (1978); Angew. Chem. Int. Ed. Engl. *17*, 771 (1978).



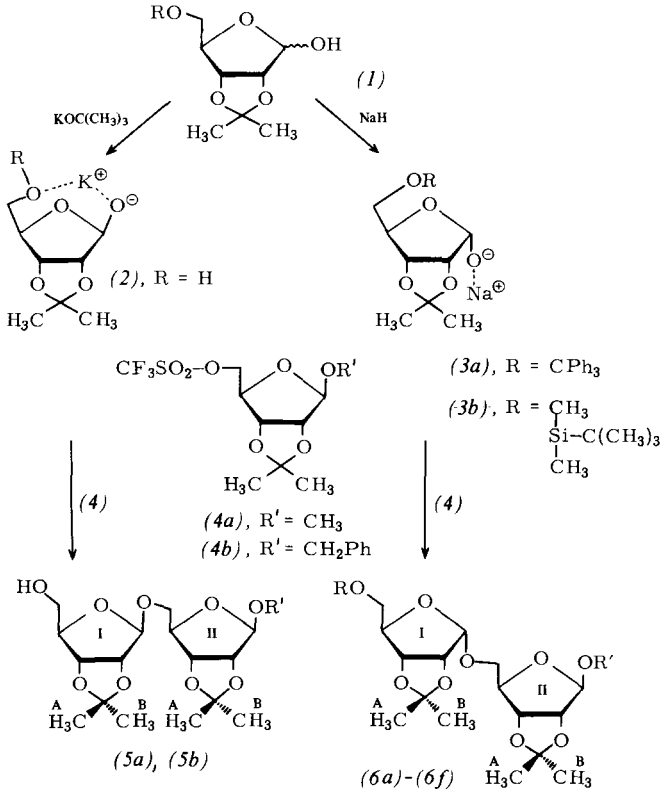
Facile, Highly Selective Synthesis of α- and β-Disaccharides from 1-*O*-Metalated D-Ribofuranoses[**]

By *Richard R. Schmidt* and *Manfred Reichrath*[*]

Dedicated to Professor Hellmut Bredereck on the occasion of his 75th birthday

Stereoselective formation of the glycosidic bond in disaccharide syntheses is generally achieved by nucleophilic displacement of a readily cleavable group at the anomeric center of the sugar[1].

The direct 1-*O*-alkylation of furanoses and pyranoses[2] or corresponding metalated derivatives[3], especially with methyl iodide and dimethyl sulfate, is already well-known, but has previously not been exploited for the chemically and stereochemically highly selective synthesis of α- or β-disaccharides[4]. We report here on an especially simple method for the synthesis of disaccharides [*(5)* and *(6)*] with high β- and α-stereoselectivity using as example the reaction of 1-*O*-metalated D-ribofuranoses *(2)* and *(3)* with 5-*O*-trifluoromethanesulfonyl-D-ribofuranosides *(4)*[6].



Stereochemical control of the reactions was accomplished by selective variation of the substituents on C-5 of the D-ribofuranose *(1)*. The ribofuranose *(1)*, R = H, reacts with potassium *tert*-butoxide in tetrahydrofuran to give the potassium salt *(2)*, which on reaction with the readily accessible trifluoromethanesulfonates *(4a)*[7] and *(4b)*[7] affords almost exclusively the β-coupled D-ribofuranosyl-(1→5)-D-ribofuranosides *(5a)* and *(5b)*[8], respectively (see Table 1). The high stereoselectivity has been discussed in terms of an intramolecular complexation in the anion of *(2)*[9].

By incorporation of a bulky protecting group on C-5, α-coupled disaccharides could be obtained. Thus, reaction of *(1) via* the sodium salt *(3a)*[9] with the trifluoromethanesulfonates *(4a)* and *(4b)* in dioxane afforded exclusively the α-disaccharides *(6a)* and *(6b)* in excellent yields[8]. The readily cleavable 5-*O*-*tert*-butyl(dimethyl)silyl group could also be used instead of the 5-*O*-trityl group: reaction of *(3b)*[9] with *(4a)* and *(4b)* furnished *(6c)* and *(6d)*, respectively, which on treatment with tetrabutylammonium fluoride could be converted almost quantitatively into the 5'-unprotected disaccharides *(6e)* and *(6f)*[8] (see Table 1).

General procedure

Compounds of type *(1)* dissolved in tetrahydrofuran or dioxane are deprotonated at 0—5 °C to *(2)* or *(3)* with equimolar amounts of potassium *tert*-butoxide or a *ca.* three- to fivefold excess of sodium hydride. After addition of base the reaction mixture is stirred for *ca.* 15 min at room temperature before adding an equimolar amount of *(4a)* or *(4b)* at 0 to 5 °C. The reaction time at room temperature is generally 5 to 20 h. [Synthesis of *(5b)*: +4 °C, 4 d, *(1)* in 1.5-fold excess.] Workup involves: extraction with $CHCl_3/H_2O$ [*(5a)*]; silica-gel filtration [*(6a)*, petroleum ether (low boiling):ethyl acetate = 7:3; *(6d)*: petroleum ether (low boiling):ethyl acetate = 8:2; *(6e)*, *(6f)*: first $CHCl_3$:ether = 9:1, then $CHCl_3:CH_3OH$ = 9:1]; bulb-to-bulb distillation [*(6c)*, 180 °C (oven temp.)/10^{-2} mbar]; chromatography on silica gel [*(5b)*: benzene:acetone = 92:8; *(6b)*: petroleum ether (low boiling):ethyl acetate = 7:8].—*(5a)*, *(5b)* and *(6a)*—*(6e)* were obtained as highly viscous oils; *(6f)*: m.p. 96 °C, from petroleum ether (low boiling).

Received: January 29, 1979 [Z 218 IE]
German version: Angew. Chem. *91*, 497 (1979)
Publication delayed at authors' request

Table 1. Disaccharides *(5a)*, *(5b)* and *(6a)*—*(6f)*. All compounds gave correct elemental analyses.

	R [a]	R'	Yield [%] [b]	^{1}H-NMR data [c] H_I-1	H_{II}-1	H_I^A	H_I^B	H_{II}^A	H_{II}^B	$[\alpha]_{578}^{20}$ [ ] [d]
(5a)	—	CH_3	89	5.15 (s)	4.98 (s)	1.31	1.47	1.31	1.47	−72.1
(5b)	—	Bn	72	5.1 (s)	5.16 (s)	1.30	1.46	1.30	1.46	−83.4
(6a)	Trityl	CH_3	87	5.1 (d)	4.92 (s)	1.32	1.57	1.28	1.45	− 1.3
(6b)	Trityl	Bn	74	5.07 (d)	5.09 (s)	1.31	1.57	1.28	1.44	−19.2
(6c)	TBDMS	CH_3	86	5.0 (dd)	4.95 (s)	1.36	1.58	1.30	1.48	−17.5
(6d)	TBDMS	Bn	77	5.0 (dd)	5.15 (s)	1.36	1.59	1.30	1.47	−37.5
(6e)	H	CH_3	93	5.0 (dd)	4.95 (s)	1.37	1.59	1.31	1.48	− 1.7
(6f)	H	Bn	87	4.98 (dd)	5.15 (s)	1.35	1.60	1.30	1.47	−28.4

[a] Abbreviations: Bn = benzyl, Trityl = triphenylmethyl, TBDMS = *tert*-butyl(dimethyl)silyl. [b] Yields of isolated products. [c] 80-MHz spectra in $CDCl_3$ with tetramethylsilane as internal standard; δ values, multiplicity in brackets. [d] $CHCl_3$ (c = 1.0).

[*] Prof. Dr. R. R. Schmidt, Dipl.-Chem. M. Reichrath
Fachbereich Chemie der Universität
Postfach 7733, D-7750 Konstanz (Germany)

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

CAS Registry numbers:
α-D-*(1)* (R = H), 70266-87-4; β-D-*(1)* (R = H), 67814-68-0; α-D-*(1)* (R = trityl), 54503-64-9; β-D-*(1)* (R = trityl), 54503-65-0; *(2)*, 70235-77-7; *(3a)*, 70209-09-5; *(3b)*, 70209-10-8; *(4a)*, 70209-11-9; *(4b)*, 70209-12-0; *(5a)*, 70209-72-2; *(5b)*, 70209-73-3; *(6a)*, 70209-74-4; *(6b)*, 70209-75-5; *(6c)*, 70209-76-6; *(6d)*, 70209-77-7; *(6e)*, 70209-78-8; *(6f)*, 70209-79-9; $KOC(CH_3)_3$, 865-47-4

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0466 $ 02.50/0

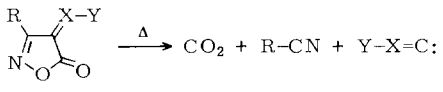
[1] *G. Wulff, G. Röhle*, Angew. Chem. *86*, 173 (1974); Angew. Chem. Int. Ed. Engl. *13*, 157 (1974); *C. Schuerch*, Acc. Chem. Res. *6*, 184 (1973), and references cited therein.
[2] *T. Purdie, J. C. Irvine*, J. Chem. Soc. *83*, 1021 (1903); *W. N. Haworth, ibid. 107*, 8 (1915); *R. Kuhn, H. Trischmann, J. Löw*, Angew. Chem. *67*, 32 (1955).
[3] *H. Bredereck, G. Hagelloch, E. Hambsch*, Chem. Ber. *87*, 35 (1954); *A. H. Haines, K. C. Symes*, J. Chem. Soc. *C 1971*, 2331, and references cited therein.
[4] Trehalose mixtures were prepared *via* this method; *H. Bredereck, E. Hambsch*, Chem. Ber. *87*, 38 (1954).
[5] *M. Reichrath*, planned Dissertation, Universität Konstanz.
[6] Investigations are currently being carried out on the application of this synthetic concept to pyranoses and reactions with secondary trifluoromethanesulfonyl groups [5].
[7] Preparation, see: *L. D. Hall, D. C. Miller*, Carbohydr. Res. *40*, C1 (1975); *R. W. Binkley, D. G. Hehemann*, J. Org. Chem. *43*, 3224 (1978).
[8] The configuration of the disaccharides *(5a)*, *(5b)* and *(6a)—(6f)* were confirmed by comparison with authentic materials [*(6e)*, *(6f)*] and by the chemical shift of the protons of the isopropylidene group: *K. H. Jung, P. Hermentin*. Dissertations, Universität Stuttgart 1977 and 1979, resp.; *R. R. Schmidt, P. Hermentin*, Chem. Ber., in press; *K. H. Jung, R. R. Schmidt*, Justus Liebigs Ann. Chem., in press.
[9] We assume that rapid and preferred formation of the β-anomer *(2)* or the α-anomer *(3)* takes place on deprotonation of the anomeric mixture *(1)*.

A New Synthesis of Fulminic Acid[**]

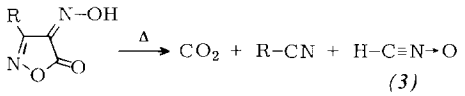
By *Curt Wentrup, Bernd Gerecht*, and *Horst Briehl*[*]

All useful syntheses of fulminic acid, HCNO, involve the dangerously explosive metal fulminates[1]. Moreover, preparation of the pure acid in bulk is extremely difficult. We now wish to report a safe and facile synthesis producing chemically pure fulminic acid in essentially quantitative yield.

The method is based on flash thermolysis of 4-substituted isoxazol-5(4*H*)-ones *(1)*, which we have previously used to prepare acetylenes, isocyanides, aminoisocyanides, and ketenimines[2]. By analogy with *(1)*, the oximes *(2)*[3] could be expected to fragment to the unknown molecule HO—NC, a tautomer of fulminic acid. However, we failed to obtain HO NC, isolating instead fulminic acid, HCNO *(3)*.



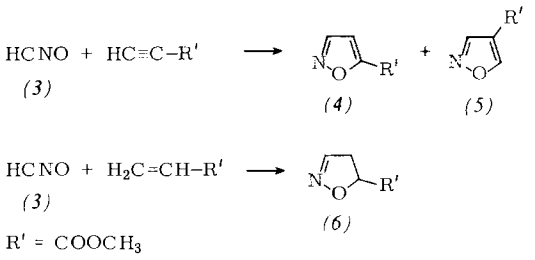
(1)



(3)

(2a), R = CH_3
(2b), R = C_6H_5

The gas-phase decomposition of *(2a)* between 200 and 800 °C gives only CO_2, acetonitrile, and HCNO. These products were isolated in a cold-trap cooled in liquid N_2 and HCNO was identified by comparison of its infrared spectrum in the gas-phase with that reported by *Beck et al.*[4a]. HCN and HNCO (isocyanic acid) were not detectable. It was also possible to observe the ν_{as}(CNO) vibration at 2190 cm^{-1} immediately upon dissolving the cold (−196 °C) pyrolyzate in CCl_4. At room temperature in solution, this absorption disappeared within a few seconds. On warming up to room temperature the fulminic acid underwent spontaneous polymerization to the known[5] mixture of tri- and tetramers.



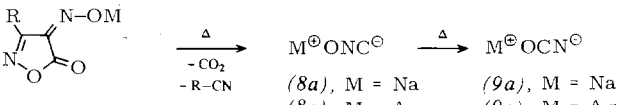
(3) *(4)* *(5)*

(3) *(6)*

R′ = $COOCH_3$

For further identification, the pyrolysis product was treated in the cold-trap with methyl propiolate and methyl acrylate. After slow warm-up to room temperature, the expected 1,3-dipolar cycloaddition products of HCNO, *(4)* and *(5)*, and *(6)*, respectively, were isolated. Notably, the ratio *(4)*/*(5)* = 84:16 was the same as from fulminic acid prepared by other means[6].

In order to obtain the chemically pure acid, it is better to use *(2b)* rather than *(2a)* as starting material. At an oven temperature of 450 °C and a sublimation temperature no higher than 120 °C, CO_2, benzonitrile, and HCNO are formed and collected in liquid N_2. CO_2 is pumped off at −80 °C, and HCNO is distilled into a second cold-trap by slow warm-up to *ca.* −10 °C in high vacuum. When sublimation temperatures higher than 120 °C were used in the pyrolysis of *(2b)*, significant amounts of HNCO were formed as a by-product. HNCO was identified by its infrared spectrum, and by its trimerization to cyanuric acid.



(7a), R = C_6H_5, M = Na
(7b), R = CH_3, M = Na
(7c), R = CH_3, M = Ag

(8a), M = Na
(8c), M = Ag

(9a), M = Na
(9c), M = Ag

The salts *(7)* of the oximes *(2)* explode when rapidly heated over a flame. Evaporation of solutions of *(7a)* occasionally resulted in non-violent decomposition with formation of benzonitrile, CO_2, and sodium cyanate, identified by their infrared spectra. This suggested initial fragmentation to sodium fulminate *(8a)*, which thermally isomerizes to the cyanate *(9a)*[4b]. When dry *(7b)* was allowed to decompose *in vacuo* at 50—55 °C (7 h) a mixture of *(8a)* and *(9a)* was formed, as identified by infrared comparison with authentic samples. Pure silver fulminate *(8c)* was formed in quantitative yield by allowing dry *(7c)* to decompose *in vacuo* at 70 to 110 °C[7].

Experimental

Fulminic acid *(3)*: The flash pyrolyses were carried out in a 30 × 2 cm electrically heated horizontal quartz tube at 10^{-3}—10^{-4} torr as previously described[8]. *(2a)* (4.0 g, 0.03 mol) was sublimed into the 450 °C pyrolysis tube from a flask held at 100—120 °C in the course of 10 h. The products were collected in a liquid N_2 trap. After bringing the system to atmospheric pressure, allowing slow warm-up to room temperature, and removing acetonitrile *in vacuo*, 1.3 g (97%) of the polymer[5] of fulminic acid was isolated. Alternatively,

[*] Prof. Dr. C. Wentrup, B. Gerecht, H. Briehl
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg (Germany)

[**] Fulminates, Part 1. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

the cold (−196 °C) pyrolyzate was treated with methyl acrylate (5.4 g, 0.06 mol). The mixture was allowed to warm up to room temperature, and acetonitrile and excess methyl acrylate were removed *in vacuo*, yielding 4.0 g (99%) of *(6)*, b. p. 70 °C/10^{-3} torr (^{1}H-NMR, see [6]).

Silver fulminate *(8c)*: Powdered *(6c)* (106 mg; 0.45 mmol) was heated at 100—110 °C for 11 h with pumping at 10 torr. The volatile products (acetonitrile and CO_2) were isolated in a cold-trap. The solid residue (68 mg, 100%) consisted of dangerously explosive silver fulminate (identified by IR comparsion with a sample prepared according to *Nef*[9]). Though no explosions have occurred during this preparation, due safety precautions should be taken.

Received: February 27, 1979;
revised: March 23, 1979 [Z 222 IE]
German version: Angew. Chem. *91*, 503 (1979)

[1] *C. Grundmann, P. Grünager:* The Nitrile Oxides. Springer, Berlin 1971, references cited therein.

[2] *C. Wentrup, W. Reichen,* Helv. Chim. Acta *59*, 2615 (1976); *W. Reichen, C. Wentrup, ibid. 59*, 2618 (1976); *C. Wentrup, H.-W. Winter,* Angew. Chem. *90*, 643 (1978); Angew. Chem. Int. Ed. Engl. *17*, 609 (1978); *C. Wentrup, U. Stutz, H.-J. Wollweber, ibid. 90*, 731 (1978) and *17*, 688 (1978); *C. Wentrup,* Chimia *31*, 258 (1977).

[3] *(2a): L. Bouveault, A. Wahl,* Ber. Dtsch. Chem. Ges. *38*, 926 (1905); *(2b): L. Claisen, W. Zedel, ibid. 24*, 140 (1891).

[4] a) *W. Beck, P. Swoboda, K. Feldl, R. S. Tobias,* Chem. Ber. *104*, 533 (1971); b) cf. *W. Beck, ibid. 95*, 341 (1962).

[5] *C. Grundmann, R. K. Bansal, P. S. Osmanski,* Justus Liebigs Ann. Chem. *1973*, 898; *C. Grundmann, G. W. Nickel, R. K. Bansal, ibid. 1975*, 1029, references cited therein.

[6] *R. Huisgen, M. Christl,* Chem. Ber. *106*, 3291 (1973).

[7] Preliminary experiments indicate that hitherto unknown organic fulminates, RO NC, may be formed in a similar manner. Thus, flash thermolysis of the *O*-benzyl and *O*-phenyl derivatives of *(2a)* gave low yields of benzyl isocyanate and phenyl cyanate, respectively (*C. Wentrup, B. Gerecht, D. Laqua, U. Stutz,* unpublished results). Benzyl cyanate would not be isolable under these conditions, since it already isomerizes to benzyl isocyanate at room temperature (*K. A. Jensen, A. Holm, J. Wolff-Jensen,* Acta Chem. Scand. *23*, 1568 (1969)). Phenyl cyanate rearranges to phenyl isocyanate at 900—1000 °C (*C. Wentrup, J.-P. Hagenbuch,* unpublished results).

[8] *N. M. Lân, C. Wentrup,* Helv. Chim. Acta *59*, 2068 (1976).

[9] *J. U. Nef,* Justus Liebigs Ann. Chem. *280*, 291 (1894).

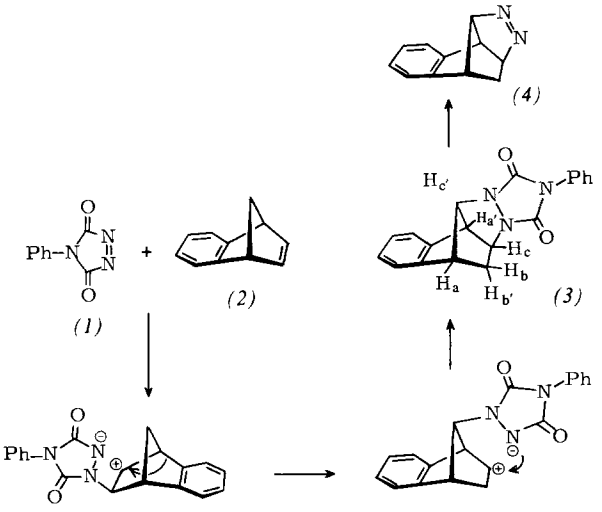
Polycyclic Azoalkanes *via* Dipolar Cycloaddition of 4-Phenyl-1,2,4-triazoline-3,5-dione with Strained Bicyclic Olefins[**]

By *Waldemar Adam, Ottorino De Lucchi,* and *Ihsan Erden*[*]

We required a convenient synthesis of the previously unknown tricyclic azoalkane *(4)* for the generation of the corresponding diradical, which is a potential intermediate of the di-π-methane rearrangement of benzonorbornadiene *(2)*[1].

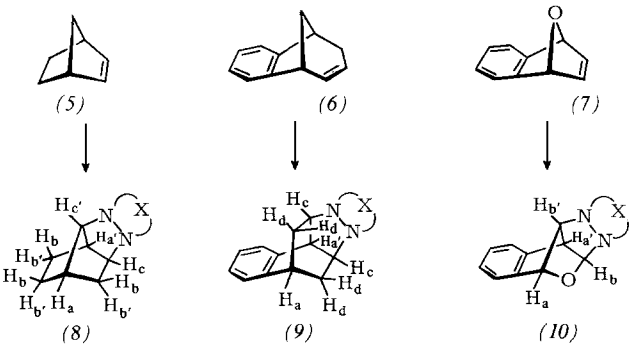
Since the highly reactive 4-phenyl-1,2,4-triazoline-3,5-dione *(1)* is known to undergo cycloaddition with strained polycyclic olefins[2], we undertook the reaction of *(1)* with the bicyclic species benzonorbornadiene *(2)*; the cycloadduct *(3)* could be reduced to *(4)* (Scheme 1). This cycloaddition could also be applied to compounds *(5)*—*(7)*.

Refluxing of stoichiometric amounts of *(1)* and *(2)* ($CHCl_3$, 30 min) led to complete decoloration of the red *(1)*. Evaporation of the $CHCl_3$ and column chromatography on Florisil,



Scheme 1

elution with CH_2Cl_2, and recrystallization from ethanol afforded the pure adduct *(3)*. Refluxing of *(3)* with KOH in isopropyl alcohol (90 min under N_2), neutralization with 3 N HCl, and treatment with $CuCl_2$ in CH_3OH, followed by 3 N NaOH, afforded the azoalkane *(4)*. It was purified by sublimation (60 °C/0.2 torr) and recrystallization from hexane.



X = –CO–NPh–CO–

Similarly, refluxing a solution of stoichiometric amounts of norbornene *(5)* with *(1)* (CH_2Cl_2, 3 h) afforded the crude cycloadduct *(8)*, which was purified by column chromatography on Florisil (eluant; CH_2Cl_2) and recrystallization from ethanol. This example clearly established that benzoannelation is not necessary for the reaction.

Refluxing of the olefin *(6)* with *(1)* in $CHCl_3$ gives the adduct *(9)* which was isolated by column chromatography on Florisil and recrystallization from ethanol[6]. Clearly the cycloaddition must involve dipolar species (cf. Scheme 1) since bromine addition to *(6)* proceeds *via* a similar cationic rearrangement[3].

Stirring stoichiometric amounts of *(7)*, *i.e.* the oxa analogue of *(2)*, and *(1)* (CH_2Cl_2, *ca.* 12 h) affords the cycloadduct *(10)*. It was purified by Florisil chromatography (CH_2Cl_2 as eluant) and recrystallization from EtOH. Physical data of all the new compounds are compiled in Table 1.

[*] Prof. Dr. W. Adam (NIH Career Awardee, 1975—80), Dr. O. De Lucchi, Dr. I. Erden
Department of Chemistry, University of Puerto Rico
Río Piedras, Puerto Rico 00931 (USA)

[**] Acknowledgments are made to the Donors of the Petroleum Research Fund (11022-AC-1), administered by the American Chemical Society, the National Science Foundation (CHE-78-12621), and the National Institutes of Health (GM-21119-03, GM-00141-04, and RR-8102-06). We thank Mr. *P. Hernández,* undergraduate research participant in the NIH sponsored SUBE program, for technical assistance.

Table 1. Physical data of the new compounds *(3)*, *(4)*, *(8)*—*(10)*. All compounds gave correct elemental analyses.

(3): m.p. 179—180°C; yield 95%; ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 1.53$ (d, $H_{b'}$; B part of AB system), 2.28 (d, H_b; A part of AB system), 3.75 (m, H_a, $H_{a'}$), 4.61 (m, H_c, $H_{c'}$), 7.15 (br. s, C_6H_4), 7.39 (br. s, C_6H_5); ^{13}C-NMR ($CDCl_3$): $\delta = 129.17, 128.36, 128.03, 127.11, 125.43, 124.08, 120.45, 76.84, 58.64, 53.43, 46.12, 34.53$ (CO resonances not recorded); IR (KBr): 3020, 1785, 1715, 1500, 1412 cm^{-1}

(4): m.p. 74—75°C; yield 74%; ^{1}H-NMR (CCl_4, TMS): $\delta = 1.20$ (m, H_b, $H_{b'}$), 2.78 (m, H_a), 3.21 (m, $H_{a'}$), 4.63 (m, H_c), 5.26 (m, $H_{c'}$), 6.88 (m, C_6H_4); IR (CCl_4): 3100, 3020, 2985, 2960, 1495, 1470, 1383, 1267, 1220 cm^{-1}

(8): m.p. 133—134°C; yield 17%; ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 1.2$—2.0 (m, $3H_b$, $3H_{b'}$), 2.60 (m, H_a, $H_{a'}$), 4.25 (m, H_c, $H_{c'}$), 7.25 (m, C_6H_5); IR (CCl_4/$CDCl_3$): 2960, 1775, 1725, 1505, 1410, 910 cm^{-1}

(9): m.p. 202—203°C; yield 31%; ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 1.98$ (m, $4H_d$), 3.07 (m, H_a), 3.48 (t, $H_{a'}$; $J(H_{a'}—H_c) = 4.0$ Hz), 4.35 (m, $2H_c$), 7.0 (br. s, C_6H_4), 7.22 (m, C_6H_5); IR ($CDCl_3$): 3080, 3060, 3040, 2960, 1770, 1705, 1600, 1500, 1400 cm^{-1}

(10): m.p. 145—146°C; yield 60%; ^{1}H-NMR $CDCl_3$, TMS): $\delta = 4.25$ (m, $H_{b'}$), 4.35 (m, $H_{a'}$), 5.22 (br. s, H_b), 5.41 (br. s, H_a), 7.08 (m, C_6H_4), 7.20 (m, C_6H_5); IR (KBr): 3040, 1790, 1710, 1600, 1495, 1400, 1320, 1260, 1230, 1150, 1090 cm^{-1}

The reactions reported here provide a synthetic entry into azoalkanes which would be difficult to prepare by classical methods and are of interest as precursors of diradical intermediates postulated in photochemical transformations.

Received: February 21, 1979 [Z 223 IE]
German version: Angew. Chem. *91*, 512 (1979)

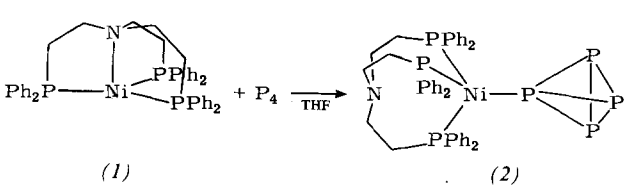
CAS Registry numbers:
(1), 4233-33-4; *(2)*, 4453-90-1; *(3)*, 70332-87-5; *(4)*, 70332-88-6; *(5)*, 498-66-8; *(6)*, 24309-43-1; *(7)*, 573-57-9; *(8)*, 70332-89-7; *(9)*, 70332-90-0; *(10)*, 35261-49-5

[1] *J. R. Edman*, J. Am. Chem. Soc. *91*, 7103 (1969).
[2] *T. J. Katz, N. Acton*, J. Am. Chem. Soc. *95*, 2738 (1973); *A. R. Browne, L. A. Paquette*, J. Org. Chem. *43*, 4522 (1978); *H. E. Zimmerman, R. J. Boettcher, N. E. Buchler, G. E. Keck, M. G. Steinmetz*, J. Am. Chem. Soc. *98*, 7680 (1976); *R. C. Cookson, S. S. H. Gilani, I. D. R. Stevens*, J. Chem. Soc. *C 1967*, 1905.
[3] *R. P. Johnson, A. Exarchon, C. W. Jefford*, J. Org. Chem. *42*, 3758 (1977).

tetrahedro-Tetraphosphorus as Monodentate Ligand in a Nickel(0) Complex

By *Paolo Dapporto, Stefano Midollini*, and *Luigi Sacconi*[*]

The existence of a P_4 unit was proposed in some rhodium complexes by *Ginsberg* and *Lindsell* but it was not clear how the P_4 was bound[1]. We have now prepared and structurally characterized a nickel(0) complex *(2)* containing as ligands the tritertiary phosphane tris(2-diphenylphosphinoethyl) amine (np_3) and a *tetrahedro*-tetraphosphorus (P_4) molecule. The P_4 unit is bonded to the metal atom by an apical P atom. The complex $[(np_3)Ni(P_4)]$ *(2)* is readily precipitated by reaction of the trigonal pyramidal complex of nickel(0)[2] *(1)* with white phosphorus in tetrahydrofuran (THF). The yellowish brown compound is diamagnetic and only slightly sensitive to air. It is insoluble in all common organic solvents.



(1) *(2)*

An X-ray diffraction analysis[3] has shown that the central nickel atom is bound in a quite regular tetrahedral geometry to the three phosphorus atoms of the np_3 ligand and to one phosphorus atom of the P_4 unit (Fig. 1). The nitrogen atom is not bonded to the metal atom (Ni...N = 3.09 Å). The Ni—P1 distance, shorter by *ca.* 0.2 Å than the sum of the covalent radii, suggests a d_π-d_π interaction between nickel and phosphorus. The nickel atom appears to attain the 18 electron configuration.

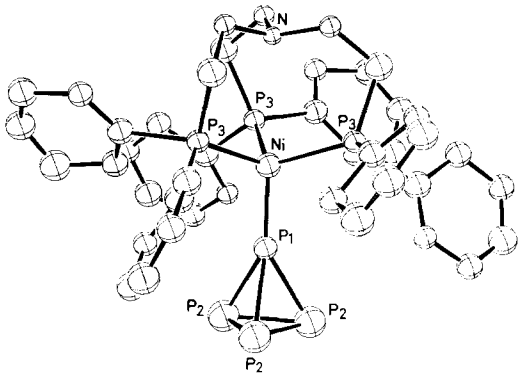


Fig. 1. ORTEP plot of $[(np_3)Ni(P_4)]$ *(2)*. Bond lengths: Ni P1 = 1.99(1), Ni P3 = 2.24(2), P1 P2 = 2.20(3), P2 P2 = 2.09(3) Å. Bond angles: P1 Ni P3 = 109.7(7), P3 Ni P3 = 109.3(7), P2 P1 P2 = 56.8(10)°.

Experimental

All operations were performed under N_2 and in oxygen-free THF. A solution of white phosphorus, P_4 (120 mg, 1 mmol) in THF (50 ml) was added to a solution of *(1)* (710 mg, 1 mmol) in THF (120 ml) at about 0 °C over a period of 15 min. Brown crystals were deposited, filtered off, washed with tetrahydrofuran and dried in a current of N_2 at room temperature (yield *ca.* 70%).

Received: February 12, 1979 [Z 231 IE]
German version: Angew. Chem. *91*, 510 (1979)

CAS Registry numbers:
(1), 52633-73-5; *(2)*, 70355-51-0

[1] *A. P. Ginsberg, W. E. Lindsell*, J. Am. Chem. Soc. *93*, 82 (1971).
[2] *L. Sacconi, C. A. Ghilardi, C. Mealli, F. Zanobini*, Inorg. Chem. *14*, 1380 (1975).
[3] Rhombohedral, space group R3; $a = 10.76$ Å, $\alpha = 108.6°$; $V = 1061$ Å^3; $Z = 1$; 296 symmetry independent reflections $[I \geq 2\sigma(I)]$, Philips PW 1100, $Mo_{K\alpha}$, graphite monochromator; solution: heavy atom method (programs X-ray 77); refinement: $R = 0.089$.

Stepwise Reaction of Phenylbis(trimethylsilyl)phosphane with Phosgene—Isolation of a (Phosphinomethylene)phosphane[1]

By *Rolf Appel* and *Volker Barth*[*]

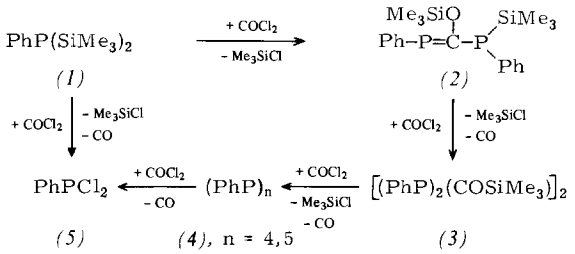
As a proven chlorinating agent in phosphorus chemistry, phosgene smoothly transforms triorganylphosphanes and triorganylphosphane oxides into the corresponding dichlorophosphoranes[2]. In contrast, its reaction with phenylbis(trimethylsilyl)phosphane *(1)* leads *via* elimination of chlorotrimethylsilane to the dichloro(phenyl)phosphane *(5)*, which

[*] Prof. Dr. L. Sacconi, Dr. P. Dapporto, Dr. S. Midollini
Istituto di Chimica Generale e Inorganica
dell'Università, Laboratorio CNR
Via J. Nardi, 39, I-50132 Firenze (Italy)

[*] Prof. Dr. R. Appel, Dipl.-Chem. V. Barth
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

fails to undergo further reaction with phosgene. Temporary appearance of a precipitate during this reaction prompted us to undertake a detailed study, especially since *Becher* and *Langer*[3] had already obtained carbonyl bis(diphenylphosphide) as an unstable product from phosgene and diphenyl(trimethylsilyl)phosphane at $-110\,^{\circ}C$.

We found that *(1)* reacts stepwise with $COCl_2$ *via* several isolable intermediates: at a molar ratio of 2:1 in pentane, these reactants first give a yellow oil shown by elemental analysis, molecular weight (cryoscopy and mass spectrometry), ^{31}P- and ^{13}C-NMR, to be phenyl[(phenyltrimethylsilylphosphino)trimethylsiloxymethylene]phosphane *(2)*. Evidence for migration of a silyl group to oxygen and for a methylenephosphane structure comes from the doublets at $\delta = +164$ and -37 in the ^{31}P-NMR spectrum and the double doublet at $\delta = 205$ in the ^{13}C-NMR spectrum[4].



Addition of $COCl_2$ to a pentane solution of *(2)* (1:2) leads to precipitation of a colorless solid substance of composition *(3)*. The signal of dicoordinate phosphorus is absent from the ^{31}P-NMR spectrum of *(3)*; a temperature-dependent AA'BB' spin system is observed which is interpretable in terms of various proposed structures. An X-ray structure determination is still in progress.

Further action of $COCl_2$ leads to dissolution of the fine precipitate of *(3)*, with simultaneous production of chlorotrimethylsilane and CO gas. The two new ^{31}P-NMR signals at $\delta = -5.9$ and -49.5 were previously observed on reaction of *(1)* with phosgene by *Baudler et al.*[5], and assigned to the cyclophosphanes *(4)*. The intermediates *(4)* are chlorinated by $COCl_2$ *via* CO elimination to give dichloro(phenyl)phosphane *(5)* as the stable final product.

Preliminary investigations show that phosgene analogues react similarly with *(1)* and that acyclic compounds having P=C bonds[4,6] are no longer mere *curiosa*.

Experimental

Phosgene (10.7 g, 108 mmol; slight excess) is condensed at 0 °C within 6 h into a stirred solution of *(1)*[7] (50.8 g, 200 mmol) in *p*-pentane (400 ml) in an evacuated vessel. After 12 h at room temperature, the solution is evaporated down to *ca.* 100 ml and stirred for another 12 h. Filtration and stripping off the solvent gives *(2)* almost quantitatively as a yellow oil which cannot be distilled without decomposition. The compound can be stored for several weeks at 0 °C in the absence of oxygen and moisture. $^{31}P\{^1H\}$-NMR (C_6D_6, 85% H_3PO_4 ext.): $\delta = +164.0$ [d, $^2J(P^aP^b) = 72.8$ Hz, P^a=C], -37.0 [d, $^2J(P^bP^a) = 72.8$ Hz, P^b—Si].—$^{13}C\{^1H\}$-NMR (CD_2Cl_2, TMS int.): $\delta = -1.0$ [dd, $^2J(P^bC) = 12.4$, $^4J(P^aC) = 6.3$ Hz, P^bSiC], $+0.3$ [dd, $^4J(P^bC) = 2.9$, $^4J(P^aC) = 0.3$ Hz, OSiC], $+205.3$ [dd, $J(P^aC) = 78.9$, $J(P^bC) = 37.7$ Hz, P^aC]; the complex spectrum of the phenyl groups was not evaluated.—$^{29}Si\{^1H\}$-NMR (CD_2Cl_2, TMS int.): $\delta = +3.7$ [dd, $J(P^bSi) = 21.0$, $^3J(P^aSi) = 12.2$ Hz, P^bSi], $+23.6$ [d, $^3J(P^bSi) = 5.0$ Hz, OSi].

Phosgene (4.95 g, 50 mmol) is condensed under similar conditions into a solution of *(2)* (39.0 g, 100 mmol) in *n*-pentane (400 ml). Since CO is liberated the reaction vessel must be equipped *via* a reflux condenser ($-60\,^{\circ}C$, cryostat cooling) with a Hg safety valve. The solution is concentrated to *ca.* 100 ml, whereupon *(3)* precipitates. Filtration over a sealed frit, washing with a small volume of *n*-pentane, and vacuum drying affords 15 g (47%) of spectroscopically pure product, m.p. 148—150 °C, which can be recrystallized from CH_2Cl_2/*n*-pentane or CH_2Cl_2/CH_3CN.—Alternatively, *(3)* can be prepared directly from *(1)* and $COCl_2$ in the molar ratio 4:3.

Received: February 12, 1979 [Z 215 IE]
German version: Angew. Chem. *91*, 497 (1979)

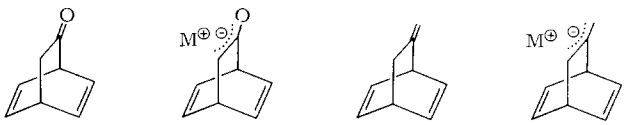
[1] Phosphorus-Carbon-Halogen Compounds, Part 17.—Part 16: *R. Appel, M. Huppertz*, Z. Anorg. Allg. Chem., in press.
[2] *R. Appel, B. Blaser, G. Siegemund*, Z. Anorg. Allg. Chem. *363*, 176 (1968); *R. Appel, W. Heinzelmann*, DBP 1192205 (1966), BASF AG.
[3] *H. J. Becher, E. Langer*, Angew. Chem. *85*, 910 (1973); Angew. Chem. Int. Ed. Engl. *12*, 842 (1973).
[4] a) *G. Becker*, Z. Anorg. Allg. Chem. *423*, 242 (1976); b) *T. C. Kleebach, R. Loureus, F. Bickelhaupt*, J. Am. Chem. Soc. *100*, 4886 (1978).
[5] Cf. *M. Baudler, B. Carlsohn, W. Böhm, G. Reuschenbach*, Z. Naturforsch. *B 31*, 558 (1976).
[6] *K. Issleib, H. Schmidt, H. Meyer*, J. Organomet. Chem. *160*, 47 (1978).
[7] *R. Appel, K. Geisler*, J. Organomet. Chem. *112*, 61 (1976).

Bicyclo[2.2.2]octa-5,7-diene-2-carboxylic Acid and 7-Methylenebicyclo[2.2.2]octa-2,5-diene[**]

By *Rudolf Gompper* and *Karl-Heinz Etzbach*[*]

Dedicated to Professor Hellmut Bredereck on the occasion of his 75th birthday

In the alkylation of the alkali-metal salts of bicyclo[2.2.2]octanone derivatives, *e.g.* those of barrelenone *(1)*, it can be calculated from the *O/C*-product ratio that an antiaromatic effect prevails, *e.g.* in the anion of *(2)*[1]. It can be expected that similar electronic circumstances are present in the anions of *(2)* and *(4)* (cf. [2]). 7-Methylenebicyclo[2.2.2]octadiene *(3)*, the potential starting material for *(4)*,



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

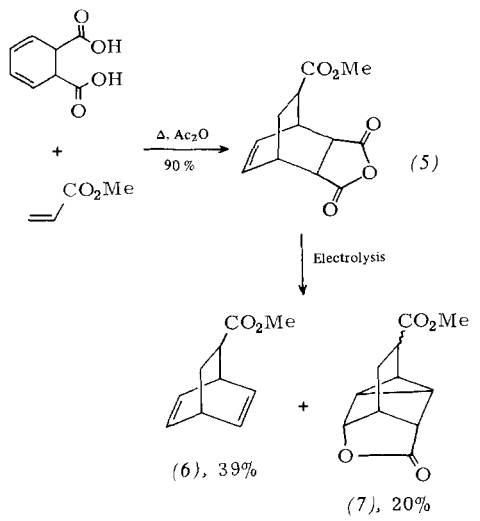
has been obtained in "very low yields" together with other products on irradiation of a solution of allene in benzene[3]. The methods developed for the synthesis of barrelenone *(1)*[1] should enable the synthesis of *(3)* on a preparative scale and, moreover, provide general access to 7-substituted bicyclo[2.2.2]octadienes.

Diels-Alder reaction of dihydrophthalic acid and methyl acrylate (cf. [4]) affords the anhydride *(5)*, subsequent electrolysis of which (10 mmol anhydride: 180 ml pyridine, 30 ml water, 5 ml triethylamine; cf. [1,5]) gives methyl bicyclo[2.2.2]octa-5,7-diene-2-carboxylate *(6)* and the tetracyclic

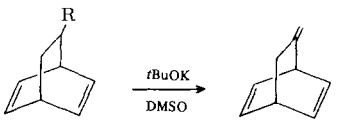
[*] Prof. Dr. R. Gompper, Dipl.-Chem. K.-H. Etzbach
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We are grateful to BASF for supplying the dihydrophthalic acid.

lactone *(7)* (consistent with the proposed structure[6]). *(6)* decomposes above 80 °C into benzene and acrylic ester.

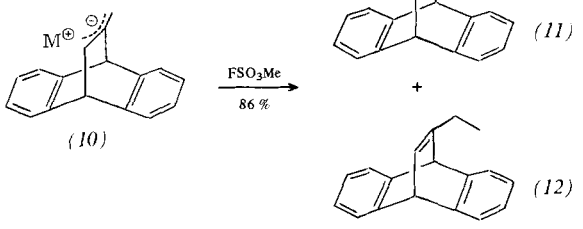


(6) can be reduced with lithium tetrahydroaluminate to the alcohol *(8)*, which without purification reacts with toluenesulfonyl chloride to give the tosylate *(9)* (chromatographic workup; silica gel, chloroform). On treatment with potassium *tert*-butoxide in dimethyl sulfoxide, *(9)* is converted into *(3)*, a colorless mobile liquid.



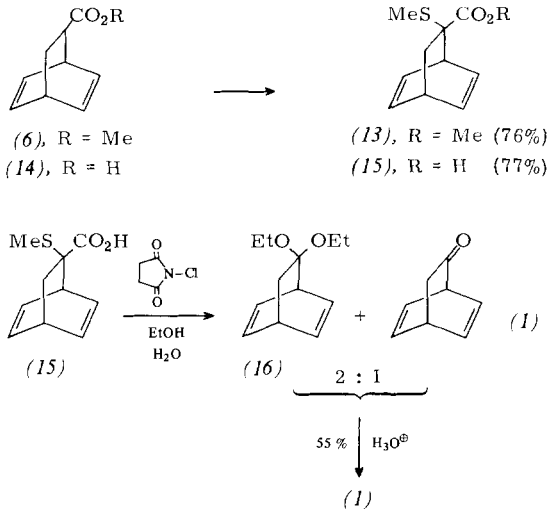
(6), R = CO_2Me
(8), R = CH_2OH(82%)
(9), R = CH_2OTos(75%)

(3) is difficult to deprotonate. It reacts with *n*-butyllithium/potassium *tert*-butoxide[7] to give, at least partially, *(4)*; further reaction with methyl fluorosulfonate affords a mixture of products which contains 7-methyl-8-methylenebicyclo[2.2.2]octadiene, together with *(3)* and an unidentified compound. More understandable is the behavior of the dibenzo derivative[8] of *(3)*. Here, reaction with *n*-butyllithium/potassium *tert*-butoxide in tetrahydrofuran (THF) at −78 °C furnishes quantitatively the deep-red salt *(10)*, which reacts



with methyl fluorosulfonate to give a 9:1 mixture of *(11)* and *(12)*. Alkylation of *(4)* and *(10)* proceeds similarly to that of *(2)* and related salts.

Sulfenylation[9] of *(6)* with (i) lithium diisopropylamide in THF/hexamethylphosphoric triamide (HMPT) at −78 °C and (ii) dimethyldisulfane affords the methylthio derivative *(13)* (chromatography on silica gel; ether). On attempted distillation (bath temperature up to 120 °C) *(13)* decomposes into benzene and α-methylthio(methyl acrylate). Since *(13)* is difficult to saponify it is advisable to obtain the carboxylic acid *(14)* [(i) 2 N NaOH, (ii) 2 N HCl, 81% yield] from *(6)* first for the preparation of *(15)*. *(14)* decomposes *via* retro Diels-Alder reaction within a few days, even at room temperature.



The dilithium salt of *(14)* can be smoothly sulfenylated to *(15)* [(i) 2 $LiN(iPr)_2$ in THF/HMPT at 0 °C; (ii) MeSSMe]. Oxidative decarboxylation[9] of *(15)* leads to a mixture of *(16)* and *(1)*. Acid hydrolysis finally yields barrelenone *(1)*. The physical data of a few compounds are given in Table 1.

Table 1. Physical data of compounds *(3)*, *(5)*, *(7)*, *(9)*, *(13)*, *(14)*.

(3): m.p. 50—60 °C/18 mbar (Kugelrohr)
(5): m.p. 121 °C (from chloroform-ligroin)
(6): colorless, sweet-smelling oil, b.p. 52 °C/10^{-2} mbar; IR (film): 1735, 1538 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.67 (mc, 2H), 2.55 (mc, 1H), 3.60 (s, 3H), 3.70 (mc, 1H), 4.00 (mc, 1H), 6.40 (mc, 4H)
(7): m.p. 74—85 °C (from ether); IR (KBr): 1780, 1735 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.43—3.13 (m, 8H), 3.73 (s, 3H), 4.80 (m, 1H)
(9): m.p. 46 °C (from hexane); IR (KBr): 1603 cm^{-1}
(13): m.p. 48 °C (from pentane); IR (KBr): 1720, 1625, 1590 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.37 (dd, J_1 = 13 Hz, J_2 = 2.5 Hz; 1H), 2.13 (s, 3H), 2.40 (dd, J_1 = 13 Hz, J_2 = 3 Hz; 1H), 3.73 (s, 3H), 3.73 (mc, 1H), 4.17 (mc, 1H), 6.43 (mc, 4H)
(14): m.p. 53 °C (from pentane); IR (KBr): 1702 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.70 (mc, 2H); 2.57 (mc, 1H), 3.67 (mc, 1H), 4.00 (mc, 1H), 6.43 (mc, 4H), 10.90 (mc, 1H)

Received: February 12, 1979 [Z 219 IE]
German version: Angew. Chem. *91*, 500 (1979)

[1] *R. Gompper, K.-H. Etzbach*, Angew. Chem. *90*, 630 (1978); Angew. Chem. Int. Ed. Engl. *17*, 603 (1978).
[2] *R. Gompper, H.-U. Wagner*, Angew. Chem. *88*, 389 (1976); Angew. Chem. Int. Ed. Engl. *15*, 321 (1976).
[3] *D. Bryce-Smith, B. E. Foulger, A. Gilbert*, J. Chem. Soc. Chem. Commun. *1972*, 664.
[4] Neth. Pat. Appl. 6409347 (1965), BASF; Chem. Abstr. *63*, P 11389d (1965).
[5] *P. Radlick, R. Klem, S. Spurlock, J. J. Sims, E. E. van Tamelen, T. Whitesides*, Tetrahedron Lett. *1968*, 5117.
[6] *L. H. Zaldow, D. R. Brannon*, J. Chem. Soc. Suppl. I *1964*, 5497.
[7] *J. Hartmann, M. Schlosser*, Helv. Chim. Acta *59*, 453 (1976).
[8] a) *P. F. Hudrlik, A. M. Hudrlik, Chung-Nan Wan*, J. Org. Chem. *40*, 1116 (1975); b) *S. J. Cristol, G. O. Mayo, ibid. 34*, 2363 (1969).
[9] *B. M. Trost*, Chem. Rev. *78*, 363 (1978).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0606-0471 $ 02.50/0*

Structure and Formation of Triorganylphosphoniocyclopropenylium Ions[**]

By *Robert Weiss, Claus Priesner,* and *Hilmar Wolf*[*]

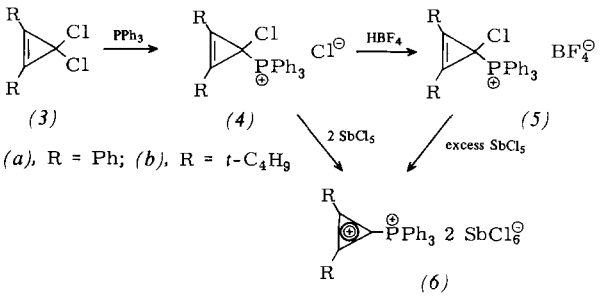
Hetero[3]radialenes *(1)*, in which X, Y, and/or Z are hetero atom functions, constitute a hitherto unexplored class of substances which could be of interest particularly in connection with ring fragmentation[1]. We have now synthesized systems of type *(2)* for the first time.



(1) *(2a)* *(2b)*

A triorganylphosphonio group served as acceptor A and the donor group Do was varied.

Reaction of the covalent dichlorides *(3)*[2] with triphenylphosphane gives quantitative yields of the cyclopropenylphosphonium salts *(4)* which can be precipitated as stable salts *(5)* from CH_2Cl_2 with ethereal HBF_4. The position of the double bond follows from spectroscopic data (Table 1). Compounds *(4)* and *(5)* are transformed by the strong Lewis acid $SbCl_5$ into the bis(hexachloroantimonates) *(6)*.

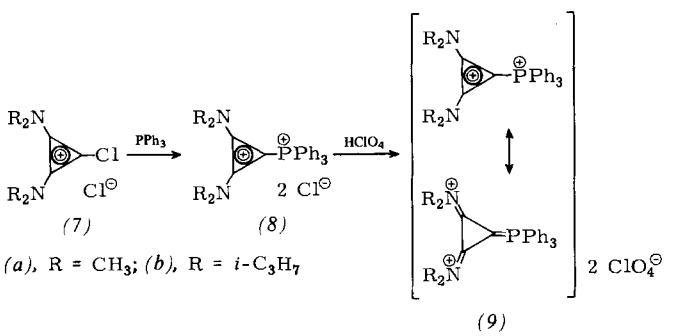


(3) *(4)* *(5)*

(a), R = Ph; *(b)*, R = t-C_4H_9

(6)

Under the same reaction conditions, the salt-like dichlorides *(7)*[3] react immediately with triphenylphosphane to give the bis(dialkylamino)triphenylphosphoniocyclopropenylium dichlorides *(8)* which can be isolated in high yield as stable bis(perchlorates) *(9)* after addition of $HClO_4$ (Table 1).



(7) *(8)*

(a), R = CH_3; *(b)*, R = i-C_3H_7

(9)

While alkyl- and aryltriphenylphosphonium salts show ^{31}P-NMR signals in the range $\delta = -20$ to -35[4], *(6b)* gave a signal at $\delta = -53.6$ and *(9a)* and *(9b)* signals at $\delta = -6.66$ and -8.44, respectively (CD_3CN; H_3PO_4 internal). The strong shielding of the phosphorus in the dications *(9)* relative to that in the system *(6b)* suggests extensive participation of the [3]radialene resonance structure in *(9)* according to the general form *(2b)*. This possibility of stabilization is reserved for systems having strong $+M$ substituents on the three-membered ring and occurs only to a limited extent, if at all, in the salts *(6)*.

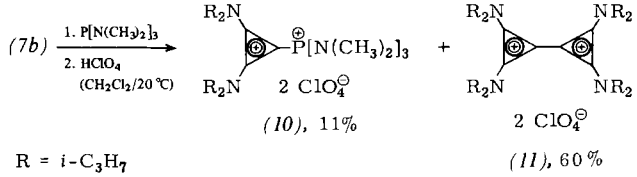
Table 1. Data of new compounds.

	M.p. [°C] [a]	IR (KBr) [cm^{-1}]	UV λ_{max} (log ε)	^{1}H-NMR τ values [b]
(5a)	163—165	1592 (m), 1485 (m), 1445 (s), 1328 (s)	310 (4.28)	2.3 (s, 10H), 2.62 (s, 15H)
(5b)	151—153	1834 (m), 1481 (m), 1438 (s), 1367 (m)	269 (3.83)	2.4 (mc, 15H), 8.88 (s, 18H)
(9a)	200	1915 (s), 1650 (vs), 1440 (m), 1410 (m), 1220 (w)	270 (4.51), 230 (4.62)	2.03 (mc, 15H), 6.48 (s, 6H), 7.17 (s, 6H)
(9b)	273	1865 (s), 1590 (vs), 1440 (m), 1380 (w), 1365 (w)	277 (4.62), 235 (4.65)	2.0 (mc, 15H), 5.59 (mc, 2H), 6.57 (mc, 2H), 8.43/8.53 (d, 12H; J=6 Hz), 9.10/9.20 (d, 12H; J=6 Hz)
(10)	290	1870 (s), 1580 (vs), 1470 (m), 1360 (m), 1300 (m)	266 (4.30), 210 (4.33)	5.77 (mc, 4H), 7.03/7.23 (d, 18H; J=12 Hz), 8.46/8.59 (d, 24H; J=7.8 Hz)

[a] All compounds decompose on melting.
[b] *(5a)*, *(5b)* in $CDCl_3$; *(9a)*, *(9b)*, *(10)* in CD_3CN.

The radialene character of *(9)* is also manifested in a high rotational barrier about the C—N bond. The ΔG^+ value of *(9a)* was found to be >24 kcal/mol[5], whereas that for bis(dialkylamino)cyclopropenylium systems without acceptor substituent lies between 17 and 20 kcal/mol[6]. The increase in positive charge of the nitrogen functions is manifested in a downfield shift of the alkyl signals by *ca.* 0.15 relative to reference systems without acceptor substituents such as *(7a)*[3].

The mode of formation of the dications *(6)* could be classified as an *addition/elimination reaction.* This would also provide a formal explanation of the formation of the dications *(9)*. However, the strong formation tendency of *(9)* is surprising in view of the high ground state stabilization of the cation *(7)* and the high-energy 1,2-bis(dialkylamino)cyclopropene intermediates postulated. In fact, the formation of the dications *(10)* and *(11)* strongly suggests that the systems *(9)* are actually produced by an *elimination/addition reaction* of a kind hitherto undescribed for the C_3^+ system.



(10), 11% *(11)*, 60%

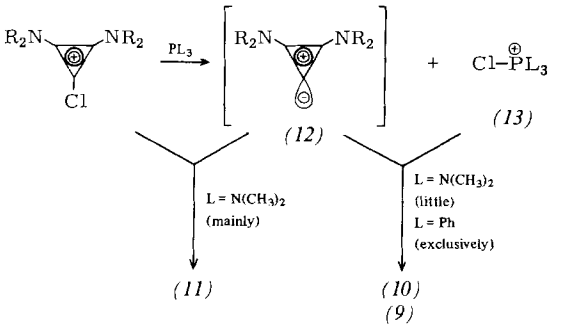
R = i-C_3H_7

Thus, reaction of *(7b)* with tris(dimethylamino)phosphane, which is more nucleophilic than PPh_3, under otherwise identical conditions no longer affords the dication *(10)*[5b] [corresponding to *(9b)*] as major product but instead the known triafulvalene dication *(11)*. These observations indicate the reaction course shown in Scheme 1.

[*] Doz. Dr. R. Weiss [+], Dr. C. Priesner, Dipl.-Chem. H. Wolf
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

[+] To whom correspondence should be addressed.

[**] Functional *cyclo*-C_3 Derivatives, Part 7. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 6: *R. Weiss, C. Priesner,* Angew. Chem. *90*, 491 (1978); Angew. Chem. Int. Ed. Engl. *17*, 457 (1978).



Scheme 1. R = i-C_3H_7.

A crucial step is the nucleophilic attack of PL_3 at the σ^* orbital or the C—Cl bond in *(7b)* with liberation of the nucleophilic carbene *(12)* and formation of the chlorophosphonium ion *(13)*. The electrophilic character of *(13)* which can be varied by way of L probably determines the further course of the reaction. The reaction observed with L = Ph is strongly reminiscent of that between CCl_4 and $P(Ph)_3$[8]. With L = $N(CH_3)_2$ this course only plays a minor role because of the greatly reduced electrophilic character of *(13)*, for *(7b)* can then successfully compete for *(12)* to give the triafulvalene dication in a coupling reaction of known kind[7b]. This reaction is also of preparative interest.

Received: February 8, 1979 [Z 224a IE]
German version: Angew. Chem. *91*, 505 (1979)

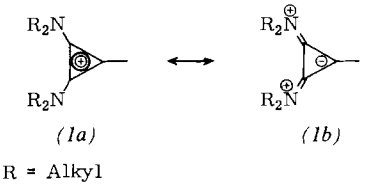
CAS Registry numbers:
(3a), 2570-00-5; *(3b)*, 66633-01-0; *(4a)*, 70287-90-0; *(4b)*, 70287-91-1; *(5a)*, 70287-93-3; *(5b)*, 70287-95-5; *(6a)*, 70304-34-6; *(6b)*, 70304-32-4; *(7a)*, 70287-96-6; *(7b)*, 66466-64-6; *(8a)*, 70287-97-7; *(8b)*, 70287-98-8; *(9a)*, 70288-00-5; *(9b)*, 70288-02-7; *(10)*, 70304-30-2; *(11)*, 61695-57-6; triphenylphosphane, 603-35-0; tris(dimethylamino)phosphane, 1608-26-0

[1] *R. West, D. C. Zecher, S. K. Koster, D. Eggerding*, J. Org. Chem. *40*, 2295 (1975).
[2] *(3b)* was obtained by analogy with *(3a)* from the pertinent cyclopropenone and $SOCl_2$ [3a].
[3] a) *C. Priesner*, Dissertation, Universität München 1978; b) *M. Hertel*, Diplomarbeit, Universität Erlangen-Nürnberg 1978.
[4] *G. M. Kosolapoff, L. Maier:* Organic Phosphorus Compounds. Wiley-Interscience, New York 1972, Vol. 27, pp. 217 ff.
[5] a) Exact determination of the rotation barrier was not possible since the coalescence temperature for the methyl signals could not be reached ($T_c > 150$ °C); b) *H. Wolf*, Diplomarbeit, Universität Erlangen-Nürnberg 1978.
[6] The rotation barrier for bis(diisopropylamino)cyclopropenylium perchlorate is 17.8 kcal/mol (*Z. Yoshida, H. Konishi, Y. Kamitori, H. Ogoshi*, Chem. Lett. *1977*, 1341) and that for bis(dimethylamino)cyclopropenylium perchlorate 20.2 kcal/mol (*R. Weiss, H. Wolf*, unpublished).
[7] a) *Z. Yoshida, H. Konishi, S. Sawada, H. Ogoshi*, J. Chem. Soc. Chem. Commun. *1977*, 850; b) *R. Weiss, C. Priesner, H. Wolf*, Angew. Chem. *90*, 486 (1978); Angew. Chem. Int. Ed. Engl. *17*, 446 (1978); c) *R. Gompper, E. Bartmann, ibid. 90*, 490 (1978) and *17*, 456 (1978).
[8] *R. Appel*, Angew. Chem. *87*, 863 (1975); Angew. Chem. Int. Ed. Engl. *14*, 801 (1975).

Synthesis of a Donor-Substituted Tris(cyclopropenylio)cyclopropenylium Salt[**]

By *Robert Weiss, Marion Hertel,* and *Hilmar Wolf*[*]

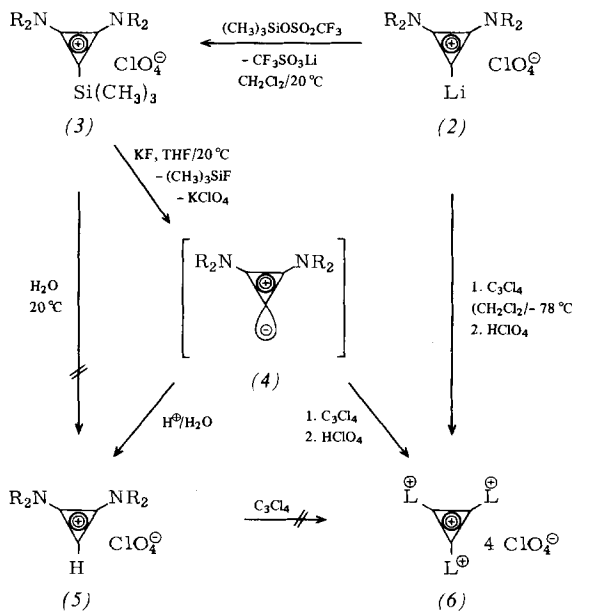
As a result of cyanine resonance, the bis(dialkylamino)cyclopropenylium group *(1)* can assume the character of a $+M$ substituent[1]. We have now exploited this property of *(1)* in order to synthesize novel polycationic cyclopropenylium systems.



Reactions of trichlorocyclopropenylium salts with arenes to form triaryl-substituted cyclopropenylium salts have been known for some time[2]. We wish to report a novel variant of this structural type in which the aromatic donor ligands are themselves cyclopropenylium systems of type *(1)*. For this purpose the carbenoid *(2)*[3a], which has meanwhile become readily accessible, was treated with trimethylsilyl trifluoromethylsulfonate (Scheme 1), giving an 82% yield of the first silyl-substituted cyclopropenylium system *(3)* as thermally stable salt showing considerable resistance to water [m.p. 131 °C; IR (KBr): 1845 (m), 1587 (m), 1535 (s), 1453 (w), 1373/1348 (m) cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\tau = 5.95$ (mc, 4H), 8.64/8.74 (d, 24H; $J = 6$ Hz), 9.58 (s, 9H)].

Compound *(3)* is a potential precursor of the nucleophilic cyclopropenylidene *(4)* (cf. ref. [1]) which has so far defied attempts at generation in the free state[3a]. The method of choice is F^--induced desilylation which has already proved of value in the case of the trimethylsilyltropylium system[4]. *(3)* is rapidly and quantitatively desilylated to *(5)* at room temperature in water on addition of one equivalent of F^-[5].

These results suggest the occurrence of the free nucleophilic carbene *(4)* (Scheme 1). Only one of the possible trapping reactions will be mentioned. While *(3)* fails to react with tetrachlorocyclopropene (C_3Cl_4) in tetrahydrofuran, in the presence of F^- ion under otherwise identical conditions the highly symmetrical stable tetracationic salt (6) is formed in *ca.* 40% yield within 24 h. This system can also be obtained in *ca.* 80% yield directly from *(2)* and C_3Cl_4 in CH_2Cl_2; however, the product thus obtained is contaminated by highly persistent dark-colored by-products.

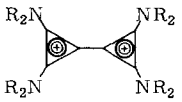


Scheme 1. R = i-C_3H_7, $L^{\oplus} = [(i\text{-}C_3H_7)_2N]_2C^{\oplus}_3$.

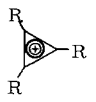
[*] Doz. Dr. R. Weiss [+], Dipl.-Chem. M. Hertel, Dipl.-Chem. H. Wolf
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)
[+] To whom correspondence should be addressed.

[**] Functional *cyclo*-C_3 Derivatives, Part 8.—This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 7: ref. [1].

Evidence supporting the structure of *(6)* as tris[bis(diisopropylamino)cyclopropenylio]cyclopropenylium tetraperchlorate comes not only from its mode of formation and its correct elemental analysis but also from the sum of the spectroscopic data. The IR spectrum shows the expected characteristic ring vibrations of the peripheral cyclopropenylium systems at 1885 (A′) and 1580 cm^{-1} (E′); the IR-active E′ vibration of the central ring cannot be assigned to any particular band owing to superposition. Important structural information comes from the UV spectrum. Simple bis(dialkylamino)cyclopropenylium systems exhibit a longest wavelength UV absorption around 225 nm ($\log\varepsilon = 4.07$—4.32)[6,7] and triafulvalene dications *(7)* show one around 250 nm ($\log\varepsilon = 4.2$)[7,8]; the longest wavelength band at 347 nm ($\log\varepsilon = 4.52$) in the system *(6)* establishes the presence of a considerably more extended π-system. The 1:1 splitting of the signals of the isopropyl protons in the ^{1}H-NMR spectrum indicates hindrance to rotation of all peripheral dialkylamino groups [^{1}H-NMR: $\delta = 5.82$ (mc, 12H), 8.42/8.52 (d, 36 H; $J = 6$ Hz), 8.47/8.57 (d, 36 H; $J = 6$ Hz)] (cf. [3b]). This rotational hindrance of the donor groups is even clearer from the ^{13}C-NMR spectrum, in which two singlets each in the ratio 1:1 are observed for the quaternary ($\delta = -58.8$ and -56.1) and for the primary C atoms ($\delta = -21.4$ and -20.0) of the alkyl groups. Moreover, three signals in the ratio 2:1:1 are recorded for quaternary C atoms ($\delta = -138.5$, -88.9, and -120.3) which are to be assigned to the three ring positions a, b, c (see Scheme 2, resonance structure C). Assignments for positions a and b are based on comparison with a series of bis(dialkylamino)-substituted cyclopropenylium compounds[7]. The chemical shift of the ^{13}C-NMR signals for the ring C atoms of cyclopropenylium compounds[9] appears to

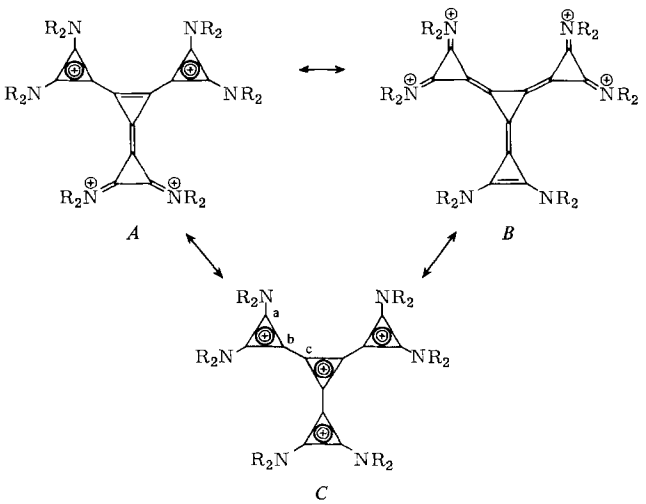


(7), R = Alkyl



(8a), R = H
(8b), R = C_6H_5
(8c), R = $N(CH_3)_2$

be highly charge dependent. Comparison of the value of $\delta = -120$ found for the central ring position c with the corresponding values of the symmetrically substituted cations *(8a)*—*(8c)* ($\delta = -175$, -154, and -117.9, respectively) leads to the conclusion that *(1)* has a donor strength comparable with that of a dialkylamino group.



Scheme 2. Resonance structures for the cation of *(6)*. R = *i*-C_3H_7.

(6) contains the first isolated tetracarbenium ion; it is essentially stabilized by the peripheral dialkylamino groups after the manner of the resonance structures A, B, and C (Scheme 2). Radialenoid, fulvenoid, and aromatic resonance structures can be formulated for each of the four rings.

In view of the pronounced stability of this compound we consider the synthesis of even more highly charged and extended polycationic polyaryls not to be impossible.

Received: February 8, 1979 [Z 224b IE]
German version: Angew. Chem. *91*, 506 (1979)

CAS Registry numbers:
(2), 66466-67-9; *(3)*, 70288-04-09; *(5)*, 57358-59-5; *(6)*, 70288-06-1; *(8a)*, 26810-74-2; *(8b)*, 12190-17-9; *(8c)*, 41893-25-8; trimethylsily trifluoromethylsulfonate, 27601-11-8

[1] *R. Weiss, C. Priesner, H. Wolf*, Angew. Chem. *91*, 505 (1979); Angew. Chem. Int. Ed. Engl. *18*, 472 (1979).
[2] *R. West, D. C. Zecher, W. Goyert*, J. Am. Chem. Soc. *92*, 149 (1970); *R. Weiss, H. Kölbl, C. Schlierf*, J. Org. Chem. *41*, 2258 (1976).
[3] a) *R. Weiss, C. Priesner, H. Wolf*, Angew. Chem. *90*, 486 (1978); Angew. Chem. Int. Ed. Engl. *17*, 446 (1978); b) *R. Weiss, C. Priesner, ibid. 90*, 484 (1978) bzw. *17*, 445 (1978).
[4] *M. Reiffen, R. W. Hoffmann*, Tetrahedron Lett. *1978*, 1107.
[5] *M. Hertel*, Diplomarbeit, Universität Erlangen-Nürnberg 1978.
[6] *Z. Yoshida*, Top. Curr. Chem. *40*, 60 (1973).
[7] *H. Wolf*, Diplomarbeit, Universität Erlangen-Nürnberg 1978.
[8] *Z. Yoshida, H. Konishi, S. Sawada, H. Ogoshi*, J. Chem. Soc. Chem. Commun. *1977*, 850.
[9] *E. V. Dehmlow, R. Zeisberg, S. S. Dehmlow*, Org. Magn. Reson. *7*, 418 (1975).

New Synthesis of Amino Acids from Halogenated Carboxylic Esters[**]

By *Franz Effenberger* and *Karlheinz Drauz*[*]

Dedicated to Professor Hellmut Bredereck on the occasion of his 75th birthday

Synthetic natural and unnatural α-amino acids are gaining increasing importance in medicine and in the fortification of foods and animal feeds[1].

Direct amination of α-halo carboxylic acids with aqueous ammonia in many cases leads to secondary and tertiary amino compounds. This multiple alkylation can be largely suppressed by addition of ammonium salts or by working in liquid ammonia[2]; separation of the various salts, though, from the amino acids also present as salt mixtures, often causes considerable experimental difficulties.—Contrary to earlier reports[3], reaction of 2,6-dihalocapronic acids with ammonia, even in the presence of ammonium salts and urotropin, yields mainly 2-piperidinecarboxylic acid, and no lysine.

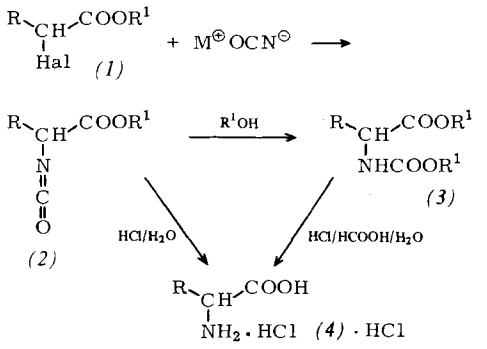
We have now found that halogenated carboxylic esters *(1)* give high yields of amino acids *(4)* on treatment with alkali cyanates in the presence of alcohols (Table 1). As in the Gabriel synthesis, the amino function is introduced in a protected form [isocyanato or alkoxycarbonylamino group in *(2)* and *(3)*, respectively], yet in a simpler and less expensive way, and the protecting group can be cleaved off under milder conditions. Scattered reports of the reaction between alkali cyanates and alkyl halides in the presence of alcohols, giving urethanes, have already been published[4]. Nothing was known, though, about reactions with derivatives of halo-

[*] Prof. Dr. F. Effenberger, Dr. K. Drauz
Institut für Organische Chemie der Universität
Pfaffenwaldring 55, D-7000 Stuttgart 80 (Germany)

[**] This work was supported by the Federal Ministry of Research and Technology and by DEGUSSA (BCT 312). We are grateful to *S. Förster* and *W. Müller* for experimental assistance.

genated carboxylic acids, or about the scope of this method for the preparation of primary amines.

The isocyanato esters *(2)* formed initially from the monohalo compounds *(1)* can be isolated and hydrolyzed to the amino acids; the cyanate-catalyzed oligomerization which is the predominant reaction of 2,6-diisocyanatohexanoic esters under standard conditions can be largely suppressed by addition of alcohol. The urethanes *(3)* can be readily isolated and purified, and are hydrolyzed almost quantitatively to analytically pure amino acid hydrochlorides, *(4)* · HCl (Table 1).



$R^1 = CH_3, C_2H_5$; Hal = Cl, Br; M = K, Na, Li

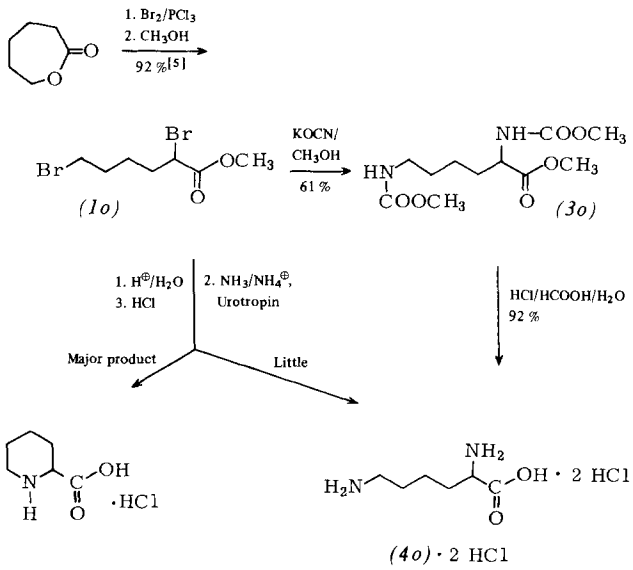
Table 1. Amino acids *(4)* from halo carboxylic esters *(1)*, X = halogen, *via* urethanes *(3)*, X = $NHCOOCH_3$ (see experimental section).

	Molecular skeleton A = $COOCH_3$	*(1)* X	*(3)* Yield [%]	*(4)*	*(4)* · HCl Yield [%]
a	XCH_2 A	Br	64	Glycine	98
b	CH_3 CHX A	Br	59	Alanine	92
c	$C_6H_5CH_2$ CHX A	Br	2.4	Phenylalanine	97
d	C_2H_5 CHX A [a]	Br	55	2-Amino-butyric acid	92
e	X $(CH_2)_3$ A	Br	67	4-Amino-butyric acid	97
f	$(CH_3)_2CH$ CHX A	Br	21	Valine	99
g	X $(CH_2)_4$ A	Br	65	5-Aminovaleric acid	96
h	n-C_4H_9 CHX A	Br	76	Norleucine	97
i		Cl	67		
j	[a]	Br	63	Norleucine	94
k	i-C_4H_9 CHX A	Br	66	Leucine	91
l	X $(CH_2)_5$ A	Cl	70	6-Amino-hexanoic acid	94
m	Cl $(CH_2)_4$ CHX A	Br	61	2-Amino-6-chloro-hexanoic acid	90
n	X $(CH_2)_2$ CHX A	Br	47	2,4-Diamino-butyric acid	98 [b]
o	X $(CH_2)_4$ CHX A	Br	61	Lysine	92 [b]

[a] $COOC_2H_5$ in place of $COOCH_3$ in *(1)* and *(3)*; $NHCOOC_2H_5$ in place of $NHCOOCH_3$ in *(3)*. [b] *(4)* · 2HCl.

The predominant formation of isocyanates *(2)* as well as the influence of the solvent and of the nature of the cation all suggest a S_N2 mechanism for this reaction. This assumption also rationalizes the observation that additional alkyl groups at the substitution center or increasing steric hindrance at the adjacent carbon atom reduce or even preclude substitution in favor of elimination, as in the case of methyl α-bromoisobutyrate. Preferred elimination thus disqualifies the method for the amination of β-halo- and β-phenyl-α-halo carboxylic esters [see, *e.g.*, *(1c)*].

Synthesis of DL-lysine from ε-caprolactone in an overall yield of 52% is an important application of the new amination procedure.



Experimental

Halo carboxylic ester *(1)* (10 mmol) in anhydrous dimethylformamide (DMF) is heated to 100 °C with stirring with finely ground and dried potassium cyanate and alcohol R^1OH (15 mmol and 35 mmol, respectively, per halogen atom to be replaced; 40—60 min for bromine compounds, 30 h for chlorine compounds). After filtration and removal of DMF by distillation, acetone (30 ml) is added to quantitatively separate the salts. The monourethanes are fractionated in a high vacuum, and the diurethanes are purified by liquid chromatography[6]. The pure urethanes *(3)* are hydrolyzed by refluxing with a mixture of equal parts of conc. hydrochloric acid, 100% formic acid, and water for 20 h at 125 °C. After removal of the mixture of acids, the residue is washed several times with acetone, and the crystalline amino acid hydrochlorides are filtered off and dried in a high vacuum.

Received: February 22, 1979 [Z 225 IE]
German version: Angew. Chem. 91, 504 (1979)

CAS Registry numbers:
(1a), 96-32-2; *(1b)*, 57885-43-5; *(1c)*, 70288-60-7; *(1d)*, 66025-42-1; *(1e)*, 4897-84-1; *(1f)*, 70332-52-4; *(1g)*, 5454-83-1; *(1h)*, 70288-61-8; *(1i)*, 70288-62-9; *(1j)*, 63927-44-6; *(1k)*, 70288-63-0; *(1l)*, 14273-89-3; *(1m)*, 70288-64-1; *(1n)*, 70288-65-2; *(1o)*, 70288-66-3; *(2a)*, 30988-17-1; *(2b)*, 30293-83-5; *(2c)*, 30293-84-6; *(2d)*, 70288-67-4; *(2e)*, 27678-30-4; *(2f)*, 30293-87-9; *(2g)*, 70288-68-5; *(2h)*, 70288-69-6; *(2j)*, 70288-70-9; *(2k)*, 30293-88-0; *(2l)*, 29640-13-9; *(2m)*, 70288-71-0; *(2n)*, 70288-72-1; *(2o)*, 70332-53-5; *(3a)*, 70288-73-2; *(3b)*, 70288-74-3; *(3c)*, 70288-75-4; *(3d)*, 70288-76-5; *(3e)*, 70288-77-6; *(3f)*, 70304-35-7; *(3g)*, 70320-18-2; *(3h)*, 70288-78-7; *(3g)*, 70288-79-8; *(3k)*, 70304-20-0; *(3l)*, 70288-80-1; *(3m)*, 70288-81-2; *(3n)*, 70288-82-3; *(3o)*, 70288-83-4; *(4a)*, 6000-43-7; *(4b)*, 25616-13-1; *(4c)*, 27172-85-6; *(4d)*, 40522-79-0; *(4e)*, 5959-35-3; *(4f)*, 25616-14-2; *(4g)*, 627-95-2; *(4h)*, 70288-84-5; *(4k)*, 2508-63-6; *(4l)*, 4321-58-8; *(4m)*, 70288-85-6; *(4n)*, 65427-54-5; *(4o)*, 617-68-5;

[1] See, *e.g.*, *Y. Izumi, J. Chibata, T. Itoh*, Angew. Chem. *90*, 187 (1978); Angew. Chem. Int. Ed. Engl. *17*, 176 (1978).
[2] *N. D. Cheronis, K. H. Spitzmueller*, J. Org. Chem. *6*, 349 (1941); H. H. Sisler, N. D. Cheronis, *ibid.* *6*, 467 (1941).
[3] *D. C. Sayles, E. F. Degering*, J. Am. Chem. Soc. *71*, 3161 (1949); *K. H. König, H. Pommer*, DAS 1296642 (1969), BASF.
[4] *D. W. Kaiser*, US-Pat. 2647916 (1953) and 2697720 (1954), American Cyan-

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0606-0475 $ 02.50/0*

mid; Chem. Abstr. *48*, 1433g (1954) and *49*, 8331i (1955); *P. A. Argabright, H. D. Rider, R. Sieck*, Org. Chem. *30*, 3317 (1965); *W. Gerhardt*, Tenside *2*, 101 (1965).
[5] *F. Effenberger, G. Clar, H. Haschke, W. Leuchtenberger, G. Schreyer, W. Schwarze*, DOS 2440212 (1976), DEGUSSA.
[6] *B. Glatz, G. Helmchen*, to be published.

The Sequences of the Membrane-Modifying Peptide Antibiotic Trichotoxin A-40

By *Hans Brückner, Wilfried A. König, Michael Greiner*, and *Günther Jung*[*]

The amphiphilic polypeptide antibiotics alamethicin[1], suzukacillin[2], and trichotoxin[3] can produce fluctuating, voltage-dependent ionic current with action potentials in lipid membranes and are therefore of interest as a model system for nerve conduction. The pores formed by aggregation of these peptides can adopt different conductance values and are especially suited for studying the mechanisms of transport phenomena.

Sequencing experiments on alamethicin[4] and suzukacillin[5] were made especially difficult by their high α-aminoisobutyric acid (Aib) content, acetylation of their N-terminals, and the presence of amino alcohols at their C-terminals.

We obtained very pure trichotoxin by extraction of the lyophilized fungal mycelium of *Trichoderma viride* NRRL 5242 with dichloromethane, chromatography on Sephadex LH-20 with methanol and separation of trichotoxin A-40[6] from A-50 by multiplicative countercurrent distribution in 2-butanol/0.015 M ammonium acetate (pH = 8.9) (see Fig. 1)[7]. We found that trichotoxin A-40 and A-50 contained the additional components isovaline (Ival) and valinol which have not previously been described. The L-configuration of the amino acids and the amino alcohols was established by chiral phase gas chromatography and separation *via* diastereomeric derivatives[8] (Ival as a (−)-enantiomer, *i.e.* D-Ival[9]).

Earlier sequencing of alamethicin, together with our own observations on suzukacillin, indicated that the peptide bond linked to the carboxy group of the α-aminoisobutyric acid was remarkably labile towards aqueous hydrochloric acid. In systematic experiments, anhydrous trifluoroacetic acid proved to be a mild, selective cleaving reagent at room temperature. The Aib-Pro bond in antiamoebin and alamethicin was also split by trifluoroacetic acid[4c].

We were able to preferentially split trichotoxin A-40 with trifluoroacetic acid in only 3 h at 37 °C into a *N*-acylated dodecapeptide (peptides I, II, III with exchange of Gly/Ala and Ala/Aib) and a C-terminal hexapeptide which began with proline and contained the amino alcohol valinol (peptides IV, V with exchange of Aib/Ival) (Fig. 1). Further acidolysis of the dodecapeptide gave Ac-Aib-OH and an undecapeptide with a free amino group. After 19 h treatment with trifluoroacetic acid, the tripeptide Ala-Aib-Aib was released from the C-terminal of the undecapeptide. This acidolysis could be reproduced with model peptides. For example, cleavage of Ac-Aib-Pro-NH_2 was approximately 50% after 15 min, that of Ac-Aib-Gly-OH and Ac-Aib-Ala-OH was

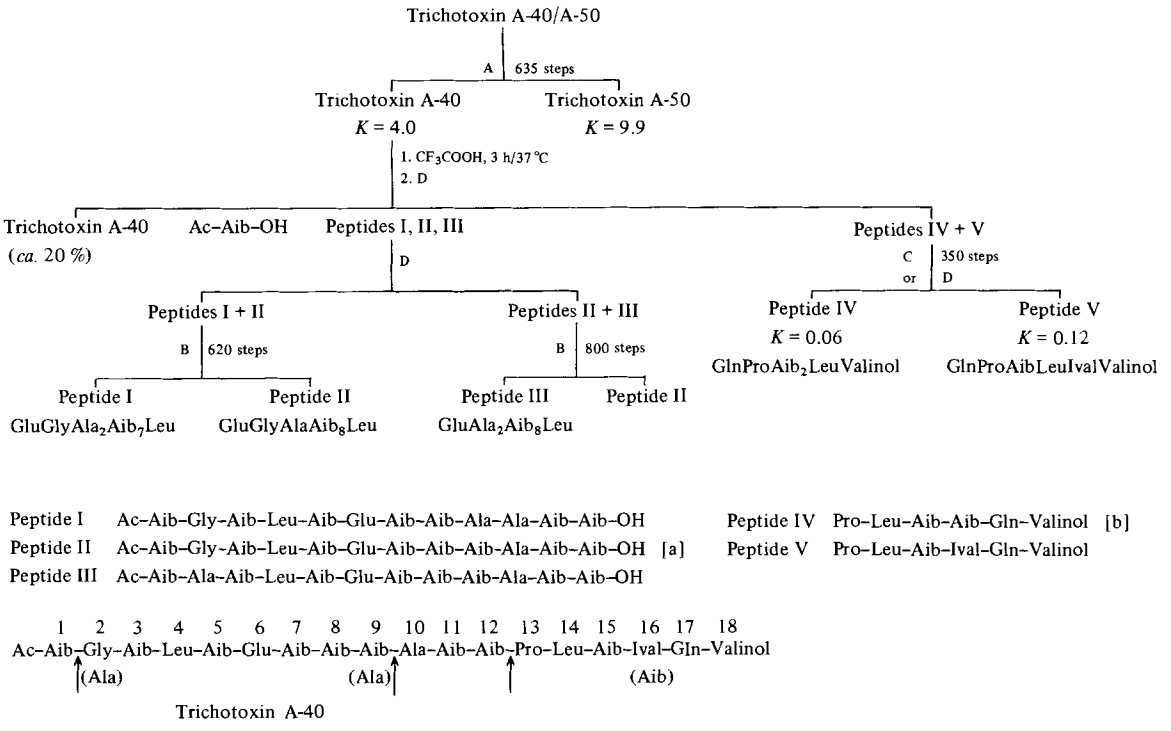


Fig. 1. Cleavage and sequencing of trichotoxin A-40. A, B, C: multiplicative countercurrent distribution. A: in 2-butanol/0.015 M ammonium acetate (pH = 8.9) 1:1 (v/v); B: in 2-butanol/ethyl acetate/methanol/0.3% ammonium acetate 3:5:2:3; C: in *n*-butanol/ethyl acetate/ammonium acetate (pH = 4.6) 2:4.5:5; *K* = distribution coefficient. D: silica gel column chromatography in chloroform/methanol/water/glacial acetic acid 65:25:4:3. [a] Sequence after cleavage of Ac-Aib-OH with trifluoroacetic acid confirmed by solid phase Edman degradation (*E. Wachter et al.*); [b] Sequence after selective cleavage of valinol with dioxane/6 N HCl (43 h/37 °C), confirmed by solid phase Edman degradation. Order of cleavage (arrows): 12—13 > 1—2 > 9—10.

[*] Prof. Dr. G. Jung [+], Dipl.-Chem. H. Brückner
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)
Prof. Dr. W. A. König, Dipl.-Chem. M. Greiner
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz, D-2000 Hamburg 13 (Germany)
[+] Author to whom correspondence should be addressed.

approximately 50% after 3 h; in contrast, Ac-Ala-Aib-OMe was only slightly attacked even after 6 h.

The trichotoxin A-40 utilized appeared to be completely homogeneous in ten TLC systems; it also showed a largely integral amino acid ratio. According to the behavior of its cleavage products on thin layer chromatography, there were, however, a total of three *N*-acetylated dodecapeptides (I, II, III) with analogous sequences and two hexapeptides (IV and V) both beginning with proline. These five peptides were separated by silica gel column chromatography and by multiplicative countercurrent distribution.

The sequences of the peptides (Fig. 1) were determined by GLC/MS analyses of the trifluoroacetylated and esterified partial hydrolyzates. The molecular weight of the hexapeptides was obtained by field desorption mass spectrometry. The α-linkage of the valinol was demonstrated by comparison of the mass spectroscopy fragmentation patterns with those of synthetic L-Gln-valinol and L-Glu(valinol)NH_2. In these experiments we observed an unusual quantitative α/γ transpeptidation.

The methods used provided sufficient quantities of defined partial sequences for ^{13}C-NMR investigations and activity studies. According to CD measurements, the helical part of trichotoxin is located, similarly to alamethicin[10], in the N-terminal dodecapeptide. The purification, cleavage, and sequencing methods can be applied to all peptide antibiotics (alamethicins, suzukacillins, *etc.*) which contain Aib.

Received: March 12, 1979 [Z 226 IE]
German version: Angew. Chem. *91*, 508 (1979)

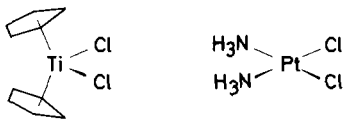
CAS Registry numbers:
Peptide I, 70320-19-3; peptide II, 70320-20-6; peptide III, 70320-21-7; peptide IV, 70320-22-8; peptide V, 70320-23-9; trichotoxin A-40, 65216-21-9

[1] *A. I. Mueller, D. O. Rudin*, Nature *217*, 713 (1968).
[2] *G. Boheim, K. Janko, D. Leibfritz, T. Ooka, W. A. König, G. Jung*, Biochim. Biophys. Acta *433*, 182 (1976).
[3] *G. Boheim, G. Irmscher, G. Jung*, Biochim. Biophys. Acta *507*, 485 (1978), and references cited therein.
[4] a) *J. W. Payne, R. Jakes, B. S. Hartley*, Biochem. J. *117*, 757 (1970); b) *Yu. A. Ovchinnikov, A. A. Kiryushkin, I. V. Kozhevnikova*, Zh. Obshch. Khim. *41*, 2085 (1971); c) *R. C. Pandey, J. C. Cook, K. L. Rinehart*, J. Am. Chem. Soc. *99*, 8469 (1977); d) *D. R. Martin, R. J. P. Williams*, Biochem. J. *153*, 181 (1976).
[5] *G. Jung, W. A. König, D. Leibfritz, T. Ooka, K. Janko, G. Boheim*, Biochim. Biophys. Acta *433*, 164 (1975).
[6] *G. Irmscher, G. Bovermann, G. Boheim, G. Jung*, Biochim. Biophys. Acta *507*, 470 (1978).
[7] *G. Jung, H. Brückner, B. Oertel*, Abstr. Symp. on Chemistry of Peptides and Proteins, Grainau 1978, p. 165.
[8] a) *K. Kruse, W. Francke, W. A. König*, J. Chromatogr. *170*, 423 (1979); b) *W. A. König, W. Rahn, J. Eyem, ibid. 133*, 141 (1977).
[9] *S. Yamada, K. Achiwa*, Chem. Pharm. Bull. *12*, 1525 (1964).
[10] *G. Jung, N. Dubischar, D. Leibfritz*, Eur. J. Biochem. *54*, 395 (1975).

Titanocene Dichloride—The First Metallocene with Cancerostatic Activity[**]

By *Hartmut Köpf* and *Petra Köpf-Maier*[*]

Dichlorobis(η^5-cyclopentadienyl)titanium(IV) (titanocene dichloride) *(1)* was first reported some 25 years ago[1], yet its cytostatic activity has remained uninvestigated. We expected *(1)* to possibly show such an activity, since it contains a *cis*-dichlorometal moiety in the neutral complex, like the well-known antitumor agent[2] *cis*-diamminedichloroplatinum(II) *(2)*. Further chemical analogies between *(1)* and *(2)* include,



(1) *(2)*

for example, the ability to undergo hydrolytic dimerization *via* oxo-[3] or hydroxo-bridges[4] and the selective reaction with aqueous ammonium polysulfide leading to the pentasulfide chelates $(C_5H_5)_2TiS_5$[5] and $(NH_4)_2[Pt(S_5)_3]$[6], respectively.

To test the antitumor activity of *(1)* we have so far carried out a series of five trial experiments on female CF_1 mice. About 6×10^6 Ehrlich ascites tumor cells[7] were implanted in each mouse by intraperitoneal injection. 24 hours after transplantation (a.t.) the mice were treated (likewise intraperitoneally) with varying amounts of *(1)* or *(2)* in 0.4 ml solution (dimethyl sulfoxide and saline 1:9 (v/v)).

In one representative experiment 84 mice were collected into groups of six animals and treated with *(1)* in doses varying between 10 and 140 mg/kg. Figure 1 shows the number of deaths caused by tumors and by toxicity as well as the proportion of surviving, apparently cured animals, up to day 30 a.t. Twelve animals served as untreated controls (0.4 ml DMSO-NaCl solution; exitus resulting from tumor growth on average 14.25 days a.t.). A further six animals were used as positive controls (10 mg/kg *(2)*; no macroscopically recognizable tumor development up to day 30 a.t.).

In other series of tests, mice treated with *(1)* have survived for ten weeks without any sign of tumor development.

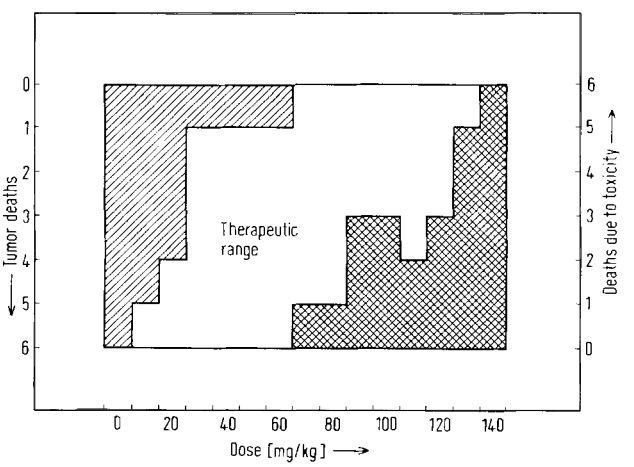


Fig. 1. Survival of mice 30 days after tumor transplantation and 29 days after treatment with *(1)* at the doses given on the abscissa. ▨ Tumor deaths without signs of substance toxicity. ▩ Deaths caused by toxicity (deaths within 8 days a.t. without macroscopically visible tumor development). □ Animals surviving on the 30th day a.t. (therapeutic range).

According to these results *(1)* is an effective antitumor agent with a cure rate in the therapeutic range of over 80%. *(1)* is the first titanium complex and the first metallocene derivative exhibiting cytostatic properties—presumably without the heavy-metal toxicity observed in the case of *(2)*.

Received: February 14, 1979 [Z 227 IE]
German version: Angew. Chem. *91*, 509 (1979)

CAS Registry numbers:
(1), 1271-19-8; *(2)*, 15663-27-1

[*] Prof. Dr. H. Köpf
Institut für Anorganische und Analytische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Dr. P. Köpf-Maier
Anatomisches Institut der Freien Universität
Königin-Luise-Strasse 15, D-1000 Berlin 33 (Germany)

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

[1] *G. Wilkinson, J. M. Birmingham*, J. Am. Chem. Soc. *76*, 4281 (1954).
[2] *B. Rosenberg, L. VanCamp, T. Krigas*, Nature *205*, 698 (1965); review: *F. K. V. Leh, W. Wolf*, J. Pharm. Sci. *65*, 315 (1976).
[3] *U. Thewalt, G. Schleussner*, Angew. Chem. *90*, 559 (1978); Angew. Chem. Int. Ed. Engl. *17*, 531 (1978).
[4] *R. Faggiani, B. Lippert, C. J. L. Lock, B. Rosenberg*, J. Am. Chem. Soc. *99*, 777 (1977).
[5] *H. Köpf, B. Block*, Chem. Ber. *102*, 1504 (1969).
[6] *H. Köpf, I. Sasmita-Wiramihardja, R. Goldmann*, unpublished work; cf. *R. Goldmann*, Dissertation, Technische Universität Berlin 1978.
[7] We thank Prof. Dr. *E. Liss*, Klinikum Steglitz der Freien Universität Berlin, for the tumor strain.

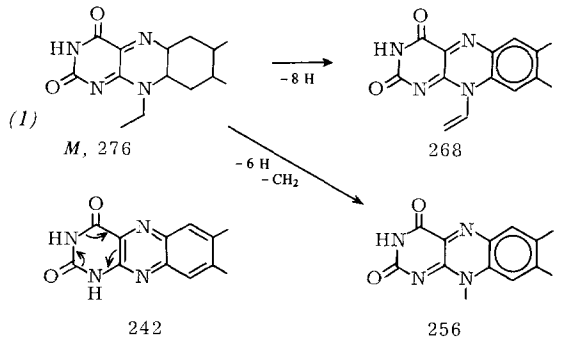
Thermal Generation of Pteridines and Flavines from Amino Acid Mixtures

By *Bettina Heinz, Walter Ried,* and *Klaus Dose*[*]

Dedicated to Professor Hermann Hartmann on the occasion of his 65th birthday

The thermal treatment of amino-acid mixtures[1] leads to formation of high-molecular products and to some hitherto unidentified heterocyclic impurities. In addition, a vivid blue fluorescence has frequently been observed[1b].

In order to elucidate the structures of the heterocycles we heated equimolar mixtures of three of the following six amino acids: glycine, alanine, valine, lysine, aspartic acid, and glutamic acid in an oil-bath (4—6 h, 160—200 °C) or metal bath (1—2 h, 180—350 °C) (cf. [1a]). The UV absorption spectra of the blue to green fluorescing material (λ_{max} *ca.* 250, 320—390, 450 nm) and the fluorescence spectra (λ_{exc} 365 nm, λ_{em} 420—480 nm), as well as the chromatographic analysis (cellulose, silica gel, aluminum oxide, Sephadex G 15 and Zipax ion-exchanger for HPLC) of the material isolated by dialysis and fractional extraction, indicated the presence of pteridine derivatives. Supporting evidence for the presence of such derivatives was also provided by chemical reactions (murexide reaction, coupling to diazotized sulfinic acid, color reaction with polytungstatophosphoric acid).



With the help of mass spectrometry we were able to detect definite pteridines; molecular ions and characteristic fragments of hydrogenated oxopteridines and aminooxopteridines (*e.g.* lumazine, xanthopterin, and isoxanthopterin) could be identified. In the case of sample 1, a strong molecular peak at $m/e = 241$ and a weaker peak at $m/e = 256$ suggest the fragmentation pattern of a lumichrome derivative *(1)* (see Table 1). For comparison, we used spectral data from the literature[2,3] and spectra of authentic samples.

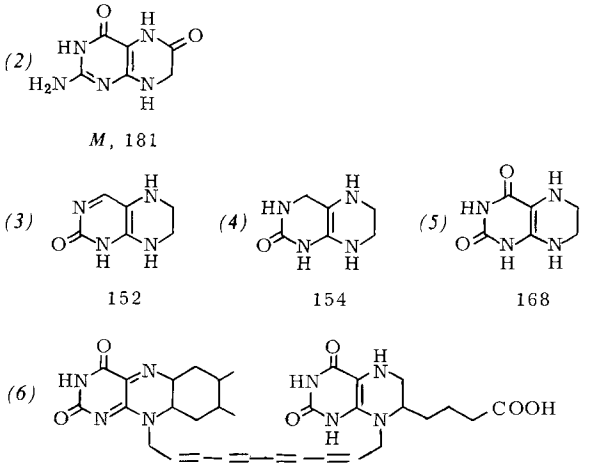


Table 1. Results of the thermolysis experiments. The starting material was fused in an oil bath (180 °C, 6 h; sample 3 under N_2). Compounds *(1)*, *(6)*, and *(7)* were isolated by gel filtration (Sephadex G-15).

Sample	Starting material (1:1:1)	Workup	Mass spectra (70 eV, 200 °C)	Compound isolated (Mol. wt. osmometric)
1	Lys Asp Gly	Melt taken up in water, solution filtered, filtrate dialyzed, contents of tube combined and freeze dried. Crude product taken up in little water, chromatographed on cellulose column, eluate concentrated, freeze dried, dried *in vacuo* over P_2O_5 at 60 °C	[a] m/e = 268 (2%), 256 (4), 242 (15), 241 (70), 227 (5), 199 (10), 171 (52), 170 (23), 156 (32), 147 (18), 146 (18), 145 (15), 144 (14), 143 (14), 142 (23), 129 (24), 126 (18), 122 (72), 117 (23), 99 (15), 85 (8), 82 (8), 74 (8), 60 (66), 45 (52), 44 (100), 43 (100)	*(1)* 276
2	Lys Asp Gly	Melt taken up in water, solution filtered, residue hydrolyzed for 5 h with 6 N NaOH; hydrolyzate purified by chromatography on cellulose column, eluate concentrated, freeze dried, dried *in vacuo* over P_2O_5 at 60 °C	[b] m/e = 181 (10%), 180 (16), 179 (15), 152 (43), 138 (22), 96 (45), 69 (27), 55 (42) [c] m/e = 168 (24%), 167 (30), 154 (20), 153 (23), 152 (42), 151 (23), 124 (13), 123 (14), 96 (45), 69 (28), 44 (100), 28 (50), 27 (37)	*(6)* 634 (?)
3	Lys Ala Gly	Workup as for sample 1	[d] m/e = 181 (8%), 152 (26), 138 (15), 96 (42), 69 (30), 55 (47)	*(7)*

[a] Given in part only. [b] Isolated fragmentation series of dihydroxanthopterin *(2)* (or dihydroisoxanthopterin). [c] Isolated fragmentation series of the partially hydrogenated oxopteridines *(3)*—*(5)* (cf. [2]). [d] Isolated fragmentation series of dihydroxanthopterin *(2)* (or dihydroisoxanthopterin); cf. sample 2.

[*] Prof. Dr. W. Ried [+], Dipl.-Chem. B. Heinz
Institut für Organische Chemie der Universität, Laboratorium Niederrad
Theodor-Stern-Kai 7, D-6000 Frankfurt/Main 70 (Germany)
Prof. Dr. K. Dose
Institut für Biochemie der Universität
Becherweg 30, D-6500 Mainz (Germany)
[+] Author to whom correspondence should be addressed.

Further characterization of the samples was provided by alkaline hydrolysis and subsequent gel filtration of the hydrolyzate on a Sephadex-G15 column with distilled water. The elution pattern at 280 nm showed essentially two peaks; the second peak consisted of substances which gave elution volumes and fluorescence colors comparable with those giv-

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0478 $ 02.50/0

[1] *G. Wilkinson, J. M. Birmingham*, J. Am. Chem. Soc. *76*, 4281 (1954).
[2] *B. Rosenberg, L. VanCamp, T. Krigas*, Nature *205*, 698 (1965); review: *F. K. V. Leh, W. Wolf*, J. Pharm. Sci. *65*, 315 (1976).
[3] *U. Thewalt, G. Schleussner*, Angew. Chem. *90*, 559 (1978); Angew. Chem. Int. Ed. Engl. *17*, 531 (1978).
[4] *R. Faggiani, B. Lippert, C. J. L. Lock, B. Rosenberg*, J. Am. Chem. Soc. *99*, 777 (1977).
[5] *H. Köpf, B. Block*, Chem. Ber. *102*, 1504 (1969).
[6] *H. Köpf, I. Sasmita-Wiramihardja, R. Goldmann*, unpublished work; cf. *R. Goldmann*, Dissertation, Technische Universität Berlin 1978.
[7] We thank Prof. Dr. *E. Liss*, Klinikum Steglitz der Freien Universität Berlin, for the tumor strain.

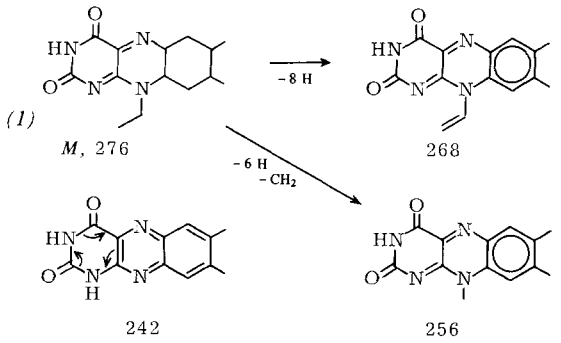
Thermal Generation of Pteridines and Flavines from Amino Acid Mixtures

By *Bettina Heinz, Walter Ried,* and *Klaus Dose*[*]

Dedicated to Professor Hermann Hartmann on the occasion of his 65th birthday

The thermal treatment of amino-acid mixtures[1] leads to formation of high-molecular products and to some hitherto unidentified heterocyclic impurities. In addition, a vivid blue fluorescence has frequently been observed[1b].

In order to elucidate the structures of the heterocycles we heated equimolar mixtures of three of the following six amino acids: glycine, alanine, valine, lysine, aspartic acid, and glutamic acid in an oil-bath (4—6 h, 160—200 °C) or metal bath (1—2 h, 180—350 °C) (cf. [1a]). The UV absorption spectra of the blue to green fluorescing material (λ_{max} *ca.* 250, 320—390, 450 nm) and the fluorescence spectra (λ_{exc} 365 nm, λ_{em} 420—480 nm), as well as the chromatographic analysis (cellulose, silica gel, aluminum oxide, Sephadex G 15 and Zipax ion-exchanger for HPLC) of the material isolated by dialysis and fractional extraction, indicated the presence of pteridine derivatives. Supporting evidence for the presence of such derivatives was also provided by chemical reactions (murexide reaction, coupling to diazotized sulfinic acid, color reaction with polytungstatophosphoric acid).



With the help of mass spectrometry we were able to detect definite pteridines; molecular ions and characteristic fragments of hydrogenated oxopteridines and aminooxopteridines (*e.g.* lumazine, xanthopterin, and isoxanthopterin) could be identified. In the case of sample 1, a strong molecular peak at $m/e = 241$ and a weaker peak at $m/e = 256$ suggest the fragmentation pattern of a lumichrome derivative *(1)* (see Table 1). For comparison, we used spectral data from the literature[2,3] and spectra of authentic samples.

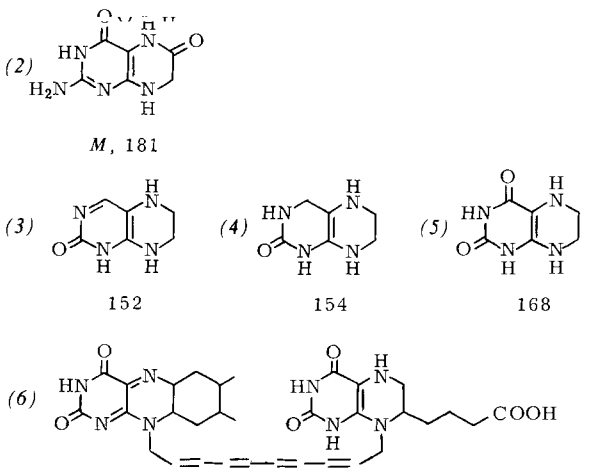


Table 1. Results of the thermolysis experiments. The starting material was fused in an oil bath (180 °C, 6 h; sample 3 under N_2). Compounds *(1)*, *(6)*, and *(7)* were isolated by gel filtration (Sephadex G-15).

Sample	Starting material (1:1:1)	Workup	Mass spectra (70 eV, 200 °C)	Compound isolated (Mol. wt. osmometric)
1	Lys Asp Gly	Melt taken up in water, solution filtered, filtrate dialyzed, contents of tube combined and freeze dried. Crude product taken up in little water, chromatographed on cellulose column, eluate concentrated, freeze dried, dried *in vacuo* over P_2O_5 at 60 °C	[a] m/e = 268 (2%), 256 (4), 242 (15), 241 (70), 227 (5), 199 (10), 171 (52), 170 (23), 156 (32), 147 (18), 146 (18), 145 (15), 144 (14), 143 (14), 142 (23), 129 (24), 126 (18), 122 (72), 117 (23), 99 (15), 85 (8), 82 (8), 74 (8), 60 (66), 45 (52), 44 (100), 43 (100)	*(1)* 276
2	Lys Asp Gly	Melt taken up in water, solution filtered, residue hydrolyzed for 5 h with 6 N NaOH; hydrolyzate purified by chromatography on cellulose column, eluate concentrated, freeze dried, dried *in vacuo* over P_2O_5 at 60 °C	[b] m/e = 181 (10%), 180 (16), 179 (15), 152 (43), 138 (22), 96 (45), 69 (27), 55 (42) [c] m/e = 168 (24%), 167 (30), 154 (20), 153 (23), 152 (42), 151 (23), 124 (13), 123 (14), 96 (45), 69 (28), 44 (100), 28 (50), 27 (37)	*(6)* 634 (?)
3	Lys Ala Gly	Workup as for sample 1	[d] m/e = 181 (8%), 152 (26), 138 (15), 96 (42), 69 (30), 55 (47)	*(7)*

[a] Given in part only. [b] Isolated fragmentation series of dihydroxanthopterin *(2)* (or dihydroisoxanthopterin). [c] Isolated fragmentation series of the partially hydrogenated oxopteridines *(3)*—*(5)* (cf. [2]). [d] Isolated fragmentation series of dihydroxanthopterin *(2)* (or dihydroisoxanthopterin); cf. sample 2.

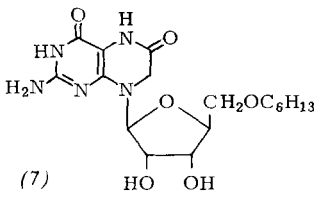
[*] Prof. Dr. W. Ried [+], Dipl.-Chem. B. Heinz
Institut für Organische Chemie der Universität, Laboratorium Niederrad
Theodor-Stern-Kai 7, D-6000 Frankfurt/Main 70 (Germany)
Prof. Dr. K. Dose
Institut für Biochemie der Universität
Becherweg 30, D-6500 Mainz (Germany)
[+] Author to whom correspondence should be addressed.

Further characterization of the samples was provided by alkaline hydrolysis and subsequent gel filtration of the hydrolyzate on a Sephadex-G15 column with distilled water. The elution pattern at 280 nm showed essentially two peaks; the second peak consisted of substances which gave elution volumes and fluorescence colors comparable with those giv-

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0478 $ 02.50/0

en by xanthopterin, isoxanthopterin, and lumazine investigated under the same conditions.

The UV spectra of the eluates were compared with those of authentic samples and showed identical absorption bands.



(7)

The concentrated eluates were dried over P_2O_5 at 60 °C *in vacuo* and then subjected to elemental analysis. From samples 1, 2, and 3 we were able to isolate the compounds *(1)*, *(6)*, and *(7)*.

Several pteridine derivatives can be synthesized on a preparative scale by the classical method of *Isay*[4], *i.e.* by fusion-condensation of 4,5-diaminopyrimidines and dicarbonyl compounds. The pteridine skeletal structure could be formed under prebiotic conditions from amino acids and the compounds allophanic acid, guanidinoformic acid, biuret, and guanidinoformamidine obtained from NH_3, CO_2 and H_2O.

Owing to the special reactivity of the amino acids we presume that the mixtures described here ("pteridine proteinoids" and "flavoproteinoids") play a significant role in the origin of life. In contrast to thermally untreated amino acid mixtures they are especially effective nutrients for microorganisms.

Received: December 1, 1978 [Z 230 IE]
revised: April 25, 1979
German version: Angew. Chem. *91*, 510 (1979)

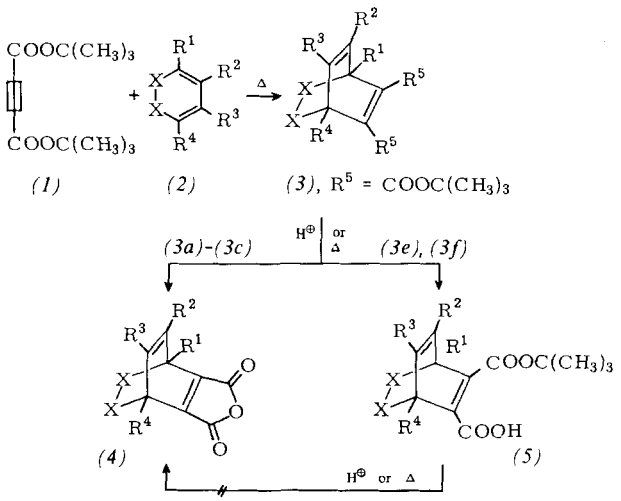
CAS Registry numbers:
(1), 70332-91-1; *(2)*, 1131-35-7; *(3)*, 28898-09-1; *(4)*, 70332-92-2; *(5)*, 38365-15-0; *(6)*, 70332-93-3; *(7)*, 70343-42-9; glycine, 56-40-6; alanine, 56-41-7; valine, 72-18-4; lysine, 56-87-1; asparagine, 70-47-3; glutaminic acid, 56-86-0

[1] a) *S. W. Fox*, Science *132*, 200 (1960); *S. W. Fox, K. Harada, ibid. 133*, 1923 (1961); b) *K. Heyns, K. Pavel*, Z. Naturforsch. *B 12*, 97, 109 (1957).
[2] *T. Goto, A. Tatamatsu, S. Matsuura*, J. Org. Chem. *30*, 1844 (1965).
[3] *J. Clark, F. S. Yates*, Org. Mass Spectrom. *5*, 1419 (1971); *P. Brown, C. L. Hornbeck, J. R. Cronin, ibid. 6*, 1383 (1972); *R. Tümmler, K. Steinfelder, E. C. Owen, D. W. West, ibid. 5*, 41 (1971).
[4] *O. Isay*, Ber. Dtsch. Chem. Ges. *39*, 250 (1906).

[2+4]-Cycloadditions with Di-*tert*-butyl Acetylenedicarboxylate[**]

By *Gisela Weber, Klaus Menke*, and *Henning Hopf*[*]

Dialkyl esters of acetylenedicarboxylic acid have long been valued as reaction partners in Diels-Alder additions as well as 1,3-dipolar and numerous other addition reactions[1]. Investigating the addition behavior of the recently described di-*tert*-butyl ester *(1)* with dienes *(2)*[2], it was observed that primary adducts of type *(3)* readily lose isobutene and water on warming, either directly or in the presence of catalytic amounts of *p*-toluenesulfonic acid, and are converted into anhydrides *(4)*. The ester *(1)* is thus equivalent to the unknown oxide of carbon, acetylenedicarboxylic anhydride (C_4O_3)[2], and could in principle be useful for the direct incorporation of the anhydride function. A communication published at the beginning of the year on the renewed preparation of *(1)*, and in which the ready cleavability of the product ester without base is also described[3], prompts us to publish a preliminary communication on further [2+4]-cycloadditions with *(1)*[4].



(1) *(2)* *(3)*, $R^5 = COOC(CH_3)_3$

(4) *(5)*

Table 1. Anhydrides *(4)* and monoacids *(5)* formed by decomposition of the primary adducts *(3)* [a].

	X X	R^1	R^2	R^3	R^4	*(3)* Yield [%]	Product Yield [%]
a	2 H	H	H	H	H	75	*(4a)* 99
b	2 H	H	CH_3	H	H	73	*(4b)* 100
c	2 H	H	CH_3	CH_3	H	75	*(4c)* 99
d	2 CH_3	CH_3	H	H	CH_3	0	—
e	O	H	H	H	H	71 [b]	*(5e)* 100
f	CH_2CH_2	H	H	H	H	51	*(5f)* 40

[a] Decomposition in the presence of catalytic amounts of *p*-toluenesulfonic acid at 60—100 °C. On thermal decomposition of the neat substance small amounts of aromatic compounds are also formed. [b] Small amounts of the four possible 2:1 adducts of furan and *(1)* are also produced.

As shown in Table 1 acyclic and cyclic model dienes *(2)* afford the esters *(3)* in good yields; the monocyclic esters *(3a)—(3c)* decompose quantitatively to the anhydrides *(4)*. In the case of the furan and 1,3-cyclohexadiene adducts *(3e)* and *(3f)*, however, the reaction stops after loss of one equivalent of isobutene: instead of the expected anhydrides *(4)*, the monoacids *(5)* are formed, which so far could not be converted into *(4)*.

For determination of the relative reactivity of *(1)* compared to that of dimethyl acetylenedicarboxylate[1] usually employed in cycloadditions we allowed both dienophiles to compete for a substoichiometric amount of 2,3-dimethyl-1,3-butadiene *(2c)*. After 16 h at 120 °C the diene had disappeared, and the two [2+4]-adducts *(3c)*, $R^5 = COOC(CH_3)_3$ and $R^5 = COOCH_3$, respectively, were formed in the ratio 26:74. Thus the ester *(1)* is *ca.* three times less reactive than its dimethyl analog towards this diene. Reactivity differences of this order of magnitude possibly suffice to terminate additions at the 1:1-adduct stage in diene systems which normally lead to 2:1 or higher Diels-Alder products[5].

[*] Prof. Dr. H. Hopf, G. Weber, Dr. K. Menke
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Alkynes and Cumulenes, Part 10. This work was supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft. Part 9: *H. Siegel, A. Germer, P. Binger, H. Hopf*, Chem. Ber. *111*, 3112 (1978).

Received: March 6, 1979 [Z 228 IE]
German version: Angew. Chem. *91*, 517 (1979)

CAS Registry numbers:
(1), 66086-33-7; *(2a)*, 106-99-0; *(2b)*, 78-79-5; *(2c)*, 513-81-5; *(2d)*, 764-13-6; *(2e)*, 110-00-9; *(2f)*, 592-57-4; *(3a)*, 70332-97-7; *(3b)*, 70332-98-8; *(3c)*, 70332-99-9; *(3e)*, 70333-00-5; *(3f)*, 70333-01-6; *(4a)*, 4773-89-1; *(4b)*, 70333-02-7; *(4c)*, 64437-91-8; *(5e)*, 70333-03-8; *(5f)*, 70333-04-9

[1] *M. Baumgarth*, Chem.-Ztg. *96*, 161 (1972); *100*, 515 (1976); *R. M. Acheson, N. F. Elmore*, Adv. Heterocycl. Chem. *23*, 263 (1978).
[2] *I. Böhm, H. Herrmann, K. Menke, H. Hopf*, Chem. Ber. *111*, 523 (1978).
[3] *W. Sucrow, F. Lübbe*, Angew. Chem. *91*, 157 (1979); Angew. Chem. Int. Ed. Engl. *18*, 149 (1979).
[4] Complete publication: *G. Weber, K. Menke, H. Hopf*, Chem. Ber., in press.
[5] For example, 1-methylpyrrole reacts with dimethyl acetyldicarboxylate to give a 1:2 adduct having the structure of a dihydroindole tetraester. The 1:1 adduct, presumably initially formed by attack at C-2 and C-5 of the diene, has so far not been isolated: *R. M. Acheson, A. R. Hands, J. M. Vernon*, Proc. Chem. Soc. *1961*, 164; cf. *R. M. Acheson, J. M. Vernon*, J. Chem. Soc. *1962*, 1148.

Methylidynetris(dimethylphosphane)[1]

By *Hans Heinz Karsch, Ulrich Schubert*, and *Dietmar Neugebauer*[*]

Alkyl-substituted methylidynetrisphosphanes were hitherto unknown. The sole example of this chemically important class of compounds is the little-characterized hexaphenyl derivative[2]. Although the analogous silicon compounds are known[3], the method adopted for their synthesis from readily accessible precursors is not applicable to the alkyl-substituted methylidynetrisphosphanes.

$$\underset{(1)}{(H_3C)_2PCH_2P(CH_3)_2} \xrightarrow[-\,BuH]{t\text{BuLi/Pentane}} \underset{(2)}{Li\{HC[P(CH_3)_2]_2\}}$$

$$(2) + (CH_3)_2PCl \xrightarrow[-\,LiCl]{Ether} \underset{(3)}{(H_3C)_2P\text{–}CH(P(CH_3)_2)\text{–}P(CH_3)_2}$$

The simplest compound, the hexamethyl derivative *(3)*, has now been obtained for the first time by metalation of the recently synthesized methylenebis(dimethylphosphane) *(1)*[4] and subsequent reaction with $(CH_3)_2PCl$.

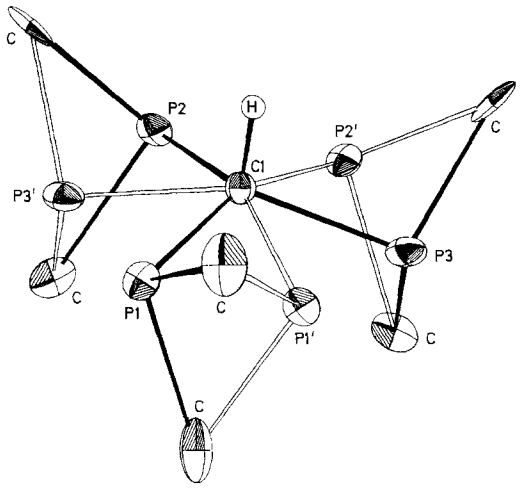


Fig. 1. View of *(3)*. The assigment to each of the two sets of atomic positions (hydrogens not shown; see text) follows from the different marking of the bonds. The C1–H group is common to both sets of positions.

[*] Dr. H. H. Karsch, Dr. U. Schubert, D. Neugebauer
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

(3) crystallizes from pentane in the form of colorless needles (m.p. 45–47 °C)[5]. On resublimation *in vacuo* large strongly-refracting crystals are obtained.

In the crystal[6], *(3)* is disordered. Referred to the positions of the common CH-group and the methyl carbons, the phosphorus atoms adopt a left-handed arrangement in one molecule and a right-handed arrangement in the other (see Fig. 1). C1 is surrounded by a distorted tetrahedral arrangement of three phosphorus atoms and one hydrogen atom with mean angles P1–C1–P of 115.4(3)° and H–C1–P of 102.6(4)° and a mean P–C1 bond length of 185.6(7) pm. The mean value of the C–P–C angle is 101.3°; the phosphorus atoms are therefore in a pseudotetrahedral arrangement.

Received: February 22, 1979 [Z 233a IE]
German version: Angew. Chem. *91*, 518 (1979)

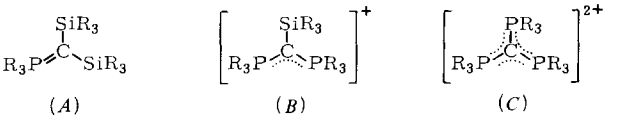
CAS Registry numbers:
(1), 64065-08-3; *(2)*, 70355-43-0; *(3)*, 70355-41-8; $(CH_3)_2PCl$, 811-62-1

[1] Part 9 of the series, "Functional Trimethylphosphine Derivatives".—Part 8: *H. H. Karsch*, Z. Naturforsch. *B 34*, 31 (1979).
[2] *K. Issleib, H. P. Abicht*, J. Prakt. Chem. *312*, 456 (1970).
[3] *G. Fritz, G. Becker, D. Kummer*, Z. Anorg. Allg. Chem. *372*, 171 (1970); *J. J. de Boer, J. A. van Doorn, C. Masters*, J. Chem. Soc. Chem. Commun. *1978*, 1005.
[4] *H. H. Karsch, H. Schmidbaur*, Z. Naturforsch. *B 32*, 762 (1977).
[5] NMR (C_6D_6, standard TMS ext. and H_3PO_4 ext.): $\delta PCH_3 = +1.14$ "t" $(X_nA)_2$, $N = 4.5$ Hz (distance between outer lines). $\delta CH = +0.58$ q, $^2J(PCH) = 1.6$ Hz; $\{^1H\}$-^{31}P: $\delta^{31}P = -48.1$ s; $\{^1H\}$-^{13}C: $\delta PCH_3 = +13.2$ "sept" $(AA_2'X)$, $N = 45.9$ Hz (distance between outer lines). $\delta CH = +33.3$ q, $^1J(PC) = 39.0$ Hz.
[6] Orthorhombic, $a = 1310(2)$, $b = 1099(2)$, $c = 838(2)$ pm; space group $Cmc2_1$; $Z = 4$. 537 structure factors ($F_0 \geq 3.92\sigma(F_0)$); $R_1 = 0.052$. Syntex $P2_1$/XTL, MoK_α radiation.

A Phosphorus Ylide with Symmetrical Resonance-Stabilized sp^2-Carbanion[1]

By *Hans Heinz Karsch, Beate Zimmer-Gasser, Dietmar Neugebauer*, and *Ulrich Schubert*[*]

Silyl substituents *(A)* considerably stabilize trialkylmethylenephosphoranes[3a]. The same applies for the iso-electronic phosphonium group *(B)*, which enables further stabilization owing to better charge delocalization and resonance[3b]. On introducing a further phosphonium group *(C)* this effect ought to be decisively increased as a result of the symmetrical geometry.

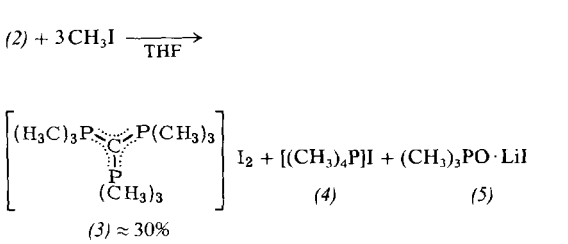


The isolation of methylidynetris(dimethylphosphane) *(1)*[2] suggested a possible access to *(3)*, the first symmetrically resonance-stabilized phosphorus ylide derivative[4], by reaction with CH_3I, but only products of a P–C cleavage reaction were obtained.

$$\underset{(1)}{[(CH_3)_2P]_3CH} + t\text{BuLi} \xrightarrow[-\,BuH]{\text{Pentane}} \underset{(2)}{Li\{C[P(CH_3)_2]_3\}}$$

[*] Dr. H. H. Karsch, D. Neugebauer, Dipl.-Chem. B. Zimmer-Gasser, Dr. U. Schubert
Anorganisch-Chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

However, conversion of *(1)* into its lithium salt *(2)* and subsequent quaternarization with CH_3I produces a lower positive charge on the phosphorus, hence reducing the tendency for P–C bond cleavage and therefore enabling the isolation of *(3)*[5].



Owing to its lower solubility in methanol, *(3)* can easily be separated from the other products; it crystallizes from water as colorless needles. A comparison of *(B)*, $R = CH_3$[3b], and *(3)* reveals the considerable gain in stability: the decomposition point increases from ≈240 to ≈330 °C; whereas *(B)*, $R = CH_3$, is only moderately air-stable and is decomposed by water, *(3)* is stable towards air, water and even trifluoroacetic acid.

The NMR spectra (in D_2O) afford no conclusive information on the configuration of *(3)*. The ^{1}H-NMR spectrum [δPCH_3: +2.85, "filled-in doublet", N = 13.1 (distance between outer lines)] and the $\{^1H\}$-^{13}C-NMR spectrum [δPCH_3: +18.2, symmetrical 6-line multiplet, N = 73.2 Hz (distance between outer lines)] would indicate a symmetrical configuration containing at least two $-\overset{+}{P}(CH_3)_3$ groups, but no resonance is observed for the central C-atom. The chemical shift of the $\{^1H\}$-^{31}P resonance ($\delta P = +19.6$ s), lying between the values for $[P(CH_3)_4]^+$ and $(CH_3)_3P{=}CH_2$, is equally not conclusive enough regarding proof of structure.

The trigonal-planar configuration could however be confirmed by X-ray structure analysis[6] (see Fig. 1).

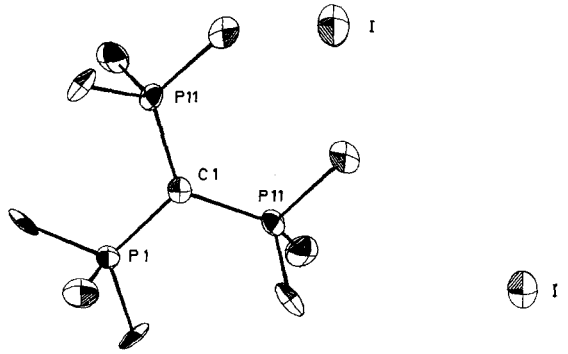


Fig. 1. View of *(6)*. The molecule has mirror symmetry. The hydrogen atoms are not shown. Bond lengths: P1–C1 = 175, P11–C1 = 175, P1–C = 180, P11–C = 178 pm; bond angles: P1–C1–P11 = 116.7, P11–C1–P11 = 126.5, C1–P1–C = 112.6, 112.6, 112.9, C1–P11–C = 115.9, 113.3, 112.5°.

The C1–P bond lengths approach those observed in other stabilized phosphorus ylides[7]. In the crystal there are at most only weak interactions between the cation and the iodide ions (minimum I...H distance: 296 pm).

Received: February 22, 1979 [Z 233b IE]
German version: Angew. Chem. *91*, 519 79)

CAS Registry numbers:
(1), 70355-41-8; *(2)*, 70377-69-4; *(3)*, 70355-42-9; *(4)*, 993-11-3; *(5)*, 70355-52-1; CH_3I, 74-88-4

[1] Part 10 of the series "Functional Trimethylphosphine Derivatives".—Part 9: [2].

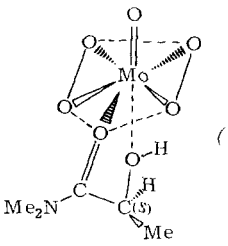
[2] *H. H. Karsch, U. Schubert, D. Neugebauer*, Angew. Chem. *91*, 518 (1979); Angew. Chem. Int. Ed. Engl. *18*, 480 (1979).
[3] a) *H. Schmidbaur*, Acc. Chem. Res. *8*, 62 (1975); b) *H. Schmidbaur, W. Tronich*, Chem. Ber. *101*, 3545 (1968).
[4] A comparable, but not completely symmetrical structural unit with phenyl substituents has been described, see *G. H. Birum, C. N. Matthews*, J. Am. Chem. Soc. *88*, 4198 (1966).
[5] As in the system $Li[H_2CP(CH_3)_2]/CH_3I$, a *C*-methylation is not observed: cf. *H. H. Karsch, H. Schmidbaur*, Z. Naturforsch. *B 32*, 762 (1977).
[6] Orthorhombic, $a = 1086(1)$, $b = 1333(2)$, $c = 1264(1)$ pm; space group $Cmc2_1$; $Z = 4$. 792 structural factors ($F_0 \geq 3.92\sigma(F_0)$); $R_1 = 0.051$. Syntex $P2_1$/XTL, MoK_α radiation.
[7] *R. Hoffmann, D. B. Boyd, S. Z. Goldberg*, J. Am. Chem. Soc. *92*, 3929 (1970).

Asymmetric Epoxidation of Simple Olefins with an Optically Active Molybdenum(VI) Peroxo Complex[**]

By *Henri B. Kagan, Hubert Mimoun, Christoph Mark*, and *Volker Schurig*[*]

The importance of chiral epoxides in biochemistry and synthetic chemistry has warranted the search for simple methods of access to this interesting class of compounds. The abiotic asymmetric epoxidation of prochiral olefins has so far been carried out with optically active peracids (optical yields 0.6—7.5%[1a]), with achiral hydroperoxides in the presence of optically active metal-complex catalysts (5—44% e.e.[1b]), and with H_2O_2 by phase-transfer catalysis with quaternized alkaloids (25% e.e.[1c]). These reactions succeeded only with activated CC double bonds (styrenes, allyl alcohols, conjugated ketones, quinones). We describe here a novel method for the asymmetric epoxidation of simple *unfunctionalized* olefins by an optically active metal-peroxo complex.

Molybdenum(VI) oxodiperoxo complexes $MoO(O_2)_2L$ (L = hexamethylphosphoric triamide HMPA, pyridine) epoxidize olefins stoichiometrically and diastereospecifically[2]. We have synthesized a stable optically active complex *(1)*[3] containing the bidentate chiral ligand (*S*)-*N*,*N*-dimethyllactamide (= L). According to X-ray structural analysis[4], the compound has the pentagonal-bipyramidal geometry *(1)* with sevenfold coordinated molybdenum.



(1)

Simple prochiral olefins such as propene or *trans*-2-butene are epoxidized stoichiometrically to optically active oxiranes

[*] Prof. Dr. H. B. Kagan
Laboratoire de Synthèse Asymétrique, LA CNRS 040255-02
Université de Paris Sud
F-91405 Orsay Cédex (France)
Dr. H. Mimoun
Laboratoire d'Oxydation, Institut Français du Pétrole
4, avenue du Bois Préau
F-92502 Rueil-Malmaison (France)
Prof. Dr. V. Schurig, Dipl.-Chem. C. Mark
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

[**] Part of a planned Dissertion by *C. Mark*. This work was supported by the Centre National de la Recherche Scientifique, the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. *C. M.* thanks the Carl-Duisberg-Stiftung for a study grant.

by *(1)* in nitrobenzene at 20 °C/1 bar (Table 1). The chemical yield (70%), the enantiomeric excess (up to 34% ee), and the configuration of the dominant oxirane enantiomer (in all cases *R*) were determined by complexation gas-chromatography on nickel(II) bis(3-heptafluorobutyryl)-1*R*-camphorate[5]. This methodology also permitted continuous kinetic monitoring of the asymmetric synthesis.

Table 1. Asymmetric epoxidation of prochiral olefins *(2)*—*(6)* by molybdenum(VI) oxodiperoxo-(*S*)-*N*,*N*-dimethyllactamide *(1)* to the oxiranes *(7)*—*(11)*. *(1)* (30 mg, ≈0.1 mmol) is suspended in nitrobenzene (3 ml) at 20 °C/1 bar. After addition of 1 mmol olefin the mixture becomes homogeneous.

Olefin		Oxirane		Enantiomeric excess [%] (±1%)	Configuration [a]
Propene	*(2)*	Methyloxirane	*(7)*	28.8	*R*
1-Butene	*(3)*	Ethyloxirane	*(8)*	31.1	*R*
3-Methyl-1-butene	*(4)*	Isopropyloxirane	*(9)*	15.5	*R*
trans-2-Butene	*(5)*	*trans*-Dimethyloxirane	*(10)*	34.8	2*R*, 3*R*
2-Methyl-2-butene	*(6)*	Trimethyloxirane	*(11)*	5.1 30.2 (−5 °C)	*R*

[a] Configuration of the dominant enantiomer. For all oxiranes, during complexation gas-chromatography on nickel(II) bis(3-heptafluorobutyryl)-1*R*-camphorate the larger peak is eluted first. Assignment of configuration: for *(7)* and *(10)* by independent synthesis; for *(8)*, *(9)*, and *(11)* by an empirical quadrant rule [5]

While a marked increase in enantiomeric yield [oxirane *(11)*] is observed on reducing the reaction rate by lowering the temperature, the increasing steric hindrance of the alkyl group [olefin *(4)*] surprisingly leads to a decrease in the asymmetric induction. The continuously monitored enantiomeric composition of the oxiranes *(2)*—*(5)* during the reaction remained constant within the experimental accuracy. This shows that the olefin epoxidation is asymmetrically induced and that no enrichment of the enantiomers of the epoxide that is formed takes place by kinetic resolution. Control experiments showed, moreover, that the slow degradation of the racemic epoxides *(2)*—*(5)* by the complex *(1)* takes place without enantiomer enrichment. The consecutive oxidation of the epoxides by *(1)* is suppressed by an excess of olefin[2]. The rate of epoxidation of olefins by *(1)* increases by about two orders of magnitude along the series ethene (48 h) < 1-butene < *trans*-2-butene < 2-methyl-2-butene (15 min). The strength of π-complexation of these olefins with $MoO(O_2)_2(HMPA)$[6] increases along the same series. The observed asymmetric induction is most likely due to enantiofacial discrimination of prochiral olefins by optically active *(1)*.

Received: February 7, 1979 [Z 229 IE]
revised: April 12, 1979
German version: Angew. Chem. *91*, 511 (1979)

CAS Registry numbers:
(1), 70355-53-2; *(2)*, 115-07-1; *(3)*, 106-98-9; *(4)*, 563-45-1; *(5)*, 624-64-6; *(6)*, 513-35-9; *(7)*, 15448-47-2; *(8)*, 3160-95-0; *(9)*, 33204-47-6; *(10)*, 1758-32-3; *(11)*, 70355-44-1

[1] a) *R. C. Ewins, H. B. Henbest, M. A. McKervey*, Chem. Commun. *1967*, 1085; *F. Montanari, I. Moretti, G. Torre, ibid. 1969*, 135; b) *S. Yamada, T. Mashiko, S. Terashima*, J. Am. Chem. Soc. *99*, 1988 (1977); *R. C. Michaelson, R. E. Palermo, K. B. Sharpless, ibid. 99*, 1990 (1977); c) *R. Helder, J. C. Hummelen, R. W. P. M. Laane, J. S. Wiering, H. Wynberg*, Tetrahedron Lett. *1976*, 1831.

[2] *H. Mimoun, I. Seree de Roch, L. Sajus*, Bull. Soc. Chim. Fr. *1969*, 1481; Tetrahedron *26*, 37 (1970).

[3] Synthesized according to the procedure given in [2]. M.p. 149 °C (dec.); IR: ν(O—O) = 865, $\nu\left(Mo\langle^{O}_{O}\right)$ sym. = 540, asym. = 585 cm^{-1}; ^{1}H-NMR: $\delta(CH_3)$ = 1.25, 1.32, 2.96, 3.08.

[4] *W. Winter, C. Mark, V. Schurig*, to be published.

[5] *V. Schurig, B. Koppenhöfer, W. Bürkle*, Angew. Chem. *90*, 993 (1978); Angew. Chem. Int. Ed. Engl. *17*, 937 (1978).

[6] *H. Arakawa, Y. Moro-oka, A. Ozaki*, Bull. Chem. Soc. Jpn. *47*, 2958 (1974).

Krypton and Xenon Inclusion Compounds of Complex Metal Cyanides

By *Manfred Kämper, Madlon Wagner*, and *Armin Weiss*[*]

Noble gas inclusion compounds—known as gas hydrates and as hydroquinone clathrates—are often stable only at low temperature and high pressure. Strictly speaking, they are not true clathrates because the host lattices are not stable on their own. We now describe the compounds $CdPt(CN)_6 \cdot 1.046$ Kr and $CdPt(CN)_6 \cdot 1.128$ Xe which exhibit high stability and vacant cage structure.

This cage structure is generally encountered in hexacyanometalates of the transition metals. Here the metal atoms are linked by the CN groups to form a three-dimensional network. The resulting Prussian blue-type cubic face-centered structure is fourfold primitive and contains eight cubic subunits per unit cell; hence two cavities exist per $MM'(CN)_6$ formula unit.

We have now found that hexacyanopalladates(IV)[1] and hexacyanoplatinates(IV)[2] of divalent transition metals, especially Mn, Zn, and Cd, are anhydrous and must therefore have vacant cavities. The compounds mentioned are obtained as large perfect cubes on gel crystallization: they also allow definite proof of their anhydrous nature.

The edge length of the cubic subunit of $CdPt(CN)_6$ (Table 1), *viz.* $a/2 = 5.47$ Å, and the diameter of a CN group (*ca.* 3.0 Å[3]) show the window in the cubic subunit to have an edge length of *ca.* 2.5 Å. Hence inclusion can only take place during growth of the compound. It also follows from the data for $CdPt(CN)_6$ that spherical atoms or molecules with a maximum diameter of *ca.* 4.7 Å (which would include H_2O) can be accommodated by the cavities. It therefore appears all the more surprising that the compounds mentioned are anhydrous although they are crystallized from water. Water molecules obviously prefer the hydrogen-bonded clusters of the solvent to being caged in the cavities of the host lattice for energetic reasons.

The cavities must be regarded as hydrophobic and thus suitable for incorporation of hydrophobic molecules from an aqueous reaction medium.

Experiments with the noble gases krypton, $d = 3.96$ Å, and xenon, $d = 4.36$ Å, yielded such inclusion compounds. Crystals of the host compound $CdPt(CN)_6$ were grown in the presence of the noble gas at 64 bar in an autoclave. The compounds obtained were characterized by analysis, mass spectrometry, and X-ray methods (Table 1).

[*] Dr. M. Kämper [*], Dipl.-Chem. M. Wagner, Prof. Dr. A. Weiss, Institut für Anorganische Chemie der Universität Meiserstrasse 1, D-8000 München 2 (Germany)
[*] To whom correspondence should be addressed.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0486 $ 02.50/0

Table 1. X-Ray data of the host compound and of the krypton and xenon inclusion compounds.

	Host compound	Kr compound		Xe compound	
Formula	$CdPt(CN)_6$	$CdPt(CN)_6 \cdot 1.046$ Kr		$CdPt(CN)_6 \cdot 1.128$ Xe	
Axis of unit cell	10.938 Å	10.955 Å		10.980 Å	
Number of reflections measured	1651	1662		1662	
Independent reflections	350 (Fm3m)	563	(F 23)	563	(F 23)
		356	(Fm3m)	356	(Fm3m)
R value	1.96%	2.95%	(F 23)	1.90%	(F 23)
		2.71%	(Fm3m)	1.89%	(Fm3m)
Occupation of site (based on formula)	—	0.614 / 0.470	(F 23)	0.566 / 0.562	(F 23)
		1.046	(Fm3m)	1.128	(Fm3m)

In compliance with the space group Fm3m the host compound $CdPt(CN)_6$ contains four formula units and eight cavities in its unit cell. However, only four cavities are occupied by noble gas atoms. Given strictly alternating occupation this corresponds to a lower tetrahedral symmetry of space group F 23; the eightfold site of the host compound resolves into two fourfold sites.

Calculation yields the same occupation of the two fourfold sites for the xenon compound, *i. e.* it becomes identical with a description in the space group Fm3m. This corresponds to two structural variants, *viz.* a purely random arrangement and a subdivision of the macrocrystal into domains each of which has one of the possible alternating occupations. No experimental distinction is possible.

The F 23 structural approach leads to 1 a slightly unsymmetrical occupation of the two fourfold sites in the case of krypton; the *R* value is slightly poorer than for the Fm3m description. However, these small deviations are hardly significant, particularly in view of the small scattering power of krypton.

Finally, these compounds could provide a technically interesting alternative to the storage of gases in steel cylinders. In the krypton compound, the krypton is present at a density corresponding to that of an ideal gas at 118 bar. If all the cavities are occupied by preparation at higher pressure this value even rises to 216 bar.

Received: February 21, 1979 [Z 232 IE]
German version: Angew. Chem. *91*, 517 (1979)

CAS Register numbers:
$CdPt(CN)_6$, 55683-97-1; Kr, 7439-90-9; Xe, 7440-63-3

[1] *H. Siebert, A. Siebert*, Angew. Chem. *81*, 575 (1969); Angew. Chem. Int. Ed. Engl. *8*, 600 (1969).
[2] *A. W. Babkow*, Dokl. Akad. Nauk SSSR *177*, 337 (1967); Proc. Acad. Sci. USSR. Chem. Sect. *177*, 1011 (1967).
[3] *W. J. Dulmage, W. N. Lipscomb*, Acta Crystallogr. *4*, 330 (1951).

A New Lithium-Nickel Polynuclear Complex: $Ni(C_{12}H_{17}NiLi)_2(THF)_4$

By *Klaus Jonas, Carl Krüger*, and *Janine C. Sekutowski*[*]

The conversion of the binary nickel(0)-olefin complexes $(C_8H_{12})_2Ni^0$ (C_8H_{12} = 1,5-cyclooctadiene) and $C_{12}H_{18}Ni^0$ ($C_{12}H_{18}$ = *all-trans*-1,5,9-cyclododecatriene) into the corresponding dilithium-nickel-olefin complexes $(C_8H_{12})_2NiLi_2(THF)_4$ (THF = tetrahydrofuran) and $C_{12}H_{18}NiLi_2(TMEDA)_2$ *(1)* (TMEDA = *N,N,N',N'*-tetramethylethylenediamine) by reaction with metallic lithium is accompanied by side reactions. This is particularly marked in the case of cyclododecatriene-nickel(0) (yields: *(1)*, *ca.* 50%; $(C_8H_{12})_2NiLi_2(THF)_4$, 80—90%).

We have now found that one of the products of the lithiation of $C_{12}H_{18}Ni^0$ is the novel polynuclear lithium-nickel complex $Ni(C_{12}H_{17}NiLi)_2(THF)_4$ *(3)*. This species is also formed if *all-trans*-cyclododecatriene-nickel(0) is allowed to react at 0 °C with a THF solution of *(1)* and precipitates out of the initially clear solution in the form of dark red crystals (30%).

$$\underset{(1)}{C_{12}H_{18}NiLi_2(TMEDA)_2} \xrightarrow[-TMEDA]{+C_{12}H_{18}Ni^0,\ +THF} \underset{(3)}{Ni(C_{12}H_{17}NiLi)_2(THF)_4}$$

We assume that *(3)* is the product of a transmetalation reaction in which, instead of exchange of lithium between two different $C_{12}H_{18}Ni^0$ molecules [eq. (a)], the metalating agent *(1)* has attached the C H bonds of the complexed double bonds of two $C_{12}H_{18}Ni^0$ molecules [eq. (b)].

$$\underset{(1)}{C_{12}H_{18}NiLi_2} + C_{12}H_{18}Ni' \rightleftarrows C_{12}H_{18}Ni + \underset{(1)'}{C_{12}H_{18}Ni'Li_2} \quad (a)$$

$$\underset{(1)}{C_{12}H_{18}NiLi_2} + 2\,C_{12}H_{18}Ni \longrightarrow \underset{(2)}{C_{12}H_{18}NiH_2} + 2\,C_{12}H_{17}NiLi \quad (b)$$

$$C_{12}H_{18}NiH_2 \longrightarrow C_{12}H_{20} + \underset{(3)}{Ni(C_{12}H_{17}NiLi)_2(THF)_4}$$

$C_{12}H_{18}$ = cyclododecatriene
$C_{12}H_{20}$ = cyclododecadiene
The n-donors bonded to lithium are shown only for isolated *(3)* in eq. (a) and (b).

(1) is converted into the unstable complex $C_{12}H_{18}NiH_2$ *(2)* which, as can be shown by protolysis of *(1)* with alcohol or by the reaction of $C_{12}H_{18}Ni^0$ with H_2[3], normally decomposes to give metallic nickel and cyclododecadiene ($C_{12}H_{20}$) or cyclododecane ($C_{12}H_{24}$). However, under the reaction conditions described here *(2)* is stabilized by reaction with two molecules of $C_{12}H_{17}NiLi$ and loss of $C_{12}H_{20}$, giving the polynuclear complex *(3)*.

Characteristic for *(3)*[3] is the linear arrangement of the Ni_3 skeleton with metal-metal interactions (Fig. 1). The central nickel atom Ni1, which occupies a crystallographic inversion center and is in an essentially planar environment, occupies a fourth coordination site at Ni2 and forces this atom *ca.* 0.5 Å out of the trigonal ligand plane of the twelve-membered

[*] Dr. K. Jonas, Priv.-Doz. Dr. C. Krüger [**], Dr. J. C. Sekutowski [**]
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr (Germany)

[**] X-ray structure analysis.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0606-0487 $ 02.50/0*

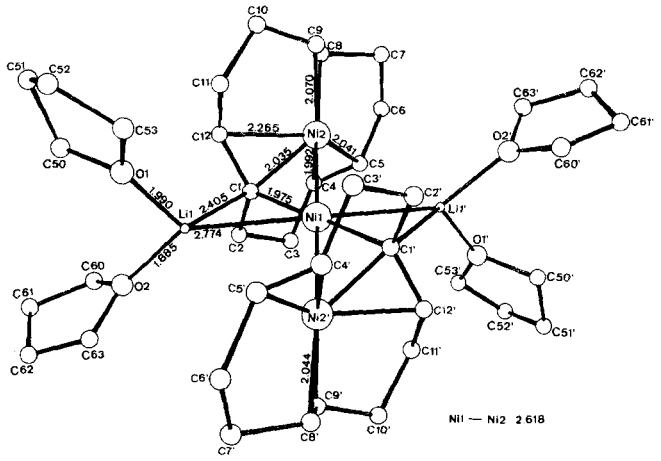


Fig. 1. Structure of the complex $Ni(C_{12}H_{17}NiLi)_2(THF)_4$ *(3)*. Bond lengths in Å.

ring[4]. A hetero-metal multicenter bond[5] is observed for the five-coordinated carbon atom (C1) of the twelve-membered ring which is bonded to Ni2 through three π-bonds. This leads to an acute angle of 78° for Ni···C1···Li which is typical for electron deficient bonds and is accompanied by considerable distortion of the π-bonded interaction Ni2C1C2 (Fig. 2).

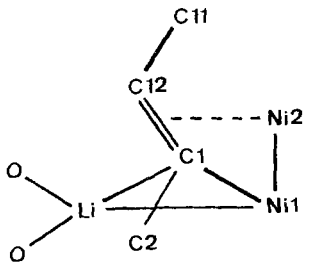


Fig. 2. The bonding situation at the site of the heterometal multicenter bond.

The molecular symmetry $\bar{1}$ (C_i) is perturbed by disorder of the aliphatic carbon atoms of the complexed twelve-membered ring. The lithium atom which interacts only with two perpendicularly oriented THF ligands appears to be coordinatively unsaturated.

The ^{13}C-NMR spectrum[6] of *(3)* in [D_6]benzene exhibits a total of eleven signals for the two identical twelve-membered rings. Six can be assigned to methylene C-atoms ($\delta = 54.5$, 44.0, 42.5, 41.8, 40.7, and 38.8 ppm, all t) and five to the C-atoms of the complexed double bonds ($\delta = 109.0$, 85.6, 84.1, 78.7, and 75.7 ppm, all d). The failure to observe the sixth olefinic C-atom (C1) is associated with its quaternary nature.

Received: March 1, 1979 [Z 234a IE]
German version: Angew. Chem. *91*, 520 (1979)

[1] *K. Jonas*, Angew. Chem. *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *14*, 752 (1975); *K. R. Pörschke*, Dissertation, Universität Bochum 1975.

[2] *G. Wilke*, Angew. Chem. *75*, 10 (1963); Angew. Chem. Int. Ed. Engl. *2*, 105 (1963).

[3] Cell data: $a = 9.268(1)$, $b = 10.723(2)$, $c = 12.738(2)$ Å; $\alpha = 68.34(1)$, $\beta = 66.78(1)$, $\gamma = 61.63(1)°$; space group $P\bar{1}$; $Z = 1$; 4048 reflections, 2574 of which were not observed; decomposition during data collection; $R = 0.103$. Atomic parameters and other data are available on request from the authors (*C. K.*).

[4] *D. J. Brauer, C. Krüger*, J. Organomet. Chem. *44*, 397 (1972); *C. Krüger*, unpublished results.

[5] *K. Jonas, D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, J. Am. Chem. Soc. *98*, 74 (1976); *D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, Angew. Chem. *88*, 52 (1976); Angew. Chem. Int. Ed. Engl. *15*, 48 (1976); *H. Bönnemann, C. Krüger, Y.-H. Tsay, ibid. 88*, 50 (1976) and *15*, 46 (1976), respectively.

[6] We thank Dr. *R. Mynott* for recording and interpreting the ^{13}C-NMR spectrum (25.2 MHz, shifts referred to TMS, multiplicities determined by off-resonance or gated-decoupling).

Nickel(0)-Induced Synthesis of Ethyllithium from Lithium, Hydrogen, and Ethylene

By *Klaus Jonas* and *Klaus Richard Pörschke*[*]

In general high reaction temperatures are necessary for the synthesis of alkali-metal hydrides from the elements[1], although sodium hydride can be formed at room temperature and normal pressure in tetrahydrofuran if both naphthalene and titanium isopropoxide are present[2]. We wish to report here, *inter alia*, on the "lithium hydride" complex $(COD)_{1.5}NiLi_2H_2(THF)_x$ (COD = 1,5-cyclooctadiene).

Reaction of binary nickel(0)-olefin complexes with metallic lithium yields well-defined dilithium-nickel-olefin complexes[3, 5], for example as in eq. (a), containing reactive lithium[4, 5]. Thus $(COD)_2NiLi_2(THF)_4$ *(2)*, which is relatively soluble in THF or dimethoxyethane (≈0.25 mol/l at room temperature), reacts with molecular hydrogen (1 atm) even at −60 °C. One H_2 per Li_2Ni-unit is taken up with elimination of 0.5 COD/Li_2Ni to produce the sparingly soluble bright-yellow powder *(3)* [eq. (b)][4].

$$(COD)_2Ni + 2\,Li \xrightarrow[-30\text{ to }0\,°C]{THF} (COD)_2NiLi_2(THF)_4 \qquad (a)$$

(1) *(2)*

$$(2) + 1\,H_2 \xrightarrow[-60\text{ to }-40\,°C]{THF} (COD)_{1.5}NiLi_2H_2(THF)_x + 0.5\,COD \qquad (b)$$

(3)

(3) contains the unchanged ligand 1,5-cyclooctadiene, as shown by reactions with cyclooctatetraene or CO in which *(3)* is dissolved and cyclooctadiene is liberated in high yield. Hydrogen is not evolved. *(3)* also dissolves in the presence of organometallic Lewis acids such as $(C_2H_5)_3Al$ if COD is added. The Li and H atoms in *(3)* are transferred from the complex to the $(C_2H_5)_3Al$ as lithium hydride [eq. (c)]. Both $Li[Al(C_2H_5)_3H]$ (75% isolated as $[Li(TMEDA)_2]^{\oplus}$-$[Al(C_2H_5)_3H]^{\ominus}$, TMEDA = *N,N,N',N'*-tetramethylethylenediamine) and *(1)* (90%) are formed in high yields.

$$(COD)_{1.5}NiLi_2H_2 + 2(C_2H_5)_3Al + 0.5\,COD \xrightarrow[-30\,°C]{THF} \qquad (c)$$

(3)

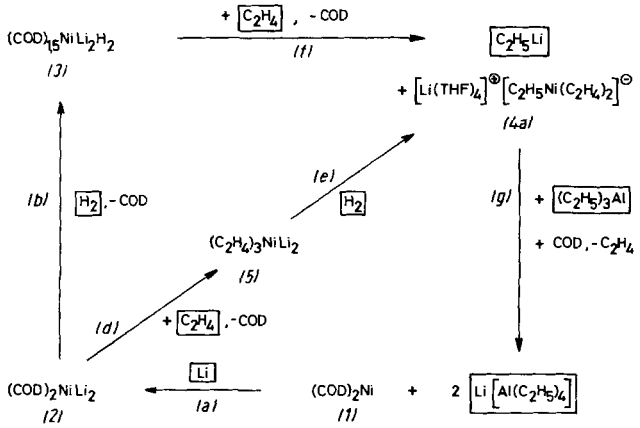
$$(COD)_2Ni + 2\,Li[Al(C_2H_5)_3H]$$

(1)

Combination of equations (a), (b), (c) gives a reaction sequence in which lithium, H_2, and $(C_2H_5)_3Al$ produce $Li[Al(C_2H_5)_3H]$ stoichiometrically at −30 °C and normal pressure. An attempted nickel(0)-catalyzed synthesis of $Li[Al(C_2H_5)_3H]$, in which *(1)*, lithium, and $(C_2H_5)_3Al$ were allowed to react at −30 °C, was unsuccessful since *(2)* does not complex with hydrogen in the presence of $(C_2H_5)_3Al$. However, the $(COD)_2Ni$ *(1)* re-formed according to eq. (c) can be re-lithiated to start the cycle again. Thus it is possible to synthesize $Li[Al(C_2H_5)_3H]$ in stages pseudocatalytically in a one-pot process.

[*] Dr. K. Jonas, Dr. K. R. Pörschke
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr (Germany)

Whereas pure lithium hydride prepared from lithium and H_2 does not add to C=C double bonds, the "lithium hydride" bound in *(3)* proves to be more reactive, *e. g.* with norbornene, propylene, or ethylene.



(3) dissolves in an ethylene-saturated THF-solution even at $-60\,^{\circ}C$ [eq. (f)]. Cooling the clear reaction solution to $-78\,^{\circ}C$ leads to the crystallization of *(4a)*, or of $[Li(TMEDA)_2]^{\oplus}[C_2H_5Ni(C_2H_4)_2]^{\ominus}$ *(4b)* if TMEDA is added, while C_2H_5Li remains in solution. Reaction of C_2H_5Li and *(4a)* with $(C_2H_5)_3Al$ and COD affords $Li[Al(C_2H_5)_4]$ and $(COD)_2Ni$ *(1)* according to eq. (g); lithiation of *(1)* leads to regeneration of *(2)* [eq. (a)]. For the preparation of *(4a)*/C_2H_5Li from *(2)*, there is a further route other than *via (3)* [eqs. (b) and (f)]. This second route also involves two steps, firstly displacement of the COD in *(2)* by ethylene, leading to the sparingly soluble *(5)*[3,4] [eq. (d)] and, secondly, treatment of *(5)* with hydrogen [eq. (e)] to give a clear solution from which *(4a)* crystallizes on cooling to $-78\,^{\circ}C$.

Received: March 1, 1979 [Z 234b IE]
German version: Angew. Chem. *91*, 521 (1979)

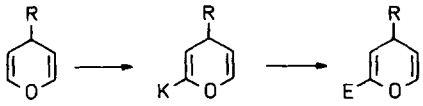
CAS Registry numbers:
(1), 1295-35-8; *(2)*, 70355-55-4; *(4a)*, 60384-04-5; *(5)*, 70355-56-5; C_2H_5Li, 911-49-4; Li, 7439-93-2; H_2, 1333-74-0; C_2H_4, 74-85-1; $(C_2H_5)_3Al$, 97-93-8; $Li[Al(C_2H_5)_4]$, 2666-13-9; $[Li(TMEDA)_2]^+$ $[Al(C_2H_5)_3H]^-$, 70377-86-5

[1] *G. F. Hüttig, A. Krajewski*, Z. Anorg. Allg. Chem. *141*, 133 (1924); *G. W. Matson, T. P. Whaley*, Inorg. Synth. *5*, 10 (1957).
[2] *E. E. van Tamelen, P. B. Fechter*, J. Am. Chem. Soc. *90*, 6854 (1968); *S. Bank, M. C. Prislopski*, Chem. Commun. *1970*, 1624.
[3] *K. Jonas*, Angew. Chem. *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *14*, 752 (1975).
[4] *K. R. Pörschke*, Dissertation, Universität Bochum 1975; *K. Jonas*, Chemiedozententagung 1976, Regensburg.
[5] *K. Blum*, Dissertation, Universität Bochum 1978.
[6] *K. Jonas, K. R. Pörschke, C. Krüger, Y.-H. Tsay*, Angew. Chem. *88*, 682 (1976); Angew. Chem. Int. Ed. Engl. *15*, 621 (1976).

Metalation of Pyrans and Dihydropyridines: When is an 8 π-System Cost Effective?[**]

By *Manfred Schlosser* and *Philippe Schneider*[*]

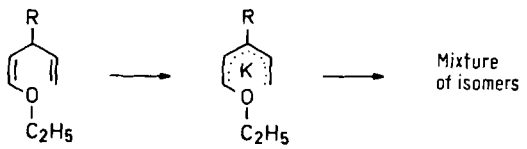
Powerful metalating agents[1] such as butyllithium in the presence of potassium *tert*-butoxide or trimethylsilylmethylpotassium promote slow hydrogen/potassium exchange at the position next to the oxygen atom, in both 4*H*-pyran *(1a)*[2a] and 4-methyl-4*H*-pyran *(1b)*[2b]. Subsequent treatment with methyl iodide, ethyl bromide, bromomethyltrimethylsilane, or chlorotrimethylsilane in petroleum ether affords 4% 2-methyl- *(2a)* and 22% 2-trimethylsilyl-4*H*-pyran *(2b)*, or 14% 2-ethyl- *(2c)*, 23% 2-trimethylsilylmethyl- *(2d)* and 48% 2-trimethylsilyl-4-methyl-4*H*-pyran *(2e)*, respectively[3].



(1a), R = H
(1b), R = CH_3

(2a), R = H, E = CH_3
(2b), R = H, E = $Si(CH_3)_3$
(2c), R = CH_3 E = C_2H_5
(2d), R = CH_3, E = $CH_2Si(CH_3)_3$
(2e), R = CH_3, E = $Si(CH_3)_3$

Thus, upon treatment with organometallic reagents the pyrans *(1a)* and *(1b)* behave like 3,4-dihydro-2*H*-pyran, in which the olefinic hydrogen adjacent to the oxygen atom can—again slowly and accompanied by side reactions—be replaced by lithium and sodium[4a]. In contrast, the open-ring analogs *(3a)* and *(3b)* are rapidly and exclusively deprotonated at the double-allylic position[4b].



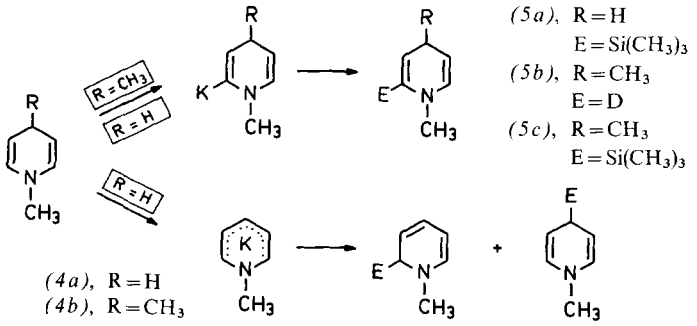
(3a), R = H
(3b), R = CH_3

Upon reaction with butyllithium and potassium *tert*-butoxide in pentane, 1,4-dimethyl-1,4-dihydropyridine *(4b)*[5] is also metalated only at the position adjacent to the heteroatom. Subsequent reaction with deuterium oxide or chloromethylsilane leads to 82% of the 2-deuteriated *(5b)* or 41% of the 2-trimethylsilylated derivative *(5c)*, respectively. On the other hand, the homologous 1-methyl-1,4-dihydropyridine *(4a)*[5] can be deprotonated, depending on the selected metalating agent[6], either again at the "geometrically acidified"[7] olefinic position or, alternatively, at the "electronically acidified"[7] methylene group. Reaction with butyllithium and potassium *tert*-butoxide in pentane followed by addition of chlorotrimethylsilane afforded 3% 1-methyl-2-trimethylsilyl-1,4-dihydropyridine *(5a)* as the sole volatile product besides starting material and resins[3]. Using trimethylsilylmethylpotassium in tetrahydrofuran, however, we were able *for the first time to remove a proton from the allylic position of a dihydropyridine derivative and thus generate an organometallic 8 π-system*[8]. The intermediate, moderately stable at $-50\,^{\circ}C$, reacts with methyl iodide or chlorotrimethylsilane to give, respectively, a 1:1 mixture of 1,2-dimethyl-1,2-dihydropyridine *(6a)* and 1,4-dimethyl-1,4-dihydropyridine *(7a)* in 55% yield or 1-methyl-4-trimethylsilyl-1,4-dihydropyridine *(7b)* (6%)[3,9].

The differing behavior of the two *N*-methyldihydropyridines *(4a)* and *(4b)* is not particularly surprising. Introduction

[*] Prof. Dr. M. Schlosser, Dipl.-Chem. P. Schneider
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project 2.467.0.75 and 2.693.0.76).

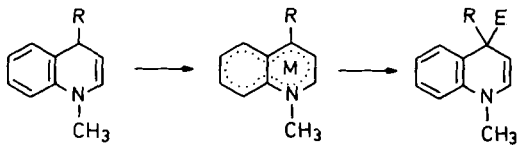


(5a), R = H, E = $Si(CH_3)_3$
(5b), R = CH_3, E = D
(5c), R = CH_3, E = $Si(CH_3)_3$

(4a), R = H
(4b), R = CH_3

(6a), E = CH_3 *(7a)*, E = CH_3
(7b), E = $Si(CH_3)_3$

of an alkyl substituent reduces the thermodynamic and, in particular, the "kinetic acidity"[7] of CH-groups. The attack at the double-allylic site being hindered by the additional methyl group [in *(4b)*], the otherwise [in *(4a)*] uncompetitive metalation at the olefinic position once again becomes more advantageous. On the other hand, attack at the site flanked by double bonds remains dominant, even after introduction of a methyl group, if the resonance area is extended, thus improving the delocalization of excess electrons. Both 1-methyl- *(8a)* and 1,4-dimethyl-1,4-dihydroquinoline *(8b)*[10] are smoothly deprotonated at the benzylic position by trimethylsilylmethylpotassium in tetrahydrofuran at −80 °C. The reaction of the two 12π-organometallic species with chloromethylsilane leads to 25% 1-methyl- *(9a)* and 47% 1,4-dimethyl-4-trimethylsilyl-1,4-dihydroquinoline *(9b)*[11], respectively.

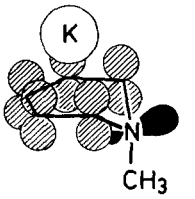


(8a), R = H
(8b), R = CH_3

(9a), *(9b)*, E = $Si(CH_3)_3$

The precise structure of the metalated heterocycles having a cyclic conjugated π-system is still unknown. The 8π-species *N*-methyldihydropyridylpotassium should, however, we assume, exist in an "envelope conformation" *(10)*, in which the horse-shoe shaped pentadienyl moiety serves as an η^5-ligand.

An analogous 8π-pyranylmetal species would present a much less favorable situation, since, due to the now unavoidable axial orientation, the second "free" electron pair on the heteroatom (O instead of N–CH_3) would produce a strong, conjugatively destabilizing ("antiaromatic") interaction with the 6π-pentadienyl system[12].



(10)

Received: February 13, 1979 [Z 214 IE]
German version: Angew. Chem. *91*, 515 (1979)

CAS Registry numbers:
(1a), 289-65-6; *(1b)*, 16855-95-1; *(2a)*, 19150-07-3; *(2b)*, 70287-77-3; *(2c)*, 70287-78-4; *(2d)*, 70287-79-5; *(2e)*, 70287-80-8; *(3a)*, 70287-81-9; *(3b)*, 70287-82-0; *(4a)*, 33666-44-3; *(4b)*, 57147-16-7; *(5a)*, 70287-83-1; *(5b)*, 70287-84-2; *(5c)*, 70287-85-3; *(6a)*, 70287-86-4; *(7b)*, 70287-87-5; *(8a)*, 30958-75-9; *(8b)*, 51483-74-0; *(9a)*, 70287-88-6; *(9b)*, 70287-89-7;

[1] *J. Hartmann, M. Schlosser*, Helv. Chim. Acta *59*, 453 (1976).
[2] a) *L. Brandsma, J. Strating* in Houben/Weyl: Methoden der organischen Chemie, Vol. VI/4, p. 109. Thieme, Stuttgart 1966; b) prepared by the same method as *(1a)*.
[3] All products gave correct elemental analyses and appropriate NMR and mass spectra. The low yields are due to incomplete metalation, but even more to the hypersensitivity of the pyran and dihydropyridine derivatives toward heat, oxygen, acids and organometallic compounds.
[4] a) *R. Paul, S. Tchelitcheff*, Bull. Soc. Chim. Fr. *1952*, 808; *V. Rautenstrauch*, Helv. Chim. Acta *55*, 594 (1972); b) *J. Hartmann, V. David, M. Schlosser*, unpublished (1975).
[5] *A. J. Birch, E. A. Karakhanov*, J. Chem. Soc. Chem. Commun. *1975*, 480.
[6] Other examples of reagent-controlled regioselectivity: cumene [1], phenylcyclopropane [*P. Schneider*, Dissertation, ETH Lausanne, Switzerland 1979].
[7] *M. Schlosser*: Struktur und Reaktivität polarer Organometalle. Springer-Verlag, Berlin 1973, pp. 64—83, 91—98.
[8] 3-Cyano- and 3-diethylamino-1-methyl-1,4-dihydropyridine have been smoothly metalated at the 2-position by lithium diisopropylamide at −80 °C [*R. R. Schmidt, C. Berger*, Chem. Ber. *109*, 2936 (1976)]. Upon treatment with butyllithium in tetrahydrofuran 1-phenyl-1,4-dihydropyridine appears to be mainly converted into the 2,6-dilithio derivative although products metalated at the *ortho* position of the phenyl ring are discussed as intermediates [*D. M. Stout, T. Takaya, A. I. Meyers*, J. Org. Chem. *40*, 563 (1975)].
[9] Subsequent treatment with trimethylsilylmethylpotassium and methyl iodide in pentane afforded 2% of a 1:1 mixture containing *(6a)* and *(7a)*.
[10] *A. J. Birch, P. G. Lehman*, J. Chem. Soc. Perkin Trans. I *1973*, 2754.
[11] In unpublished experiments *H. Ahlbrecht* and *K. Reucker* (cf. *K. Reucker*, Dissertation, Universität Giessen 1977) were able to deprotonate 1,3-dimethyl-2-phenyl-1,4-dihydroquinoline, activated by an additional aromatic moiety, at the methylene group and to obtain a series of 4-substituted derivatives.
[12] Evidence for the instability of 8π-pyranylmetal compounds was obtained by *R. R. Schmidt, U. Burkert, R. Prewo*, Tetrahedron Lett. *1975*, 3477; 2,4,6-triphenyl-4*H*-pyran, when establishing the acid/base equilibrium in the presence of lithium diisopropylamide at −80 °C, is deprotonated (at position 4) to the extent of only 50%. Under the same conditions, 2,6-diphenyl-4*H*-pyran does not undergo any noticeable change.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0606-0490 $ 02.50/0

Ullmanns Encyklopädie der technischen Chemie. Editorial board: *E. Bartholomé, E. Biekert, H. Ley* (deceased), *W. M. Weigert* (deceased), and *E. Weise.* Verlag Chemie, Weinheim—New York 1978, 4th Edit. Vol. 15: Korrosion bis Lacke (Corrosion to Paints and Varnishes). xv, 726 pp., bound, DM 475.00.—Vol. 16: Lagerwerkstoffe bis Milch (Bearing Materials to Milk). x, 734 pp., bound, DM 425.00.

With the appearance of Volumes 15 and 16, ten of the eighteen planned alphabetical volumes (7—24) of the 4th edition of Ullmann are now available[*]. The next few years will see the completion of this new edition of the encyclopedia—a truly impressive accomplishment by the editors, editorial board, and publisher.

Almost half of Volume 15 (302 pages) is devoted to the keyword plastics which merely considers general properties and processes—individual kinds of plastics are described under their own headings. The subject matter is presented in the following sections: historical (4 pages), introduction (35 pages), states of order and properties (34 pages), additives (21 pages), coloring (5 pages), processing (73 pages), testing (16 pages), analysis (26 pages), standardization (4 pages), economic significance and applications (9 pages), utilization of wastes (9 pages), plastics with special properties (28 pages), plastics as electrical insulators (38 pages). The introduction provides a terse survey of physicochemical and physical fundamentals of polymers, *i.e.* thermodynamics, reaction kinetics, and structure of macromolecular materials. The section on utilization of wastes deals with a highly topical development which is becoming more and more important (references up to 1978!).

Other keywords in Volume 15 are: corrosion (59 pages), crystals (83 pages with sections on crystallography and crystal properties), copper (100 pages, including copper alloys and copper compounds), cresols and xylenols (17 pages), artificial leather (8 pages), artists' colors (7 pages), paints and varnishes (138 pages).

Like the entry on plastics, those concerned with crystals and paints and varnishes have the character of introductory monographs. The large number of literature references given here, and elsewhere in Ullmann, are of great value in penetrating further into the field in question.

Volume 16 contains a great variety of keywords. For example lithium (17 pages), magnesium (39 pages), manganese (56 pages), with their alloys and compounds, and metallurgy (17 pages) come from the realm of inorganic chemistry. Organic chemistry is represented by maleic acid, malonic acid, melamine, methacrylic acid and methacrylates, methane, methanol, methylamines, organometallic compounds, and dyestuffs chemistry by methine dyes (35 pages), leuco vat dyes, metal complex dyes, and microscopy stains. From the field of natural products we have leather (69 pages), lignin, foodstuffs (76 pages, including sections on general aspects, preservation, additives, and packaging), milk and milk products (37 pages), lecithin, margarines and shortenings. Entries having a more technological slant will be found under inorganic phosphors (29 pages), generation of light (38 pages), magnetic materials (38 pages), magnetic media, solvents (33 pages), membranes (21 pages), microcapsules, bearing materials, soldering and brazing, protection of materials, metals/surface treatment.

Of course, entries under comprehensive keywords such as organometallic compounds and foodstuffs deal only with facts common to the whole field and with fundamental relationships; this is immediately apparent from the number of pages (*e.g.* 21 pages on organometallic compounds). More specialized information (say about organomagnesium compounds) will be found in the relevant entries (magnesium in the case mentioned).

As always, the individual keywords provide useful information about economic aspects (including production and consumption figures), quality demands, environmental problems, safety questions, and legal requirements. In this connection, special mention should be made of two tables from the contribution on solvents in this volume, which list physical properties as well as safety and physiological data.

It only remains to say that these two volumes fully comply with the high standard of presentation and product set by previous volumes of Ullmann.

Ulfert Onken [NB 467 IE]

Kirk-Othmer: Encyclopedia of Chemical Technology. Editors: *H. F. Mark, D. F. Othmer, C. G. Overberger,* and *G. T. Seaborg.* John Wiley & Sons, New York 1978, 3rd Edit. Vol. 2. Alkoxides, Metal to Antibiotics (Peptides). xxv, 1036 pp., bound, £ 50.00.—Vol. 3. Antibiotics (Phenazines) to Bleaching Agents. xxv, 958 pp., bound, £ 50.00.

Volumes 2 and 3 of the new edition of *Kirk-Othmer*[*] are now available. Both volumes are again distinguished by a purposeful selection of keywords, skilful subdivision, and a remarkable balance within the individual entries.

This can be seen in the article about ammonia (Vol. 2), which contains sections on: the physical and chemical properties of ammonia; thermodynamic and kinetic fundamentals of its production; production of synthesis gas (from coal, heavy hydrocarbon fractions, or natural gas); ammonia synthesis (including energetic and environmental aspects); storage and shipment of ammonia; production capacities and quantities together with production costs and prices; specifications, analytical methods, and questions of safety; uses (especially for production of fertilizers, plastics, and explosives).

A similar subdivision is found under the heading "benzene" (Vol. 3), where there are sections on: physical and chemical properties of benzene; production from petroleum (by reforming processes and cracking), from coal, and from other sources; production capacities and quantities, with prices; specifications, analytical methods, and aspects of safety; uses (*e.g.* for production of ethylbenzene, cumene, cyclohexane, nitrobenzene/aniline, maleic anhydride, chlorobenzene, *etc.*).

All the other entries concerned with substances (*e.g.* alkyl resins, aluminum/aluminum alloys, amines, amino acids, anthraquinone/anthraquinone derivatives, antibiotics, antistatics, asphalt, azo dyes, biopolymers) and with methodology and other topics (*e.g.* analytical methods, azeotropic and extractive distillation, batteries and electric cells) are without exception first-class presentations.

R. Steiner [NB 468 IE]

[*] Cf. Angew. Chem. Int. Ed. Engl. *18*, 88 (1979).

[*] Cf. Angew. Chem. Int. Ed. Engl. *18*, 237 (1979).

Ozonation in Organic Chemistry. Vol. 1: Olefinic Compounds. By *P. S. Bailey*. Academic Press, New York 1978. xiv, 272 pp., bound, £ 18.50.

Many summaries have appeared on the ozonolysis of alkenes, but up to now there has been no authoritative representation and discussion of the current state of affairs. The present monograph fills this gap. It is a fitting tribute to *Rudolf Criegee*, "a true gentleman, a dedicated scientist and teacher"; the author received the decisive stimulus for his scientific work in the Karlsruhe Laboratory.

Unlike "Organic Syntheses", the book is not a collection of recipes intended for hurried searchers; it is rather a conscientious account of a slice of chemical history. Ozonolysis is a prime example of the way in which mechanistic thinking acts as a stimulus to new experiments. The reviewer feels that the central part of the book consists of Chapters VI and VII, which describe the dramatic development in the determination of the mechanism of ozonolysis over the last 15 years.

Ozonides are formed by 1,3-dipolar cycloaddition, followed by a 1,3-dipolar cycloreversion of the primary ozonide and a renewed 1,3-dipolar cycloaddition of the carbonyl oxide to the carbonyl bond. If the carbonyl oxide had been generally recognized as a 1,3-dipole, the analogy with nitrones would have allowed the *syn,anti* isomerism to have been foreseen and have saved some false trails; the alternative mechanisms proposed by *Story* and *Murray* have not stood up to testing. *Criegee* himself lived to see the reinstatement of his mechanism of ozonolysis, and contributed to it with some brilliant experiments.

Much effort is still being devoted to the question of how the structure and the reaction conditions affect the *cis,trans* ratio of ozonides.

Advances in the oxidation and reduction of ozonides over the last two decades are also reported in detail (Chapter VIII), as are the numerous types of anomalous ozonolysis reactions (Chapter IX). The competition between ozonide formation and epoxidation (Chapter XI) can now be regarded as well understood, while gas phase ozonation (Chapter XII) is still very unclear in its mechanism and, because of the low yields, is also unattractive.

The literature (717 references) has been covered until the end of 1976. This volume is to be followed by a second, which will deal with the ozonation of alkynes, arenes, and heterocyclics, and with the reactions of ozone with nucleophilic agents and the CH bond. This first volume, in itself, deserves wide circulation.

Rolf Huisgen [NB 464 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Molecular Movements and Chemical Reactivity as Conditioned by Membranes, Enzymes, and Other Macromolecules. XVIth Solvay Conference on Chemistry, Brussels, November 22—November 26, 1976. Edited by *R. Lefever* and *A. Goldbeter*. John Wiley & Sons, London 1978. xiii, 346 pp., bound, £ 25.50.—ISBN 0-471-03541-6

Terpenoids and Steroids, Vol. 8. Senior Reporter: *J. R. Hanson*. The Chemical Society, London 1978. ix, 301 pp., bound, DM 115.00.—ISBN 0-85186-326-4.—A volume in the series "Specialist Periodical Reports"

Luminescence Spectroscopy. Edited by *M. D. Lumb*. Academic Press, London 1978. ix, 375 pp., bound, £ 24.00.—ISBN 0-12-459550-2

Electron Spectroscopy: Theory, Techniques, and Applications, Vol. 2. Edited by *C. R. Brundle* and *A. D. Baker*. Academic Press, New York 1978. xi, 287 pp., bound, $ 36.25.—ISBN 0-12-137802-0

Übungsbuch Höhere Festigkeitslehre. Elastizitätstheorie, Plastizitätstheorie, Viskoelastizitätstheorie. By *H. Göldner*. Physik-Verlag, Weinheim 1978. 367 pp., bound, DM 28.00.—ISBN 3-87664-037-7

Erratum

Due to an unfortunate printing error in the communication: Synthesis of Thymosin α_1, a Polypeptide of the Thymus by *Ch. Birr* and *U. Stollenwerk*, Angew. Chem. Int. Ed. Engl. *18*, 394 (1979), the yield given in reference [4b] *(S.-S. Wang et al.)* should read 9.2%.

Registered names, trademarks, etc. used in this journal, even without specific indication thereof, are not to be considered unprotected by law.

© Verlag Chemie, GmbH, D-6940 Weinheim, 1979. – Printed in West Germany by Zechnersche Buchdruckerei, Speyer/Rhein.

All rights reserved (including those of translation into foreign languages). No part of this issue may be reproduced in any form – by photoprint, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Only single copies of contributions, or parts thereof, may be reproduced for personal use. Copies reproduced and used other than for private purposes in an industrial or commercial undertaking are subject to copyright and, in such cases, a copyright fee must be paid to the VG WORT, Abteilung Wissenschaft, Goethestr. 49, 8000 München 2, from whom conditions of payment can be obtained on request.

Valid for users in the USA: The appearance of the code at the bottom of the first page of an article in this journal (serial) indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the condition, however, that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc., for copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Law. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For copying from back volumes of this journal see 'Permissions to Photo-Copy: Publisher's Fee List' of the CCC.

Editorial office: Boschstraße 12, D-6940 Weinheim, Germany, Telephone (06201) 14036. Telex 465516 vchwh d.

Editor: *O. Smrekar* · **Translation Editors:** *A. J. Rackstraw* and *A. Stimson*.

Publishers: Verlag Chemie, GmbH. (Managing Directors *Jürgen Kreuzhage* and *Hans Schermer*) Pappelallee 3, D-6940 Weinheim, Germany

Correspondence concerning advertisements should be addressed to Verlag Chemie, GmbH. (Advertising Manager *R. J. Roth*). Pappelallee 3. P.O. Box 1260/1280, D-6940 Weinheim, Germany. Telephone Weinheim (06201) 14031, Telex 465516 vchwh d.

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 7
July 1979
Pages 493 – 562

Synthesis and Biosynthesis of Alkoxylipids[**]

By Helmut K. Mangold[*]

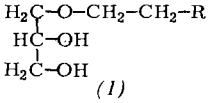
Chromatographic methods have shown that lipids with long alkyl or 1-alkenyl chains—called alkoxylipids or ether lipids—are widely distributed in human and animal tissues. These compounds comprise neutral alkoxylipids, *i.e.* 1-*O*-alkyl or 1-*O*-(1-alkenyl)-2,3-di-*O*-acylglycerols, and alkoxylipids which are linked by a phosphate residue at C-3 to aminoethanol, choline or serine. 1-*O*-Alkylglycerols, 1-*O*-(1-alkenyl)glycerols and other natural alkoxylipids can be synthesized in high yields. 2-Alkyl, 1,3-dialkyl and trialkylglycerols which are not found in nature are also accessible by synthesis. The neutral alkoxylipids are employed in biomedical investigations, *e.g.* as substrates in acyl-hydrolase systems or in fat absorption studies. The principal features of alkoxylipid biosynthesis have been elucidated. The alkyl residue is derived from a saturated or monounsaturated fatty acid *via* the corresponding alcohol. 1-*O*-(1-alkenyl)-2-*O*-acylglycerophosphoryl aminoethanols ("plasmalogens") are apparently formed from the appropriate 1-alkyl compounds; this is not possible in the case of the choline series. Both "aminoethanol" and "choline" plasmalogens are, nevertheless, present in most tissues.

1. Introduction

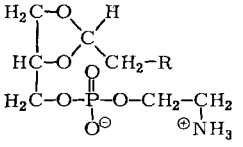
Water-soluble alkali salts of the higher fatty acids together with glycerol are formed almost exclusively after alkaline hydrolysis—"saponification"—of most plant and animal fats and oils which mainly consist of tri-*O*-acylglycerols ("triglycerides"). Saponification of lipids from tissues and organs of many marine animals results, on the other hand, in a high proportion of water-insoluble, neutral compounds which can be extracted from the aqueous alkaline reaction mixture with organic solvents. The unsaponifiable substances in the liver lipids of marine fish and mammals are chiefly hydrocarbons, particularly squalene[1], sterols[2] and long-chain alcohols with one[3] or more hydroxy groups[2,4].

In 1922 *Tsujimoto* and *Toyama*[5] discovered two compounds in the "unsaponifiable material" from the liver oils of sharks and rays which they called "batyl" and "selachyl alcohols". *Toyama*[6], who isolated a similar compound, "chimyl alcohol", from the liver of the ratfish *(Chimaera monstrosa)* suspected these three compounds to contain ether linkages formed from glycerol and long-chain alcohols but their structures were first elucidated by *Heilbron et al.* between 1928 and 1933[7–9]. Chimyl, batyl and selachyl alcohols are indeed 1-*O*-alkylglycerols *(1)* [hexadecyl, octadecyl and *cis*-9-octadecenylglycerols, respectively; strictly speaking selachyl alcohol is a 1-*O*-(9-alkenyl)glycerol][9]. *Baer* and *Fischer*[10] synthesized the D and L forms of chimyl and batyl alcohols and established that the natural compounds belong to the D series—they are 1-*O*-alkyl-*sn*-glycerols[10].

In 1924 *Feulgen* and *Voit*[11] discovered substances in animal tissues—"plasmalogens"—from which long-chain aldehydes could be liberated with acid. In the late thirties *Feulgen* and *Bersin*[12] isolated "aldehydogenic lipids" from bovine skeletal muscle to which they assigned an acetal phosphatide *(2)* structure. *Baer* and *Fischer*[10] advanced the hypothesis that alkylglycerols *(1)* and acetal phosphatides *(2)* might be biogenetically related.



(1)



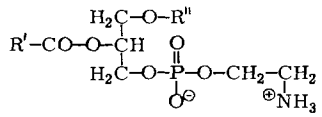
(2)

[*] Prof. Dr. H. K. Mangold
Institut für Biochemie und Technologie – H. P. Kaufmann-Institut – der Bundesanstalt für Fettforschung
Piusallee 68, D-4400 Münster (Germany)

[**] Based on a lecture given on the occasion of the presentation of the Heinrich Wieland Prize on October 28, 1977 in München (Germany).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/07 07-0493 $ 02.50/0*

Klenk and *Debuch*[13] obtained alkylglycerol derivatives by catalytic hydrogenation of plasmalogens. Since they could also detect acyl residues in the plasmalogens, they ruled out

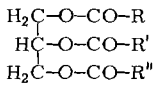


(3), R'' = CH=CH–R
(4), R'' = CH_2–CH_2–R
(5), R'' = CO–CH_2–R

the acetal phosphatide structure *(2)*. Studies in several laboratories[14-17] showed that plasmalogens are 1-*O*-(1-alkenyl)-2-*O*-acylglycerophospholipids such as *(3)*; in human and animal tissues they are always present together with the corresponding 1-*O*-alkyl compounds such as *(4)* as minor compounds associated with the 1-2-diacyl derivatives of type *(5)*[18]. It should be noted that "alkyl" and "1-alkenyl" alkoxylipids include substances which contain one double bond in the chain and/or one in the vinyl ether group.

In addition to compounds *(3)*—*(5)*, corresponding phospholipids have been found, particularly in central and peripheral nervous tissue, which contain choline or serine instead of ethanolamine. Human and animal depot fats have, in addition to triacylglycerols *(6)*, a usually small proportion of 1-*O*-alkyl- *(7)* and 1-*O*-(1-alkenyl)-2,3-*O*-diacylglycerols *(8)*[19] (cf. Scheme 1).

(Squalus acanthias) contains, in addition to 54% triacylglycerols *(6)*, approximately 38% alkyldiacylglycerols *(7)* and 0.5% alkenyldiacylglycerols *(9)*[29]. The liver lipids of the atlantic and pacific ratfish *(Chimaera monstrosa* and *Hydrolagus colliei*, respectively) consist of 66% *(7)* and 6% *(8)*[29,31].

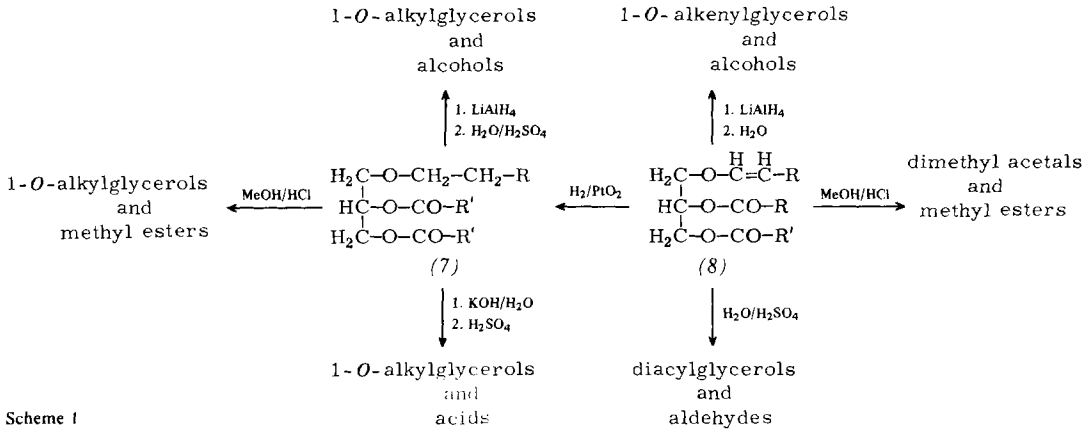


(6)

Compounds of type *(6)*—*(8)* can be separated from one another by thin-layer chromatography[21,30,33]. The neutral alkoxylipids in human adipose depots, as well as animal tissues and organs represent a fraction of less than 0.5%[30,32]; they are first concentrated by chromatography on "thick" layers of silica gel and then isolated from the concentrate[31,33].

The lipids of human and animal tumors contain considerably higher proportions of alkyldiacylglycerols *(7)* than normal tissues[34].

Ionic alkoxylipids are mainly found in the brain and peripheral nervous tissue of higher animals. The chromato-



Scheme 1

Ionic, *e.g. (3)* and *(4)*, and neutral derivatives of alkyl- and alkenylglycerols, *e.g. (7)* and *(8)*, were always identified earlier in mixtures by means of their cleavage products. These usually rather difficult studies were simplified considerably when, in 1960, complex mixtures of alkoxylipids and acyl lipids were resolved by thin-layer chromatography into classes of compounds[20-22]; each of these classes was subsequently separated into its components by gas chromatography[22-24]—or the acyl, alkyl and alkenyl residues could at least be analyzed. Methods for the synthesis of alkyl- and alkenylglycerols were soon greatly improved[25,26] and radioactively labeled alkoxylipids were synthesized[27]. In 1972 *Snyder*[28] published a comprehensive volume on the alkoxylipids.

2. Distribution, Isolation and Characterization of Alkoxylipids

The neutral alkoxylipids occur in especially high proportions in the liver of cartilaginous fish. The liver of the dogfish

graphic behavior of these phospholipids is chiefly determined by their polar groups; the influence of the long-chain residues is slight. Neither compounds *(3)*—*(5)*, nor the three corresponding choline or serine forms could be separated from one another. Mixtures of non-polar derivatives of these compounds can, however, be resolved into their diacyl, alkylacyl and alkenylacyl forms[35]. For analytical purposes it is, however, much more convenient to first split off the polar groups with phospholipase C from *Bacillus cereus*[36], then to acetylate the disubstituted glycerols[20,36] and fractionate the acetyl derivatives. The products can be completely separated from one another by adsorption chromatography[36,37].

Diacylglycerophospholipids such as *(5)* are more quickly saponified by dilute alkali than the alkoxylipids, the latter can thus be concentrated on a preparative scale[38]. Alkylacyl- and alkenylacylglycerophosphoryl cholines can be obtained by employing preferential hydrolysis of diacylglycerophosphoryl cholines with phospholipase C from *Clostridium welchii*[17] or phospholipase D from cabbage[39]. The ionic alkoxylipids can also be isolated after selective hydrolysis of

the 1-acyl residues of *(5)* or the corresponding cholines with pancreatic lipase[40,41].

IR[30,42] and NMR spectra[43] of alkoxylipids are of little use for the identification and characterization of these compounds. The characteristic, strong absorption band at 1667–1670 cm^{-1} is very useful for recognition of *cis*-1-alkenyl ethers[17,44].

The alkoxylipids, like most long-chain compounds, are polymorphous[45,46]. Hexadecyldipalmitoyl- and octadecyldistearoylglycerol both occur in two forms, (1-hexadecenyl)dipalmitoyl- and (1-octadecenyl)distearoylglycerol each exist in four forms[45]. These polymorphic lipids are well characterized by their critical solution temperatures with nitromethane or acetonitrile[47].

Very dilute chloroform solutions of batyl alcohol *(1)*, R = octadecyl, are weakly dextrorotatory, 10 percent solutions exhibit no optical activity whereas more concentrated solutions are weakly levorotatory[10,48]. The diacetates and the isopropylidene derivatives of 1-*O*-alkylglycerols have a considerably higher specific rotation than batyl alcohol[10]. Alkyldiacyl- *(7)* and alkenyldiacylglycerols *(8)* from the liver of the ratfish have a higher specific rotation than the nonacylated compounds[49].

Gas chromatographic analysis with "internal standards"[50] is the most reliable technique for the quantitative estimation of neutral and ionic lipids containing alkyl or alkenyl residues. Using the isotopic derivative technique[20], alkyl and alkenyldiacetylglycerols with labeled acetyl residues are resolved by thin-layer chromatography and determined radiometrically[51].

The acyl, alkyl and alkenyl residues of alkoxylipids such as *(7)* and *(8)* are usually analyzed by gas chromatography in the form of methyl esters, alkylisopropylideneglycerols, or aldehydes or dimethyl acetals. Scheme 1 shows how the alkoxylipids can be converted into these derivatives[30,52].

Specific reactions and separations are required for the analysis of the acyl residues of ionic alkoxylipids in mixtures of glycerophospholipids containing the same base[53].

Alkyl- and 1-alkenylglycerols can be obtained from neutral[30,31] and ionic alkoxylipids[54,55] by using water to split the complexes formed with $LiAlH_4$. This deacylation reaction is suitable for the isolation and analysis of alkyl- and 1-alkenylglycerols from very small quantities of material.

The alkylglycerols are purified by thin-layer chromatography and then separated by gas chromatography after having been converted into alkylisopropylideneglycerols[30,56] or alkylglycolaldehydes[24,57].

In order to analyze the 1-alkenyl groups, mixtures of aldehydes are obtained by acid-catalyzed hydrolysis of the neutral *(8)* or ionic plasmalogens, *e.g. (3)*[30,58], or mixtures of dimethyl acetals are produced by reaction with methanol[30,52]. The aldehydes[30,52] and their dimethyl acetals[30] can easily be separated by gas chromatography. Interference due to formation of *cis*- and *trans*-1-alkenylalkyl ethers[59] can be overcome by reducing the aldehydes to alcohols, which are then acetylated and analyzed[30,31].

If the acid-catalyzed hydrolysis of the 1-alkenyl derivatives is carried out directly on the thin-layer chromatogram, the reaction products can be separated from one another and from the unmodified diacyl- and alkylacylglycerolipids[60].

Whereas in the lipids of human and animal tissues saturated and unsaturated fatty acids with up to six double bonds are esterified[52], the alkyl and 1-alkenyl residues of the alkoxylipids contain a maximum of one double bond, besides a vinyl ether double bond. Table 1 shows a typical example.

Apart from alkyl and 1-alkenyl moieties with 16 or 18 carbon atoms, only small quantities of residues with other chain lengths are found. In the light of these findings, a biogenetic relationship between lipids which contain alkyl and 1-alkenyl moieties[10] seems indeed to be reasonable. This hypothesis is supported by the fact that alkyl and 1-alkenyl moieties with 18 carbon atoms in alkoxylipids from the liver of cartilaginous fish have their additional double bond mainly in the 9-position[62,63], the additional double bond of residues with 20 carbon atoms is in the 13-position[62]. Surprisingly, the 1-*O*-acyl, -alkyl and -1-alkenyl residues from the neutral lipids of liver of the ratfish contain a relatively large proportion of branched chains (2.6, 5.0 and 16.4% respectively) whereas the 2-*O*-acyl residues are almost all unbranched[37]. The alkoxylipids of the heart and milk of ruminants are also rich in branched alkyl and alkenyl moieties[53,64].

A variety of glyceroglycolipids in human and animal tissues are also derived from 1-*O*-alkylglycerols[65].

The unsaponifiable fraction of the neutral and ionic lipids from the liver of the Greenland shark *(Somniosus microce-*

Table 1. Alkyl and 1-alkenyl groups in the alkoxylipids of human heart [a] [61] (Tr. = trace). *(7)*: alkyldiacylglycerols; *(4)* and *(14)*: alkylacylglycerophosphoryl aminoethanols and cholines, respectively; *(8)*: 1-alkenyldiacylglycerols; *(3)* and *(3a)*: 1-alkenylacylglycerophosphoryl aminoethanols and cholines, respectively.

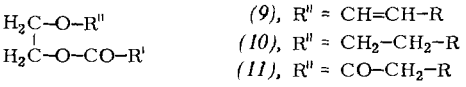
Chain length : No. of double bonds [b]	Alkyl groups in			1-Alkenyl groups in		
	(7) [%]	*(4)* [%]	*(14)* [%]	*(8)* [%]	*(3)* [%]	*(3a)* [%]
< 14	Tr.	4.1	3.8	—	—	—
14 : 0 br.	—	1.9	—	—	—	—
14 : 0	Tr.	1.5	1.5	Tr.	Tr.	Tr.
15 : 0 br.	Tr.	Tr.	Tr.	Tr.	Tr.	Tr.
15 : 0	Tr.	1.0	1.7	1.5	0.4	1.0
16 : 0 br.	Tr.	—	—	Tr.	Tr.	Tr.
16 : 0	35.3	41.9	50.5	60.8	35.3	62.6
17 : 0 br. / (16 : 1)	Tr.	Tr.	Tr.	3.0	Tr.	Tr.
17 : 0	Tr.	Tr.	Tr.		3.2	Tr.
18 : 0 br.	—	Tr.	Tr.	Tr.	Tr.	3.5
18 : 0	39.0	31.9	21.5	20.4	38.9	16.8
18 : 1	25.7	17.7	21.0	14.3	20.5	14.2
18 : 2	Tr.	Tr.	Tr.	Tr.	1.6	1.9
> 18	Tr.	Tr.	Tr.	Tr.	Tr.	Tr.

[a] Woman, 42 years old. [b] The number before the colon signifies the chain length, that after the colon the number of double bonds. br. = branched.

phalus)[66] and other marine organisms[67] contains 1-*O*-(2-methoxyhexadecyl)- and 1-*O*-(2-methoxyoctadecyl)glycerols. Derivatives of these methoxyalkylglycerols also occur in bone marrow, in the erythrocytes and milk of humans and various animals[68]. Particularly in the liver of the Greenland shark—as opposed to almost all animal tissues so far studied—there are also lipids with polyunsaturated methoxyalkyl residues[67]. In addition to the esters of 1-*O*-alkyl- and 1-*O*-(2-methoxyalkyl)glycerols, the liver oil of the Greenland shark contains 1-*O*-(2-hydroxyalkyl)glycerol esters[69]. The Harderian gland of the rabbit contains hydroxysubstituted alkyldiacylglycerols whose hydroxy groups are esterified with long-chain fatty acids and are located in the middle of the alkyl chains[70].

Very small quantities of the phospholipids which are derivatives of 1,2-di-*O*-alkyl-*sn*-glycerols are found in human[71] and bovine[72] heart. The halophilic bacterium *Halobacterium cutirubrum* contains relatively high proportions of phospho- and glycolipids derived from 2,3-di-*O*-phytanyl-*sn*-glycerol[73,74]. Similar compounds have been found in *Sulfolobus acidocaldarius*[75] and *Thermoplasma acidophilum*[76].

The tissues of marine invertebrates and also other organisms contain, in addition to lipids with a glycerol backbone, long-chain diol derivatives with two to five carbon atoms. These "diol lipids" together with diol phospholipids and glycolipids are widely distributed in the plant and animal kingdoms[77,78]. The starfish *Distolasterias nipon* is especially rich in diol lipids[78]. Approximately 35% of its lipids are derived from ethanediol; they contain—in addition to diacylethanediols *(11)*—alkylacyl- *(10)* and 1-alkenylacylethanediols ("neutral diol plasmalogens") *(9)*[78]. The diol lipids are generally identified indirectly *via* their cleavage fragments[77,78], but at least the neutral ones can be separated from the corresponding glycerol derivatives[79,80].



It remains to be mentioned that alkyl ethers of cholesterol[81] are present in bovine heart and that very small quantities of the corresponding 1-alkenyl ethers are found in bovine and pig heart[82]. The jaw of the dolphin *Phocoena phocoena* also contains unusual alkoxylipids, di-*O*-alkylpentanediols whose alkyl moieties have almost exclusively 18 carbon atoms[83].

Methods for isolating and identifying natural alkoxylipids have been described in detail[84].

The natural alkoxylipids and often their symmetrical analogs are used in biomedical investigations. Methods for the characterization and analysis of these unusual lipids have been developed[85–87]. The trialkylglycerols which are accessible by synthesis only[88] are utilized, especially in fat absorption studies and clinical tests. A lipid fraction from the preputial gland of the mouse which was considered to consist of trialkylglycerols[89], was identified as a mixture of alkyl acetates[90].

3. Synthesis of Alkoxylipids

As chromatographic methods became available for lipid analysis, it was possible to study the synthesis of these natural products with better prospects of success. Systematic syntheses for natural alkoxylipids and related compounds were developed in the sixties.

3.1. Alkyl Ethers

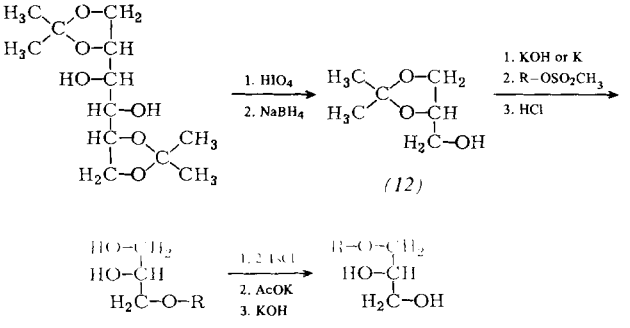
Methods for synthesizing 1-*O*-alkylglycerols *(1)* are of special interest because many other alkoxylipids can be obtained from these compounds relatively simply.

An earlier procedure based on alkylation of allyl alcohols with long-chain alkyl halides and subsequent oxidation of the alkyl allyl ethers[2,91] is, of course, only suitable for the synthesis of saturated alkylglycerols—as racemic mixtures. The classical synthesis starts with isopropylideneglycerol *(12)* which is alkylated with alkyl iodides[10] or tosylates[92]. The 1-*O*-alkylglycerols *(1)* are obtained from the alkylisopropylideneglycerols after splitting off the protecting group with aqueous inorganic acid[10,92]. Since, in the synthesis of selachyl alcohol according to the above method, most of the *cis*-9-octadecenyl moiety is converted into the *trans* moiety, the compound is obtained by reacting isopropylideneglycerol tosylate with sodium *cis*-9-octadecenoate[93]. Transalkylation occurs however[25], so that a dialkyl ether is formed as the main product and the yield of selachyl alcohol is under 20%[93].

Alkylation of the two optically active isopropylideneglycerols *(12)* with alkyl iodides or tosylates forms the basis for investigations which permit the configurational characterization of the natural alkylglycerols. They belong to the D series and are thus 1-*O*-alkyl-*sn*-glycerols[10].

A comparison of methods for the synthesis of these compounds led to the development of a procedure[25] which has since been used almost exclusively: isopropylideneglycerol *(12)* is condensed with an alkylmethanesulfonate ("alkyl mesylate") in boiling benzene in the presence of potassium; if this reaction is performed in xylene in the presence of potassium hydroxide then the water produced is removed by azeotropic distillation[25]. 1-*O*-Alkylglycerols *(1)* are obtained with yields of up to 80% by cleavage of the protecting group with hydrochloric acid. This procedure is suitable for the synthesis of saturated, mono- and polyunsaturated 1-*O*-alkylglycerols, also in their optically active forms[49] (Scheme 2). In this way we were able to synthesize a useful, radioactively labeled compound, 1-*O*-[1'-^{14}C]hexadecylglycerol.

Scheme 2 also shows how the naturally occurring D-isomers can be obtained from the easily accessible "unnatural" 3-*O*-alkyl-*sn*-glycerols, the L-isomers: Walden inversion of the L-*(1)* tosylate with potassium acetate in ethanol and subsequent alkaline hydrolysis leads to the desired products[94].



Scheme 2 L-*(1)* D-*(1)*

1-*O*-(2′-Methoxyalkyl)glycerols[66,67] can be obtained from methyl 2-bromopalmitate *via* methyl 2-methoxypalmitate, 1-methoxyhexadecanol, subsequent reaction of the tosylate or mesylate with isopropylideneglycerol *(12)* and cleavage of the protecting group[66,95]. 1-*O*-(2-Hydroxyalkyl)glycerols have also been synthesized[96].

The symmetrical 2-*O*-alkylglycerols, which have not as yet been detected in nature, have proved to be of value in biomedical investigations. 2-*O*-Alkylglycerols—also those with double bonds — can easily be synthesized by alkylation of 1,3-benzylideneglycerol with alkyl iodides[97], tosylates[98] or in especially good yields with alkylmethanesulfonates[87] and subsequent acid-catalyzed cleavage of benzaldehyde.

The isomeric alkylglycerols can be converted into their diesters with acyl chlorides in benzene/pyridine[85,87,99]; 1-*O*-alkyl-2-acylglycerols[100] and 1-acyl-2-*O*-alkylglycerols[87] result from the diesters by enzymatic hydrolysis of the ester bond in the α-position.

The 1,2-di-*O*-alkylglycerols can be obtained by alkylation of α-trityl[73,101] or α-tetrahydropyranylglycerol[102] and cleavage of the protecting group. Both methods are suitable if optically active glycerol derivatives are used as starting materials and also for the synthesis of enantiomeric 1,2-di-*O*-alkylglycerols; they cannot be used, however, if two different alkyl residues are to be introduced into positions 1 and 2 of glycerol. Such "mixed" compounds can be produced by alkylation of 1-*O*-alkyl-3-*O*-tritylglycerols and cleavage of the protecting group[88].

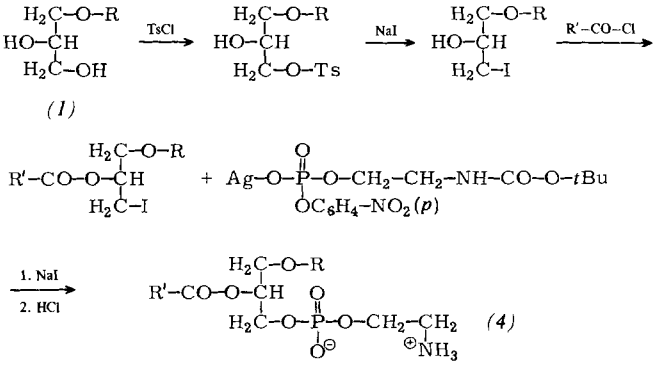
1,3-Di-*O*-alkylglycerols can be synthesized by partial alkylation of 1-*O*-alkylglycerols[88] or by alkylation of 2-*O*-benzylglycerol and subsequent hydrogenolytic cleavage of the protecting group[103]. The first procedure leads, however, to mixtures which must be separated by chromatography whilst the second method can only be used for the synthesis of saturated compounds. 1,3-Di-*O*-alkylglycerols, and also those with double bonds, are furnished by reaction of 1,3-dichloropropanol with sodium alkoxides; the yields, however, are not satisfactory[87].

The synthesis of trialkylglycerols is relatively complicated. It has not yet been possible to alkylate glycerol with alkyl halides or mesylates in good yields, nor to react alkoxides with tribromopropane or tri-*O*-mesylglycerol to give trialkylglycerols. This is not due so much to the different solubilities of the reaction partners but to steric hindrance. It seems worthwhile, however, to try out the phase transfer technique. The isomeric alkylglycerols[87,88], like the isomeric dialkylglycerols[87,102], can be further alkylated in approximately equally good yields. Ideally, triacylglycerols *(6)* should be converted directly into trialkylglycerols. Reduction with $LiAlH_4$ and BF_3 in ether affords the desired compounds but with yields of under 5%[104].

Glycol cleavage of 1-*O*-alkylglycerols with sodium periodate in pyridine[57] gives alkylglycolaldehydes which can be reduced with $LiAlH_4$ to *O*-alkylethanediols[79]; both reactions are quantitative. Di-*O*-alkylethanediols and dialkyl ethers of other diols can be obtained by alkylation of diols[105] or alkyl diols[79].

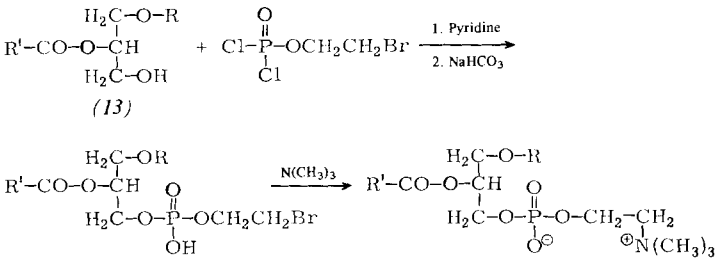
Alkyl ethers of cholesterol are produced in good yields if mesylates are reacted with cholesterol in the presence of potassium hydroxide in boiling benzene[106].

Methods for the synthesis of diacylglycerophosphoryl aminoethanols *(5)* and cholines are also suitable for the synthesis of alkylacyl- and dialkylglycerophospholipids (see [107,108]).



(1) *(4)*

These and similar phospholipids can be synthesized by condensation of disubstituted glycerophosphoric acid with a "protected" aminoethanol[100,109].



(13)

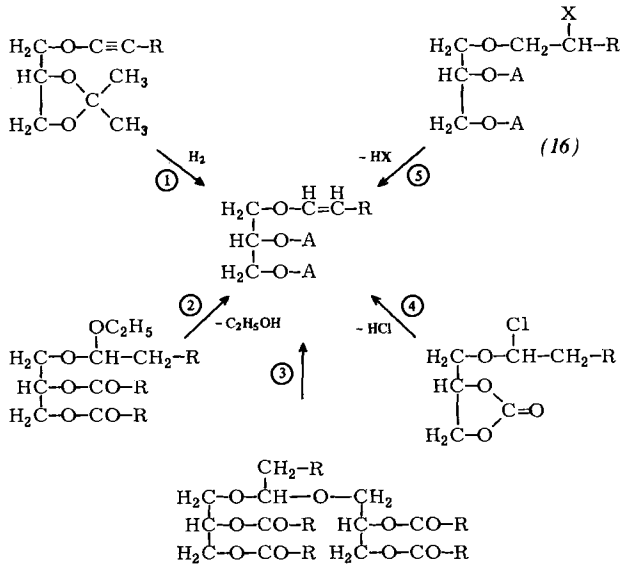
Disubstituted glycerophosphoryl cholines[110] such as 1-*O*-alkyl-2-acyl- *(14)*[100,108], 1-acyl-2-*O*-alkyl-[41,111], 1,2- and 1,3-di-*O*-alkylglycerophosphoryl cholines[112,113] together with the lyso compounds (*e. g.* 1-*O*- and 2-*O*-alkylglycerophosphoryl cholines[114]) can be produced from the glycerol derivatives *(13)*.

Phosphorylation of *(13)* with phosphorus oxide chloride and reaction of the product with choline chloride in pyridine yields disubstituted glycerophosphoryl cholines[94].

The methods described are also suitable for the synthesis of diol phospholipids. In addition to the natural ionic alkoxylipids, analogous compounds are often used in biochemical investigations. The synthesis of these substances has been described in two reviews[115].

3.2. 1-Alkenyl Ethers

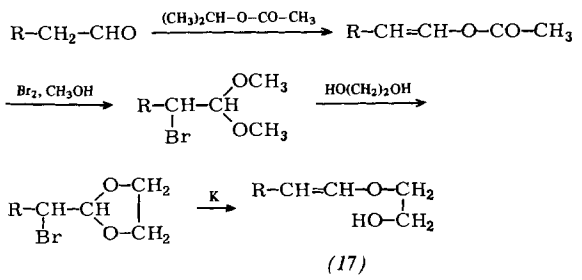
Several groups of workers have tried to synthesize 1-*O*-(1-alkenyl)glycerols (Scheme 3, A = H or CO R). Attempts to obtain these substances by partial hydrogenation of a 1-alkynyl derivative with the Lindlar catalyst (method 1) failed[116]. Elimination of ethanol (method 2) or cleavage of diacylglycerol (method 3) from the acetals *(15)* proved to be of limited use[117,118]. On thermal decomposition of such acetals, *trans*-1-alkenyl derivatives are formed almost exclusively[119], whereas the natural plasmalogens have a *cis* configuration[17,44]. Elimination of hydrogen chloride from 1-*O*-(1-chloroalkyl)glycerol carbonate (method 4) can be utilized[119]. *Cis-trans* mixtures are also formed in this reaction but there is a relatively large proportion of the desired *cis* compound and it can be isolated by argentation chromatog-



Scheme 3 (15)

raphy[120]. This synthesis (method 4) also provides optically active substances corresponding to the natural 1-*O*-(1-alkenyl)-*sn*-glycerols and the neutral and ionic plasmalogens[120,121]. As is the case with the enantiomeric 1-*O*-alkylglycerols *(1)*[94], the *sn*-1 and *sn*-3 isomeric 1-*O*-(1-alkenyl)glycerols can be converted into one another by Walden inversion *via* their ditosylates (see Scheme 2)[122]. The elimination of *p*-toluenesulfonic acid or hydrogen iodide from the substituted derivatives *(16)* (method 5) is suitable for the synthesis of 1-*O*-(1-alkenyl)glycerols and their esters *(8)*[123]. Plasmalogens of type 3[124] and a "cardiolipin plasmalogen"[125] have been synthesized by this procedure.

The synthesis of neutral and ionic diol plasmalogens is much simpler than that of the corresponding glycerol derivatives. In the synthesis of 1-alkenylethanediols *(17)*, *cis-trans* mixtures are produced which can be separated by chromatography on silver-nitrate-impregnated silica gel[126]. Acylation of *cis* and *trans (17)* gives neutral diol plasmalogens and their *trans* isomers [cf. *(9)*][127].



(17)

Syntheses which include a reaction with a halogen or hydrogen halide are not suitable for compounds containing an additional double bond in their 1-alkenyl residues. Such glycerol and ethanediol derivatives can, however, be easily obtained from animal tissues. Hydrogenolysis of the total lipids from bovine heart gives a mixture of alcohols, alkylglycerols and 1-alkenylglycerols—providing the resulting complexes with $LiAlH_4$ are cleaved with water and not acid (cf. Scheme 1)[55]. The 1-alkenylglycerols can be easily isolated as a class of lipids by silica gel chromatography; the pure compounds can then be isolated by reversed-phase chromatography. Periodate cleavage of 1-*O*-(1-alkenyl)glycerol mixtures in pyridine gives the 1-alkenyl derivatives of glycolaldehyde; reduction of these compounds furnishes 1-alkenylethanediols which can be separated by chromatography[55]. The isolation of alkenylglycerols and their conversion to alkenylethanediols has, in contrast to all purely synthetic methods, the advantage that separation of the desired *cis* compounds from the *trans* isomers is not necessary. An interesting chapter is devoted exclusively to the chemistry of the "aldehydogenic lipids"[128].

4. Biosynthesis and Metabolism of Alkoxylipids

1-*O*-Alkylglycerols are synthesized relatively quickly in the animal organism and then undergo further reactions. In the mid-fifties, radioactively labeled substrates had already been used to demonstrate that the starfish *Asterias rubens* incorporated glycerol and acetate into its acyl lipids (ester lipids) and alkoxylipids (ether lipids)[129]. The rat absorbs alkylglycerols administered with its food almost completely in the small intestine[130]. In the gastrointestinal tract some of these compounds are esterified and some are cleaved; the corresponding fatty acids are formed in the presence of molecular oxygen[130,131].

4.1. Biosynthesis

The prime interest in investigations aimed at elucidating alkoxylipid biosynthesis was to answer the following questions:

1. What is the relationship between the alkoxylipids (ether lipids) and the acyl lipids (ester lipids)?
2. Are the alkyl residues formed from 1-alkenyl residues or *vice versa*?
3. Why do the alkyl and 1-alkenyl residues contain, in addition to the vinyl ether double bond a maximum of one double bond, while the acyl residues can be polyunsaturated?

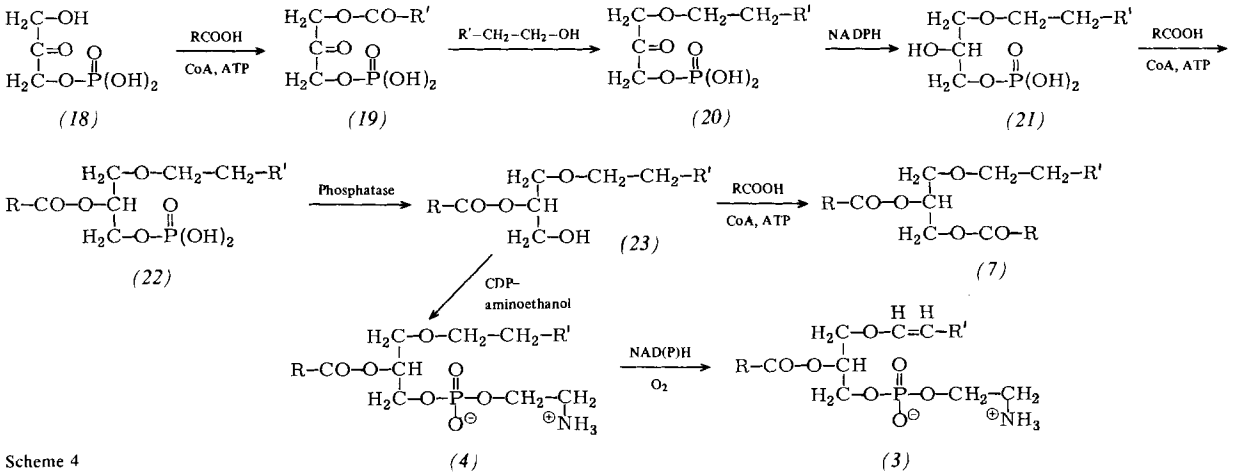
Comparison of the double bond positions in the monounsaturated chains of the neutral alkoxylipids from the liver of the ratfish showed there was a great deal of similarity between the structures of the alkyl, 1-alkenyl and acyl chains[62]. This finding supported the hypothesis that the long-chain alkyl and 1-alkenyl residues are formed from the corresponding fatty acids (cf. also[63,132]).

The results from experiments on dog heart-lung preparations indicated that saturated long-chain alcohols are incorporated into the 1-alkenyl residues of ionic plasmalogens more quickly than aldehydes or acids[133]. The same applies to the digestive organ of the starfish *Asterias forbesi*[134] and the isolated shark stomach[135]. Experiments on the snail *Arion ater* and on *Tetrahymena pyriformis* finally demonstrated that derivatives of 1-*O*-(1-alkenyl)glycerols — plasmalogens—can be produced from 1-*O*-alkylglycerols[136]. According to metabolic studies with radioactively labeled palmitic or stearic acid or the corresponding aldehydes, alcohols or alkylglycerols, the alkyl and 1-alkenyl moieties of alkoxylipids are apparently synthesized as follows:

Fatty acid → aldehyde → alcohol → alkyl chain → 1-alkenyl chain

"Free" aldehydes have been detected in rat and dog heart[137]. In addition, the corresponding "free" alcohols have been isolated from bovine heart[138]. The alcohols and aldehydes in animal tissues are always saturated or monounsaturated and they mostly have chains with 16 or 18 carbon atoms[90, 137, 139].

About ten years ago systematic investigations in several laboratories led to the elucidation of alkoxylipid biosynthesis in animal tissues (see Scheme 4). If liver mitochondria or



(18) (19) (20) (21) (22) (23) (7) (4) (3)

Scheme 4

heart microsomes are incubated with dihydroxyacetone phosphate *(18)* and a long-chain alcohol in the presence of ATP, CoA, NaF and Mg^{2+}, 1-*O*-alkyldihydroxyacetone phosphate *(20)* is formed[140]. The same reaction is inhibited by *p*-chloromercuribenzoate in microsomes from the intestinal mucosa of the rat[141]—glyceraldehydephosphoric acid does not act as an acceptor for the alkyl residue[142].

If an acyldihydroxyacetone phosphate *(19)* is used as alkyl acceptor, the 1-*O*-alkyl derivative *(20)* is formed in the absence of CoA[143]. Compounds of type *(20)* have been characterized as intermediates in alkoxylipid biosynthesis[144] but it is still not clear how acyl/alkyl exchange is achieved. If [^{18}O]-hexadecanol is employed as substrate *in vivo* or *in vitro*, ^{18}O is found in the alkoxy groups of the alkoxylipids which are produced[145]. In the reaction *(19)*→*(20)*, a hydrogen atom is released from C-1 of the *sn*-glycerol residue[146] and replaced by a hydrogen atom from the medium[147]; the configuration of the substituents at C-1 is retained[148]. 1-*O*-Alkyl-*sn*-glycero-3-phosphate *(21)* results from 1-*O*-alkyldihydroxyacetone phosphate *(20)* in a NADPH-dependent reaction which is catalyzed by a microsomal enzyme[149]; *(21)* is acylated to *(22)*[140, 149]. This compound is dephosphorylated by a Mg^{2+}-dependent microsomal enzyme to 1-*O*-alkyl-2-*O*-acyl-*sn*-glycerol *(23)*[150]; neutral and ionic 1-*O*-alkylglycerol derivatives, *e.g. (7)* and *(4)*, are synthesized from *(23)* by reactions which are known from the biochemistry of the 1-2-diacylglycerols[150].

It has been shown that the alkyl residues are not formed from 1-alkenyl residues[151, 152].

Experiments on animal tissues[100, 152] and cell-free systems[153, 154] have demonstrated that the 1-*O*-alkyl-2-*O*-acyl-*sn*-glycerophosphoryl aminoethanols *(4)* are the direct precursors of the 1-*O*-(1-alkenyl) derivatives ("aminoethanol plasmalogens") *(3)*. The 1-alkenyl residues are produced by *cis*-elimination of the (1*S*) and (2*S*) hydrogen atoms of the alkyl residue[155]. The enzyme catalyzing this reaction is bound to the microsomal membrane. It requires molecular oxygen and NAD(P)H as cofactors[153, 154] and probably also cytochrome b_5[154, 156]. This desaturase is stimulated by proteins[153, 157].

The cholines *(14)* corresponding to the aminoethanols *(4)* are not dehydrated to plasmalogens[153, 158].

Each step of alkoxylipid biosynthesis has been studied exclusively with substrates which have saturated chains with 16 or 18 carbon atoms. It cannot therefore be seen from Scheme 4 why the alkyl and 1-alkenyl moieties of the alkoxylipids contain, in addition to the vinyl ether double bond, at the most one double bond.

If food rich in lipids containing polyunsaturated fatty acids or aldehydes are given to rats, this does not influence the composition of the alkyl and 1-alkenyl residues[159, 160]. If the animals are fed, however, with polyunsaturated alcohols[159, 161], polyunsaturated chains are found in these residues[159-163].

The lack of polyunsaturated alkyl and 1-alkenyl residues in the alkoxylipids of human and animal tissues is apparently due to the fact that their precursors, *i.e.* polyunsaturated alcohols, are not present in these tissues. It seems reasonable to assume that, as has long been known[164], saturated fatty acids are reduced to alcohols in the organism—probably *via* aldehydes; the same applies to monounsaturated but not to polyunsaturated fatty acids.

Several authors have indeed demonstrated that the CoA derivatives of saturated fatty acids are reduced to aldehydes[165] and also that aldehydes are reduced to alcohols[166, 167]. It is thus understandable that only saturated and monounsaturated alcohols can be found in animal tissues[139] and excrement[159, 168, 169], even if the animals have ingested highly unsaturated triacylglycerols[159] or fatty acids[168].

Several groups of workers have recently investigated the substrate specificity of the enzymes involved in alkoxylipid biosynthesis. Equimolar mixtures of acids[169] and also equimolar mixtures of aldehydes[170], alcohols[171] and alkylglycerols[172] were fed to rats and the incorporation of these compounds in the alkoxylipids of the intestinal mucosa determined. One group of these mixtures consisted of saturated substances with 13, 15, 17 and 19 carbon atoms whilst the other group contained compounds with 19 carbon atoms and 0, 1 and 2 double bonds[173]. Since the lipids of rat tissues

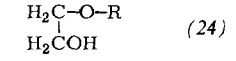
only contain very small proportions of chains with an odd number of carbon atoms, it is easy to follow the metabolism of the compounds in the mixtures given by gas chromatographic analysis of the alkyl, 1-alkenyl and acyl groups. It has to be assumed, of course, that the components of the mixed substrates are not converted into one another. This condition is satisfied, at least in the case of the aldehydes, alcohols and alkylglycerols.

Analysis of the alkyl and 1-alkenyl residues in the ionic alkoxylipids of the rat intestinal mucosa showed that the enzymes involved in the biosynthesis of the alkoxylipids from fatty acids exhibit strong substrate specificity as regards both chain length and the number of double bonds in the precursors[159, 162, 170, 172].

Metabolic studies on complex lipids should therefore not be performed solely with substrates of a defined chain length and containing a defined number of double bonds—and also not only with minute quantities of radioactively labeled compounds. If the components do not react with one another, it would seem advantageous to feed a mixture of substrates instead of single compounds. In contrast to metabolic studies employing radioactively labeled compounds, substrate saturation in such a nutritional experiment is assured.

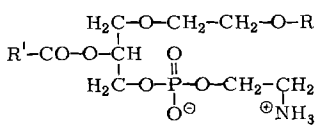
The possibility of modifying lipid composition by dietetic methods and thus of altering the absorption properties of the intestinal mucosa may be of interest for the therapy of diseases of the alimentary canal.

Long-chain 1,2-diols are incorporated into 1-*O*-(2-hydroxyalkyl)glycerophosphoryl aminoethanols and cholines in rat brain[174]; long-chain ketoalcohols give rise to the corresponding 1-*O*-(1-oxoalkyl)glycerols[175].

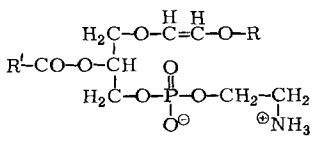


(24)

It may be expected that the 1-alkenyl derivatives of ethanediol such as *(17)* can, like the glycerol compounds, result from alkyl ethers of type *(24)*. This is, however, not the case; the derivatives *(24)* are treated by the organism like simple long-chain alcohols[176]. 1-(2-Alkoxyethyl)-2-*O*-acylglycerophosphoryl aminoethanol *(25)* is thus formed which can also be dehydrogenated to the plasmalogen analog *(26)*[176].



(25)



(26)

In addition to *(25)*, a choline derivative is also produced; however, in analogy with the glycerophospholipids, this is not dehydrogenated to a plasmalogen analog[175].

4.2. Metabolism

1-*O*-Alkylglycerols[161, 172, 177] and their esters[178] given in food are well tolerated by man and animals, even in relatively large amounts. Some of the alkylglycerols are absorbed in their unmodified form[130, 161, 179] and some are cleaved whereby the alkyl residues give rise to the corresponding fatty acids[130, 179]. It is remarkable that the natural 1-*O*-alkyl-*sn*-glycerols are acylated in the intestinal mucosa but the "unnatural" 3-*O*-alkyl-*sn*-glycerols are not[180]. 1-*O*-Alkylglycerophosphoryl aminoethanols and cholines are also rapidly acylated in the mucosa[100]. Plasmalogens are synthesized from 1-*O*-alkyl-2-*O*-acylglycerophosphoryl aminoethanols *(4)* but not from the corresponding cholines *(14)*[100]. Alcohols added to feed are found in the alkyl residues but not in the 1-alkenyl residues of the alkoxylipids in the blood of experimental animals[181]; the alcohols do not seem to penetrate the blood-brain barrier[182]. Little is known about the behavior of 2-*O*-alkylglycerols and their esters in animal organisms.

The toxicity of the isomeric di-*O*-alkylglycerols and their esters has not yet been studied. By using radioactively labeled 1,2- and 1,3-di-*O*-alkylglycerols it has been established that absorption of these compounds does not depend on the position of the alkyl residues but to a great extent on their chain lengths. Over 50% of the two isomeric dioctylglycerols but only 10% of the dioctadecylglycerols are absorbed intact[112]. The 1,2-di-*O*-alkylglycerols are acylated more quickly in the digestive tract than their symmetrical isomers[112]. 1,2-Di-*O*-alkylglycerophosphoryl aminoethanols and cholines are poorly absorbed[112]. It is interesting that the absorption of sterols is inhibited by dialkylglycerophosphoryl cholines[183].

The trialkylglycerols are not toxic[184, 185, 188]. As long as these compounds have chains with more than 12 carbon atoms they are not hydrolytically cleaved in the alimentary canal of the rat[186, 188] or the pig[187] but are excreted in unmodified form[186, 188]. As trialkylglycerols do not affect the absorption of fats and fat-soluble vitamins[188], edible fats can be "diluted" with these "non-fattening fats"—and thus their nutritional value can be reduced—without significantly changing their physical and organoleptic properties[184]. The utilization of trialkylglycerols in the food industry is hindered by the high cost of these substances. Moreover, the trialkylglycerols are oxidized much more easily than the triacylglycerols, the proper "fats"[185, 189].

It is not yet known what the function of the alkoxylipids in the organism may be.

5. Use of Alkoxylipids in Biomedical Investigations

Alkoxy- and acyl-lipids have similar physical properties; they behave differently, however, towards acids, bases and lipolytic enzymes. Lipids which contain alkyl moieties can normally be used as stable model substances in biological systems in which acyl lipids are enzymatically cleaved.

The stereospecificity of lipoprotein lipase from human and animal tissues has been studied with enantiomeric alkyldiacylglycerols containing ^{3}H- and ^{14}C-labeled alkyl or acyl chains[190]. 1,2-Di-*O*-alkyl-3-*O*-acylglycerols and 1,3-di-*O*-alkyl-2-*O*-acylglycerols with radioactively labeled acyl residues were similarly used to determine the positional specificity of lipoprotein lipases[191, 192]. According to these experiments, the specificity of these enzymes encompasses the substrate configuration, the position of the acyl group at the glycerol, the chain length and the number of double bonds[192, 193].

Radioactively labeled 1-*O*- and 2-*O*-alkylglycerols[194] together with 1,2- and 1,3-di-*O*-alkylglycerols[112] have been employed in research on fat absorption. It was deduced from absorption studies with labeled trialkylglycerols[187, 188, 195] that triacylglycerols, "fats", cannot be absorbed intact, *e.g.* by pinocytosis[186].

After it had been appreciated how unreliable the ^{131}I-triolein test was for quantitative determination of fat malabsorption[196], clinical methods of investigation were developed which were based on the utilization of radioactively labeled trialkylglycerols[187, 197, 198]. It was recommended that patients be given ([9,10-$^3H_2$]hexadecyl)didodecylglycerol as a non-absorbable indicator together with ([1-^{14}C]trioleoyl)glycerol as "fat". The proportion of fat absorbed can be calculated from the change in the isotope ratio (^{3}H:^{14}C) after passage of the two compounds through the alimentary canal[197].

1-*O*-Alkylglycerophosphoryl cholines and their derivatives[199], together with 1-*O*-alkyl-2-acyl- *(14)* and 1,2-di-*O*-alkylglycerophosphoryl cholines[200] have been used in studies on lipid-lipid and lipid-protein interactions; these investigations should provide a contribution towards the understanding of the construction and function of biological membranes.

6. Outlook

Many questions are still open: Why do plant tissues not contain any or only small quantities of alkoxylipids? What are the functions of the plasmalogens in the brain? Which physiological processes can be influenced by changing the alkoxylipid composition of the organs? Why do cancerous cells have considerably larger proportions of alkyldiacylglycerols than normal cells?

Reports concerning the amazing actions of alkoxylipids have appeared repeatedly for over 30 years. Alkylglycerols are supposed to have bactereostatic action, protect against radiation, aid in the healing of wounds and inhibit tumor growth. Until recently, these effects were obtained solely with substances isolated from animal tissues. Synthetic compounds were, on the other hand, inactive. The biological effects so far observed are probably due to impurities in the alkoxylipids.

Received: September 8, 1978 [A 276 IE]
German version: Angew. Chem. *91*, 550 (1979)

[1] *M. Tsujimoto*, Ind. Eng. Chem. *8*, 889 (1916).
[2] *C. Dorée*, Biochem. J. *4*, 72 (1909).
[3] *E. Andre, M. T. François*, C. R. Acad. Sci. *183*, 663 (1926); *T. P. Hilditch, J. A. Lovern*, J. Soc. Chem. Ind. *48*, 365 (1929).
[4] *A. Kossel, S. Edlbacher*, Hoppe-Seylers Z. Physiol. Chem. *94*, 264 (1915).
[5] *M. Tsujimoto, Y. Toyama*, Chem. Umschau Geb. Fette, Öle, Wachse, Harze *29*, 27, 35, 43 (1922); *Y. Toyama, ibid. 29*, 237, 245 (1922).
[6] *Y. Toyama*, Chem. Umschau Geb. Fette, Öle, Wachse, Harze *31*, 61 (1924).
[7] *I. M. Heilbron, W. M. Owens*, J. Chem. Soc. *1928*, 942.
[8] *G. G. Davies, I. M. Heilbron, W. M. Owens*, J. Chem. Soc. *1930*, 2542.
[9] *W. H. Davies, I. M. Heilbron, W. E. Jones*, J. Chem. Soc. *1933*, 165.
[10] *E. Baer, H. O. L. Fischer*, J. Biol. Chem. *140*, 397 (1941).
[11] *R. Feulgen, K. Voit*, Pflügers Arch. Gesamte Physiol. Menschen Tiere *206*, 390 (1924).
[12] *R. Feulgen, Th. Bersin*, Hoppe-Seylers Z. Physiol. Chem. *260*, 217 (1939).
[13] *E. Klenk, H. Debuch*, Hoppe-Seylers Z. Physiol. Chem. *296*, 179 (1954).
[14] *M. M. Rapport, R. E. Franzl*, J. Biol. Chem. *225*, 851 (1957); *M. M. Rapport, B. Lerner, N. Alonzo, R. E. Franzl, ibid. 225*, 859 (1957).
[15] *G. V. Marinetti, J. Erbland, E. Stotz*, J. Am. Chem. Soc. *80*, 1624 (1958); *81*, 861 (1959).
[16] *H. Debuch*, Hoppe-Seylers Z. Physiol. Chem. *311*, 266 (1958); *317*, 182 (1960).
[17] *H. R. Warner, W. E. M. Lands*, J. Am. Chem. Soc. *85*, 60 (1963).
[18] *H. E. Carter, D. B. Smith, D. N. Jones*, J. Biol. Chem. *232*, 681 (1958); *L. Svennerholm, H. Thorin*, Biochim. Biophys. Acta *41*, 371 (1960).
[19] *J. C. M. Schogt, P. Haverkamp-Begemann, J. Koster*, J. Lipid Res. *1*, 446 (1959).
[20] *H. K. Mangold*, Fette, Seifen, Anstrichm. *61*, 877 (1959).
[21] *H. K. Mangold, D. C. Malins*, J. Am. Oil Chem. Soc. *37*, 383 (1960).
[22] *D. C. Malins, H. K. Mangold*, J. Am. Oil Chem. Soc. *37*, 576 (1960).
[23] *R. Blomstrand, J. Gürtler*, Acta Chem. Scand. *13*, 1466 (1959).
[24] *D. C. Malins*, Chem. Ind. (London) *1960*, 1359.
[25] *W. J. Baumann, H. K. Mangold*, J. Org. Chem. *29*, 3055 (1964).
[26] *J. Gigg, R. Gigg*, J. Chem. Soc. *C 1968*, 16.
[27] *H. K. Mangold*, J. Labelled Compd. *4*, 3 (1968).
[28] *F. Snyder*: Ether Lipids, Chemistry and Biology. Academic Press, New York 1972.
[29] *H. K. Mangold, K. D. Mukherjee*, J. Chromatogr. Sci. *13*, 398 (1975).
[30] *H. H. O. Schmid, H. K. Mangold*, Biochem. Z. *346*, 13 (1966).
[31] *H. H. O. Schmid, W. J. Baumann, H. K. Mangold*, Biochim. Biophys. Acta *144*, 344 (1967).
[32] *N. Tuna, H. K. Mangold* in *R. D. Jones*: Evolution of the Atherosclerotic Plaque. University of Chicago Press, Chicago 1963.
[33] *H. H. O. Schmid, L. L. Jones, H. K. Mangold*, J. Lipid Res. *8*, 692 (1967).
[34] *R. Wood, F. Snyder*, J. Lipid Res. *8*, 494 (1967); *F. Snyder, R. Wood*, Cancer Res. *28*, 972 (1968); *29*, 251 (1969).
[35] *O. Renkonen*, Acta Chem. Scand. *21*, 1108 (1967); J. Lipid Res. *9*, 34 (1968).
[36] *O. Renkonen*, Biochim. Biophys. Acta *125*, 288 (1966).
[37] *W. J. Baumann, T. Takahashi, H. K. Mangold, H. H. O. Schmid*, Biochim. Biophys. Acta *202*, 468 (1970).
[38] *D. J. Hanahan, R. Watts*, J. Biol. Chem. *236*, PC 59 (1961); *O. Renkonen*, Acta Chem. Scand. *17*, 634 (1963).
[39] *W. E. M. Lands, P. Hart*, Biochim. Biophys. Acta *98*, 532 (1965).
[40] *G. H. de Haas, L. Sarda, J. Roger*, Biochim. Biophys. Acta *106*, 638 (1965).
[41] *A. J. Slotboom, G. H. de Haas, P. P. M. Bonsen, G. J. Burbach-Westerhuis, L. L. M. van Deenen*, Chem. Phys. Lipids *4*, 15 (1970).
[42] *W. J. Baumann, H. W. Ulshöfer*, Chem. Phys. Lipids *2*, 114 (1968).
[43] *J. Cymerman Craig, D. P. G. Hamon*, J. Org. Chem. *30*, 4168 (1965); *H. H. O. Schmid, W. J. Baumann, H. K. Mangold*, J. Am. Chem. Soc. *89*, 4797 (1967).
[44] *W. T. Norton, E. L. Gottfried, M. M. Rapport*, J. Lipid Res. *3*, 456 (1962).
[45] *A. Seher, F. Spener, H. K. Mangold* in *H. G. Wiedemann*: Thermal Analysis. Birkhäuser, Basel 1972, Vol. 3, p. 109.
[46] *A. Seher*, Chem. Phys. Lipids *8*, 134 (1972); *A. Seher, G. Werner, ibid. 11*, 203 (1973).
[47] *H. H. O. Schmid, H. K. Mangold, W. O. Lundberg, W. J. Baumann*, Microchem. J. *11*, 306 (1966).
[48] *Y. Toyama, T. Ishikawa*, J. Chem. Soc. Jpn. *59*, 1367 (1938).
[49] *W. J. Baumann, V. Mahadevan, H. K. Mangold*, Hoppe-Seylers Z. Physiol. Chem. *347*, 52 (1966).
[50] *K. L. Su, H. H. O. Schmid*, Lipids *9*, 208 (1974).
[51] *H. K. Mangold*, unpublished work.
[52] *H. H. O. Schmid, N. Tuna, H. K. Mangold*, Hoppe-Seylers Z. Physiol. Chem. *348*, 370 (1967).
[53] *H. H. O. Schmid, T. Takahashi*, Biochim. Biophys. Acta *164*, 141 (1968).
[54] *G. A. Thompson, Jr., P. Lee*, Biochim. Biophys. Acta *98*, 151 (1965).
[55] *W. J. Baumann, H. H. O. Schmid, J. K. G. Kramer, H. K. Mangold*, Hoppe-Seylers Z. Physiol. Chem. *349*, 1677 (1968).
[56] *D. J. Hanahan, J. Ekholm, C. M. Jackson*, Biochemistry *2*, 630 (1963).
[57] *W. J. Baumann, H. H. O. Schmid, H. K. Mangold*, J. Lipid Res. *10*, 132 (1969).
[58] *Z. L. Bandi*, Chem. Phys. Lipids *3*, 309 (1969).
[59] *V. Mahadevan, F. Phillips, C. V. Viswanathan*, Chem. Phys. Lipids *2*, 183 (1968).
[60] *H. H. O. Schmid, H. K. Mangold*, Biochim. Biophys. Acta *125*, 182 (1966); *L. A. Horrocks*, J. Lipid Res. *9*, 469 (1968).
[61] *F. Spener, H. K. Mangold*, J. Lipid Res. *10*, 609 (1969).
[62] *H. H. O. Schmid, P. C. Bandi, H. K. Mangold, W. J. Baumann*, Biochim. Biophys. Acta *187*, 208 (1969).
[63] *F. Spener, H. K. Mangold*, J. Lipid Res. *12*, 12 (1971).
[64] *J. C. M. Schogt, P. Haverkamp-Begemann, J. H. Recourt*, J. Lipid Res. *2*, 142 (1961).
[65] *W. T. Norton, M. Brotz*, Biochem. Biophys. Res. Commun. *12*, 198 (1964); *I. Ishizuka, M. Suzuki, T. Yamakawa*, J. Biochem. (Tokyo) *73*, 77 (1973); *B. L. Slomiany, A. Slomiany, G. B. J. Glass*, Eur. J. Biochem. *78*, 33 (1977).

[66] *B. Hallgren, G. Ställberg*, Acta Chem. Scand. *21*, 1519 (1967).
[67] *B. Hallgren, A. Niklasson, G. Ställberg, H. Thorin*, Acta Chem. Scand. *B 28*, 1035 (1974).
[68] *B. Hallgren, A. Niklasson, G. Ställberg, H. Thorin*, Acta Chem. Scand. *B 28*, 1029 (1974).
[69] *B. Hallgren, G. Ställberg*, Acta Chem. Scand. *B 28*, 1074 (1974).
[70] *K. Kasama, W. T. Rainey, Jr., F. Snyder*, Arch. Biochem. Biophys. *154*, 648 (1973).
[71] *M. Popović*, Hoppe-Seylers Z. Physiol. Chem. *340*, 18 (1965); *E. L. Pugh, M. Kates, D. J. Hanahan*, J. Lipid Res. *18*, 710 (1977).
[72] *G. V. Marinetti, J. Erbland, E. Stotz*, Biochim. Biophys. Acta *33*, 403 (1959).
[73] *M. Kates, B. Palameta, L. S. Yengoyan*, Biochemistry *4*, 1595 (1965).
[74] *M. Kates, L. S. Yengoyan, P. S. Sastry*, Biochim. Biophys. Acta *98*, 252 (1965); *M. Kates, B. Palameta, M. B. Perry, G. A. Adams, ibid. 137*, 213 (1967).
[75] *T. A. Langworthy, W. R. Mayberry, P. F. Smith*, J. Bacteriol. *119*, 106 (1974).
[76] *T. A. Langworthy*, Biochim. Biophys. Acta *487*, 37 (1977).
[77] *O. Lindberg*, Ark. Kemi *16 A*, N 15 (1943); *23 A*, N 2 (1946); *L. D. Bergelson, V. A. Vaver, N. V. Prokazova, A. N. Ushakov, G. A. Popkova*, Biochim. Biophys. Acta *116*, 511 (1966).
[78] *V. A. Vaver, N. A. Pisareva, B. V. Roznov, A. N. Ushakov*, Chem. Phys. Lipids *7*, 75 (1971).
[79] *W. J. Baumann, H. H. O. Schmid, H. W. Ulshöfer, H. K. Mangold*, Biochim. Biophys. Acta *144*, 355 (1967).
[80] *H. P. Kaufmann, H. K. Mangold, K. D. Mukherjee*, J. Lipid Res. *12*, 506 (1971); *M. Calderon, W. J. Baumann*, Biochim. Biophys. Acta *210*, 7 (1970); review: *L. D. Bergelson*, Fette, Seifen, Anstrichm. *75*, 89 (1973).
[81] *H. Funasaki, J. R. Gilbertson*, J. Lipid Res. *9*, 766 (1968).
[82] *J. R. Gilbertson, H. H. Garlich, R. A. Gelman*, J. Lipid Res. *11*, 201 (1970).
[83] *U. Varanasi, D. C. Malins*, Science *166*, 1158 (1969).
[84] Reviews: *C. V. Viswanathan*, Chromatogr. Rev. *98*, 129 (1974); *H. H. O. Schmid, P. C. Bandi, K. L. Su*, J. Chromatogr. Sci. *13*, 478 (1975); *H. K. Mangold, K. D. Mukherjee*, Ergeb. Exp. Med. *20*, 118 (1976).
[85] *W. J. Baumann, H. K. Mangold*, Biochim. Biophys. Acta *116*, 570 (1966).
[86] *H. H. O. Schmid, W. J. Baumann, J. M. Cubero, H. K. Mangold*, Biochim. Biophys. Acta *125*, 189 (1966); *R. Wood, W. J. Baumann, F. Snyder, H. K. Mangold*, J. Lipid Res. *10*, 128 (1969).
[87] *G. F. Cegla, H. K. Mangold, H. Greten*, J. Am. Oil Chem. Soc., in press.
[88] *W. J. Baumann, H. K. Mangold*, J. Org. Chem. *31*, 498 (1966).
[89] *F. M. Helmy, M. H. Hack*, Comp. Biochem. Physiol. *23*, 329 (1967).
[90] *F. Spener, H. K. Mangold, G. Sansone, J. G. Hamilton*, Biochim. Biophys. Acta *192*, 516 (1969).
[91] *N. Kornblum, H. N. Holmes*, J. Am. Chem. Soc. *64*, 3045 (1942).
[92] *E. Baer, L. J. Rubin, H. O. L. Fischer*, J. Biol. Chem. *155*, 447 (1944).
[93] *E. Baer, H. O. L. Fischer, L. J. Rubin*, J. Biol. Chem. *170*, 337 (1947).
[94] *G. K. Chacko, D. J. Hanahan*, Biochim. Biophys. Acta *164*, 252 (1968).
[95] *G. Ställberg*, Chem. Ser. *7*, 31 (1975).
[96] *T. Muramatsu, H. H. O. Schmid*, Chem. Phys. Lipids *9*, 123 (1972).
[97] *T. H. Bevan, T. Malkin*, J. Chem. Soc. *1960*, 350.
[98] *S. C. Gupta, F. A. Kummerow*, J. Org. Chem. *24*, 409 (1959).
[99] *L. J. Stegerhoek, P. E. Verkade*, Rec. Trav. Chim. Pays-Bas *75*, 143 (1956).
[100] *F. Paltauf*, Biochim. Biophys. Acta *260*, 352 (1972).
[101] *P. J. Thomas, J. H. Law*, J. Lipid Res. *7*, 453 (1966).
[102] *F. Paltauf, F. Spener*, Chem. Phys. Lipids *2*, 168 (1968).
[103] *R. Damico, R. C. Callahan, F. H. Mattson*, J. Lipid Res. *8*, 63 (1967).
[104] *H. C. Go, A. L. Branen*, J. Am. Oil Chem. Soc. *52*, 427 (1975).
[105] *D. A. Shirley, J. R. Zietz, Jr., W. H. Reedy*, J. Org. Chem. *18*, 378 (1953).
[106] *F. Paltauf*, Monatsh. Chem. *99*, 1277 (1968).
[107] Review: *A. J. Slotboom, H. M. Verheij, G. H. de Haas*, Chem. Phys. Lipids *11*, 295 (1973); *F. J. M. Daemen, G. H. de Haas, L. L. M. van Deenen*, Rec. Trav. Chim. Pays-Bas *82*, 487 (1963).
[108] *F. Paltauf, H. Hauser, M. C. Phillips*, Biochim. Biophys. Acta *249*, 539 (1971).
[109] *F. Paltauf*, Chem. Phys. Lipids *17*, 148 (1976); *I. Barzilay, Y. Lapidot, ibid. 3*, 280 (1969); *R. Aneja, J. S. Chadha, A. P. Davies*, Biochim. Biophys. Acta *218*, 102 (1970); *F. Paltauf, A. Holasek*, J. Biol. Chem. *248*, 1609 (1973).
[110] *R. Hirt, R. Berchtold*, Pharm. Acta Helv. *33*, 349 (1958).
[111] *H. U. Weltzien, O. Westphal*, Justus Liebigs Ann. Chem. *709*, 240 (1967).
[112] *F. Paltauf*, Biochim. Biophys. Acta *176*, 818 (1969).
[113] *H. Eibl, D. Arnold, H. U. Weltzien, O. Westphal*, Justus Liebigs Ann. Chem. *709*, 226 (1967).
[114] *D. Arnold, H. U. Weltzien, O. Westphal*, Justus Liebigs Ann. Chem. *709*, 234 (1967).
[115] Reviews: *F. Paltauf*, Chem. Phys. Lipids *11*, 270 (1973); *A. F. Rosenthal*, Methods Enzymol. *35*, 429 (1975).
[116] *M. V. Berezovskaya, I. K. Sarycheva, N. A. Preobrazhenskii*, Zh. Obshch. Khim. *34*, 543 (1964); *G. K. Chacko, K. Schilling, E. G. Perkins*, J. Org. Chem. *32*, 3698 (1967).
[117] *E. N. Zvonkova, I. K. Sarycheva, N. A. Preobrazhenskii*, Dokl. Akad. Nauk SSSR *159*, 1079 (1964); *T. V. Serebryakova, E. N. Zvonkova, G. A. Serebrennikova, N. A. Preobrazhenskii*, Zh. Org. Khim. *2*, 2004 (1966).
[118] *A. J. Slotboom, G. H. de Haas, L. L. M. van Deenen*, Chem. Phys. Lipids *1*, 192 (1967).
[119] *J. Cunningham, R. Gigg*, J. Chem. Soc. *1963*, 2968.
[120] *J. Gigg, R. Gigg*, J. Chem. Soc. *C 1967*, 431.
[121] *J. Gigg, R. Gigg*, J. Chem. Soc. *C 1967*, 1865.
[122] *V. I. Titov, G. A. Serebrennikova, T. P. Sobesskaya, R. P. Evstigneeva*, Zh. Org. Khim. *6*, 2412 (1971).
[123] *I. B. Vtorov, G. A. Serebrennikova, R. P. Evstigneeva*, Tetrahedron Lett. *1971*, 4605; *I. B. Vtorov, G. A. Serebrennikova, N. A. Preobrazhenskii*, Zh. Org. Khim. *6*, 669 (1970).
[124] *G. A. Serebrennikova, A. V. Chebyshev, I. B. Vtorov, G. N. Fedorova, R. P. Evstigneeva*, Khim. Prir. Soedin. *7*, 825 (1971); Zh. Org. Khim. *8*, 1171 (1972).
[125] *V. I. Titov, G. A. Serebrennikova, R. P. Evstigneeva*, Zh. Org. Khim. *8*, 1166 (1972).
[126] *J. K. G. Kramer, H. K. Mangold*, Chem. Phys. Lipids *3*, 176 (1969).
[127] *J. K. G. Kramer, H. K. Mangold*, Chem. Phys. Lipids *4*, 332 (1970).
[128] *N. A. Preobrazhenskii, G. A. Parfenov* in *R. Bognár, V. Bruckner, Cs. Szántay*: Recent Developments in the Chemistry of Natural Carbon Compounds. Akadémiai Kiadó, Budapest 1971, Vol. 4, p. 19.
[129] *M. L. Karnovsky, A. F. Brumm*, J. Biol. Chem. *216*, 689 (1955).
[130] *S. Bergström, R. Blomstrand*, Acta Physiol. Scand. *38*, 166 (1956).
[131] *A. Tietz, M. Lindberg, E. P. Kennedy*, J. Biol. Chem. *239*, 4081 (1964).
[132] *F. Snyder, M. L. Blank*, Arch. Biochem. Biophys. *130*, 101 (1969).
[133] *R. W. Keenan, J. B. Brown, B. H. Marks*, Biochim. Biophys. Acta *51*, 226 (1961).
[134] *J. Ellingboe, M. L. Karnovsky*, J. Biol. Chem. *242*, 5693 (1967).
[135] *S. J. Friedberg, R. C. Greene*, J. Biol. Chem. *242*, 5709 (1967).
[136] *G. A. Thompson, Jr.*, Biochim. Biophys. Acta *152*, 409 (1968); *V. M. Kapoulas, G. A. Thompson, Jr., ibid. 187*, 594 (1969).
[137] *J. R. Gilbertson, W. J. Ferrell, R. A. Gelman*, J. Lipid Res. *8*, 38 (1967).
[138] *J. R. Gilbertson, R. C. Johnson, R. A. Gelman, C. Buffenmeyer*, J. Lipid Res. *13*, 491 (1972).
[139] *T. Takahashi, H. H. O. Schmid*, Chem. Phys. Lipids *4*, 243 (1970); *M. L. Blank, F. Snyder*, Lipids *5*, 337 (1970).
[140] *A. K. Hajra*, Biochem. Biophys. Res. Commun. *37*, 486 (1969).
[141] *F. Paltauf*, Biochim. Biophys. Acta *260*, 345 (1972).
[142] *F. Snyder, B. Malone, R. L. Wykle*, Biochem. Biophys. Res. Commun. *34*, 40 (1969).
[143] *A. K. Hajra*, Biochem. Biophys. Res. Commun. *39*, 1037 (1970).
[144] *F. Snyder, B. Malone, M. L. Blank*, J. Biol. Chem. *245*, 1790 (1970).
[145] *F. Snyder, W. T. Rainey, Jr., M. L. Blank, W. H. Christie*, J. Biol. Chem. *245*, 5853 (1970).
[146] *S. J. Friedberg, A. Heifetz, R. C. Greene*, J. Biol. Chem. *246*, 5822 (1971); Biochemistry *11*, 297 (1972).
[147] *S. J. Friedberg, A. Heifetz*, Biochemistry *12*, 1100 (1973).
[148] *S. J. Friedberg, A. Heifetz*, Biochemistry *14*, 570 (1975); *S. J. Friedberg, R. D. Alkek, ibid. 16*, 5291 (1977).
[149] *R. L. Wykle, C. Piantadosi, F. Snyder*, J. Biol. Chem. *247*, 2944 (1972).
[150] *F. Snyder, M. L. Blank, B. Malone*, J. Biol. Chem. *245*, 4016 (1970).
[151] *H. Fürniss, J. Strosznajder, H. Debuch*, Hoppe-Seylers Z. Physiol. Chem. *354*, 697 (1973).
[152] *F. Paltauf*, FEBS Lett. *17*, 118 (1971).
[153] *F. Paltauf, A. Holasek*, J. Biol. Chem. *248*, 1609 (1973).
[154] *R. L. Wykle, M. L. Blank, B. Malone, F. Snyder*, J. Biol. Chem. *247*, 5442 (1972).
[155] *W. Stoffel, D. LeKim*, Hoppe-Seylers Z. Physiol. Chem. *352*, 501 (1971).
[156] *F. Paltauf, R. A. Prough, B. S. S. Masters, J. M. Johnston*, J. Biol. Chem. *249*, 2661 (1974).
[157] *R. C. Baker, R. L. Wykle, J. S. Lockmiller, F. Snyder*, Arch. Biochem. Biophys. *177*, 299 (1976); *F. Paltauf*, Eur. J. Biochem. *85*, 263 (1978).
[158] *H. H. O. Schmid, T. Muramatsu, K. L. Su*, Biochim. Biophys. Acta *270*, 317 (1972); *F. Paltauf*, FEBS Lett. *20*, 79 (1972).
[159] *Z. L. Bandi, E. Aaes-Jørgensen, H. K. Mangold*, Biochim. Biophys. Acta *239*, 357 (1971).
[160] *Z. L. Bandi, I. Reichwald-Hacker, H. K. Mangold*, unpublished work.
[161] *Z. L. Bandi, H. K. Mangold, G. Hølmer, E. Aaes-Jørgensen*, FEBS Lett. *12*, 217 (1970).
[162] *Z. L. Bandi, H. K. Mangold*, unpublished work.
[163] *K. L. Su, H. H. O. Schmid*, J. Lipid Res. *13*, 452 (1972).
[164] *D. Stetten, Jr., R. Schoenheimer*, J. Biol. Chem. *133*, 347 (1940).
[165] *R. C. Johnson, J. R. Gilbertson*, J. Biol. Chem. *247*, 6991 (1972); *C. O. Rock, V. Fitzgerald, F. Snyder*, Arch. Biochem. Biophys. *186*, 77 (1978).
[166] *R. J. Kessler, W. J. Ferrell*, Int. J. Biochem. *5*, 365 (1974).
[167] *J. C. Kawalek, J. R. Gilbertson*, Arch. Biochem. Biophys. *173*, 649 (1976).
[168] *Z. L. Bandi, H. K. Mangold*, FEBS Lett. *13*, 198 (1971).
[169] *Z. L. Bandi, H. K. Mangold*, FEBS Lett. *31*, 97 (1973).
[170] *I. Reichwald-Hacker, H. Becker, H. K. Mangold*, unpublished work.
[171] *Z. L. Bandi, H. K. Mangold*, Nutr. Metab. *22*, 190 (1978).
[172] *I. Reichwald, H. K. Mangold*, Nutr. Metab. *21* (Suppl. 1), 198 (1977).

[173] H. K. Mangold, H. Becker, U. Cramer, F. Spener, Chem. Phys. Lipids 17, 176 (1976).
[174] T. Muramatsu, H. H. O. Schmid, J. Lipid Res. 12, 740 (1971).
[175] N. Chang, H. H. O. Schmid, J. Biol. Chem. 250, 4877 (1975).
[176] H. H. O. Schmid, P. C. Bandi, Th. H. Madson, W. J. Baumann, Biochim. Biophys. Acta 488, 172 (1977).
[177] W. E. Carlson, H. S. Bayley, Can. J. Anim. Sci. 48, 315 (1968).
[178] R. Hardy, P. R. Mackie, J. Sci. Food Agric. 22, 382 (1971).
[179] R. Blomstrand, Proc. Soc. Exp. Biol. Med. 102, 662 (1959).
[180] F. Paltauf, Biochim. Biophys. Acta 239, 38 (1971).
[181] S. J. Friedberg, Lipids 11, 587 (1976).
[182] R. A. Gelman, J. R. Gilbertson, Nutr. Metab. 18, 169 (1975).
[183] P. J. O'Connor, J. B. Rodgers, Biochim. Biophys. Acta 450, 402 (1976).
[184] H. K. Mangold, A. Meizies, H. Becker, I. Reichwald, G. Cegla, Proc. 4th Internatl. Rapeseed Conference, Giessen 1974, p. 719.
[185] V. Müller, Fette, Seifen, Anstrichm. 78, 412 (1976).
[186] F. Spener, F. Paltauf, A. Holasek, Biochim. Biophys. Acta 157, 368 (1968).
[187] W. E. Carlson, H. S. Bayley, Br. J. Nutr. 28, 295 (1972).
[188] R. G. H. Morgan, A. F. Hofmann, J. Lipid Res. 11, 223 (1970).
[189] N. Yanishlieva, H. Becker, H. K. Mangold, Chem. Phys. Lipids 18, 149 (1977).
[190] F. Paltauf, F. Esfandi, A. Holasek, FEBS Lett. 40, 119 (1974); F. Paltauf, E. Wagner, Biochim. Biophys. Acta 431, 359 (1976).
[191] H. Greten, R. I. Levy, H. Fales, D. S. Fredrickson, Biochim. Biophys. Acta 210, 39 (1970); G. Assmann, R. M. Krauss, D. S. Fredrickson, R. I. Levy, J. Biol. Chem. 248, 7184 (1973).
[192] H. Greten, H. K. Mangold, G. Cegla, unpublished work.
[193] N. E. Hoffman, W. J. Simmonds, R. G. H. Morgan, Aust. J. Exp. Biol. Med. Sci. 50, 803 (1972); K. Y. Lee, D. M. Hurley, W. J. Simmonds, Biochim. Biophys. Acta 337, 214 (1974); S. J. Brand, R. G. H. Morgan, ibid. 369, 1 (1974).
[194] W. W. Christie, Lipids 9, 876 (1974); A. Tietz, H. Weintraub, Y. Peled, Biochim. Biophys. Acta 388, 165 (1975).
[195] K. Y. Lee, W. J. Simmonds, N. E. Hoffman, Biochim. Biophys. Acta 249, 548 (1971); R. W. St. Clair, N. D. M. Lehner, Th. E. Hamm, Lipids 10, 25 (1975).
[196] N. Tuna, H. K. Mangold, D. G. Mosser, J. Lab. Clin. Med. 61, 620 (1963).
[197] R. G. H. Morgan, A. F. Hofmann, J. Lipid Res. 11, 231 (1970).
[198] J. Hoving, A. J. Valkema, J. H. P. Wilson, M. G. Woldring, J. Lab. Clin. Med. 86, 286 (1975).
[199] H. U. Weltzien, Biochim. Biophys. Acta 311, 6 (1973); Exp. Cell Res. 92, 111 (1975); D. Sellin, D. F. H. Wallach, H. U. Weltzien, K. Resch, E. Sprenger, H. Fischer, Eur. J. Immunol. 4, 189 (1974); H. U. Weltzien, B. Arnold, A. Blume, H. G. Kalkoff, Chem. Phys. Lipids 16, 267 (1976).
[200] F. T. Schwarz, F. Paltauf, P. Laggner, Chem. Phys. Lipids 17, 423 (1976); F. T. Schwarz, F. Paltauf, Biochemistry 16, 4335 (1977); J. W. Fong, L. J. Tirri, D. S. Deshmukh, H. Brockerhoff, Lipids 12, 857 (1977); L. J. Tirri, P. C. Schmidt, R. K. Pullarkat, H. Brockerhoff, ibid. 12, 863 (1977).

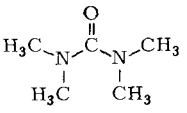
Ureas as Solvents for Chemical Investigations

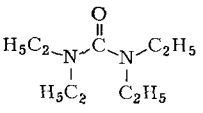
By Barbara J. Barker, Joseph Rosenfarb, and Joseph A. Caruso[*]

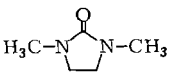
N-Alkylated ureas, including cyclic derivatives, are readily obtained pure. These stable compounds are already used as industrial solvents owing to their considerable solvent power, their wide liquid range, and their favorable dielectric constants and dipole moments. They are being increasingly employed as reaction media for electrochemical and analytical studies.

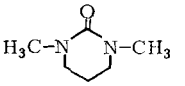
1. Introduction

Since *Lüttringhaus* and *Dirksen*[1] published their article on tetramethylurea (TMU), a considerable number of investigations into the behavior of this substance and other ureas have been undertaken in order to determine the usefulness of liquid ureas as nonaqueous media. Other solvents of primary interest are tetraethylurea (TEU), which is also acyclic like TMU, as well as the cyclic analogs 1,3-dimethyl-2-imidazolidinone ("dimethylethyleneurea", DMEU) and 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone ("dimethylpropyleneurea", DMPU). All of these substances are liquid at room temperature because hydrogen bridges are prevented by alkyl substitution on the nitrogen. Notable physical properties (with respect to the potential of ureas as electrolytic solvents) include wide liquid ranges as well as favorable dielectric constants and dipole moments.


TMU


TEU


DMEU


DMPU

Since there has been increasing dependence on nonaqueous solvents as media for inorganic and organic reactions, fundamental investigations of the general physical properties of ureas and of electrolyte behavior in these solvents warrant attention. Titrimetric and electroanalytical studies suggest possible analytical applications of the liquid ureas. Presented here is a comprehensive review of advances made since the authoritative article by *Lüttringhaus* and *Dirksen*[1] appeared some 14 years ago.

[*] Prof. Dr. B. J. Barker [†]
Department of Chemistry
Xavier University
Cincinnati, Ohio 45207 (USA)
Dr. J. Rosenfarb
Department of Chemistry
University of Florida
Gainesville, Florida 32611 (USA)
Dr. J. A. Caruso
Department of Chemistry
University of Cincinnati
Cincinnati, Ohio 45221 (USA)
[†] To whom correspondence should be addressed.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/07 07-0503 $ 02.50/0*

2. Preparation and Purification

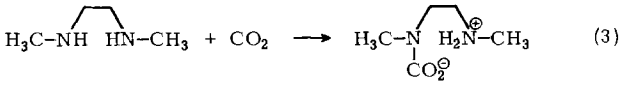
Tetramethylurea (TMU) and tetraethylurea (TEU), which are available commercially from various chemical suppliers, can be purified by vacuum distillation through a column packed with a suitable drying agent such as granular barium oxide[2,3]. TMU is somewhat hygroscopic; however, both purified solvents retain a very low specific conductance for months when stored under nitrogen. The purified solvents usually have a water content of less than 0.01%. There are several methods of preparing TMU (cf. [1]); an especially useful one is aminolysis of aryl carbonates [eq. (1) and (2)].

$$(C_6H_5O)_2CO + HN(CH_3)_2 \rightarrow C_6H_5O{-}CO{-}N(CH_3)_2 + C_6H_5OH \quad (1)$$

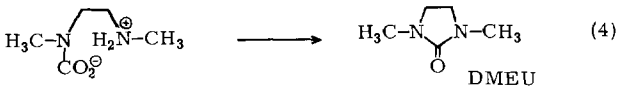
$$C_6H_5O{-}CO{-}N(CH_3)_2 + HN(CH_3)_2 \rightarrow (CH_3)_2N{-}CO{-}N(CH_3)_2 + C_6H_5OH \quad (2)$$

TMU

The cyclic ureas DMEU and DMPU may be synthesized by a variety of established methods, and are also commercially available. A procedure developed by *Mulvaney* and *Evans*[4] employs cyclization of the respective carbamate (made by the addition of carbon dioxide to the appropriate alkylamine) at elevated temperatures and pressures.

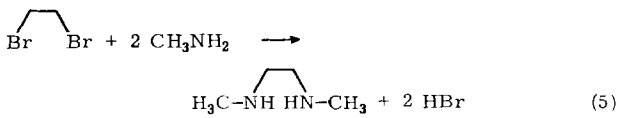


(3)

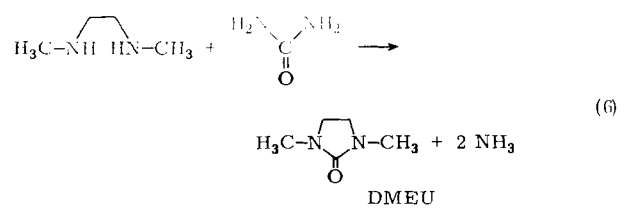


DMEU (4)

Reactions (3) and (4) have proved suitable for industrial preparation of the solvent. (Acyclic ureas have also been prepared from carbon monoxide and alkylamines at elevated temperatures and pressures[5].) *Rosenfarb, Huffman,* and *Caruso*[6] have described the synthesis of several *N,N*-dimethyl-substituted cyclic ureas by a modified procedure based on that reported earlier by *Jansen* and *Stokes*[7]. This preparation involved alkylation of the nonalkylated cyclic ureas in aqueous formaldehyde/formic acid media. *Lien* and coworkers prepared numerous alkylated ureas by adding the appropriate α,ω-dibromoalkanes to an alkylamine and by subsequently adding urea to the system [eq. (5) and (6)][8-11].



(5)



DMEU (6)

Other syntheses of cyclic ureas exist[12-14]; however, many of them require elaborate conditions and apparatus.

Purification of the cyclic ureas is readily accomplished by vacuum distillation over barium oxide[2,3,6]. Fractional freezing has been shown to be very useful for purifying DMEU[6] since its freezing point is 8.2 °C. Among the cyclic ureas, DMEU has been shown to be the most stable to heating[15]; however, the ureas in general are fairly stable under reflux conditions.

3. Physical Properties

Of the many ureas, only TMU, TEU, DMEU, and DMPU have been thoroughly studied with respect to their physical properties. These four ureas are clear and colorless when carefully purified, and each has a characteristic sharp odor. Table 1 presents selected physical properties.

Table 1. Physical properties of liquid ureas.

	TMU [1, 2]	TEU [3, 6]	DMEU [6]	DMPU [6]
B.p. [°C/torr]	176.5/760	81–82/7	220/754	230/754
M.p. [°C]	−1.2	—	8.2	< −20
Density [g/ml] at 25 °C	0.9619	0.9027	1.0519	1.0596
Viscosity [cP] at 25 °C	1.401	2.363	1.944	2.934
Dielectric constant (1 MHz) at 25 °C	23.45	14.39	37.60	36.12
Specific conductance [Ω^{-1} cm^{-1}] at 25 °C	2×10^{-8} – 8×10^{-8}	7×10^{-9} – 15×10^{-9}	1×10^{-8} – 7×10^{-8}	2×10^{-8} – 9×10^{-8}
Dipole moment [Debye]	3.37	3.45	4.09	4.23
Index of refraction at 25 °C	1.4493	1.4448	1.4707	1.4881

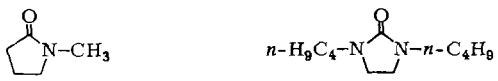
The dielectric constants and dipole moments[6,8] of the cyclic ureas are greater than those of the acyclic compounds[1,2,6,7]. An increase in chain length of the *N*-alkyl group(s) within a series of compounds normally decreases the dielectric constant; this may be seen on comparing the dielectric constants of DMEU/DMPU and TMU/TEU. A similar trend has been observed within homologous series of amides[16]. Although DMPU has a large liquid range, moderate dielectric constant, and high polarity, its higher viscosity may limit its use as a solvent, as compared to the lower viscosity, equivalent dielectric constant medium, DMEU. Likewise, the lower dielectric constant and higher viscosity of TEU limit its use as a solvent, when compared to TMU. Molecular associations have been investigated in several of the liquid ureas[6]. The parallel dipole-dipole associations suggested in the liquid ureas cannot be substantiated, since the Kirkwood *g* factors[17] were only slightly greater than unity.

4. Industrial and Pharmacological Applications

The acyclic ureas have been utilized to a greater extent than their cyclic homologs as industrial solvents[1,18,19]. However, liquid ureas in general have been commercially used in lubrication[20], in detergent production[21], as slow acting fertilizers[5], and in pre-treatment of catalysts[22] and textiles, especially in "permanent press" finishing[23-25].

Several alcohols derived from cyclic ureas (DMEU and DMPU, for example) have shown promise as bacterial growth inhibitors for textile materials. TMU and TEU have been used as catalysts for industrially significant reactions[26,27], including the reaction of elemental tin with alkyl halides and that of thionyl chloride with dibasic acids.

Lien and co-workers have investigated the pharmacological activities of a number of ureas[8, 11]. In studies with white rats, DMEU and DMPU appear to have a toxicity comparable with that of *N*-methyl-2-pyrrolidone[28], a widely used "universal" solvent. However, 1,3-dibutyl-2-imidazolidinone ("dibutylethyleneurea", DBEU) has a considerably higher toxicity[8] as a depressant on the central nervous system.



DBEU

Small amounts of TMU have been shown to increase the solubility of drugs[29]. (Generally, an increase in *N*-methylation also appears to increase the solubility of a variety of biologically active compounds.) TMU may be quite useful for drug titrations[30] although the recovery data (97.5 to 101.5%) were not as desirable as those for other organic compounds[31, 32]. TMU is a differentiating solvent for barbiturates and a leveling solvent for sulfa drugs.

A number of acid-base titration studies have been undertaken in tetramethylurea. These include potentiometric[30, 31] and indicator[30, 32] titrations of phenols, carboxylic acids, barbiturates and sulfa drugs with tetrabutylammonium hydroxide as the titrant. Typical curves for potentiometric titrations are shown in Figure 1; water levels as high as 5% in TMU could be tolerated without significantly affecting the results.

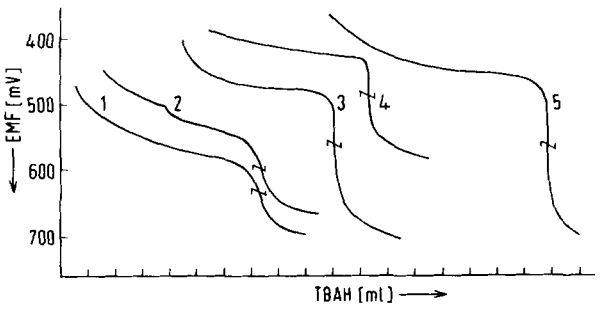


Fig. 1. Titration curves of some weak monoprotic acids against tetrabutylammonium hydroxide (TBAH) in tetramethylurea (TMU). 1, phenol; 2, benzoic acid + phenol; 3, 1-nitroso-2-naphthol; 4, *p*-nitrophenol; 5, benzoic acid.

In the indicator titrations, thymol blue was found to be suitable for analysis of carboxylic acids and bromophenol blue was a good indicator for the bases.

Satisfactory recoveries were also obtained from conductometric titrations with diphenylguanidine (DPG) as the titrant for *p*-nitrobenzoic, *o*-nitrobenzoic, and picric acids in TEU[3]. 2,4-Dinitrophenol and benzoic acid could not be determined with sufficient accuracy by this technique.

5. Fundamental Investigations

5.1. Conductance Studies

As in other nonaqueous solvents, conductance methods have been used to investigate the behavior of alkali metal and tetraalkylammonium salts in TMU[2, 33], TEU[3], DMEU[34, 35], and DMPU[34, 35]. The behavior of these salts in solution has been discussed in terms of limiting equivalent electrolyte (Λ_0) and ionic ($\lambda_0\pm$) conductances, association constants (K_A), and electrolyte "sizes" in solution (a_j, d). Conductance data in these studies were evaluated by:

1) the Fuoss-Shedlovsky y-x and Λ_0'-C methods[36]

$$1/\Lambda S_z = 1/\Lambda_0 + C\Lambda S_z f^2 K_A/\Lambda_0^2$$
$$y = 1/\Lambda S_z \text{ and } x = C\Lambda S_z f^2$$
$$\Lambda_0' = (\Lambda + \beta C^{1/2})/(1 - \alpha C^{1/2})$$

2) the Fuoss-Onsager equation for associated and unassociated electrolytes[37]

$$\Lambda = \Lambda_0 - S(C\gamma)^{1/2} + EC\gamma \log C\gamma + JC\gamma - K_A C\gamma\Lambda f^2$$

3) the Fernández-Prini expanded form[38] of the Pitts[39] and Fuoss-Hsia[40] equations

$$\Lambda = \Lambda_0 - S(C\gamma)^{1/2} + EC\gamma \log C\gamma + J_1 C\gamma - J_2(C\gamma)^{3/2} - K_A C\gamma\Lambda f^2$$

4) the full Pitts equation[39, 41] (see previous studies[35])[*].

As Table 2 reveals, the limiting equivalent conductances in the series of alkali metal ions generally increase as the crystallographic radii of the cations increase. As the crystallographic radii increase, the effective size of the cations decreases because of decreasing solvation. However, in TMU (and TEU), the λ_0^+ value of the sodium ion is about 0.5 unit higher than that of the potassium ion. In DMEU and DMPU, the sodium and potassium ions are isoconducting. The unusual conductance behavior of sodium salts found in the ureas is also observed in other structurally similar nonaqueous solvents such as dimethylacetamide[42], dimethylpropionamide[43], dimethylbutyramide[44], and *N*-methyl-2-pyrrolidone[45]. As expected, the limiting equivalent conductances of the tetraalkylammonium ions decrease as the crystallographic radii of these ions increase. The order of magnitude of λ_0^+ indicates that the effective size of the solvated alkali metal ions in the ureas investigated is comparable with that of the large tetraalkylammonium ions.

Table 2. Ionic limiting equivalent conductances (λ_0^+) (butyl(triisoamyl)ammonium tetraphenylborate as reference electrolyte) at 25 °C (cf. [2]).

	TMU [2, 33]	DMEU [34, 35]	DMPU [34, 35]
Na^+	15.74	11.46	6.96
K^+	15.26	11.51	7.00
Rb^+	15.63	11.46	7.36
Cs^+	16.52	12.52	8.00
NMe_4^+	22.22	16.92	11.30
NEt_4^+	21.61	16.78	11.01
NPr_4^+	16.60	12.46	8.03
NBu_4^+	15.00	10.73	6.89
SCN^-	33.44	23.28	16.66
I^-	29.12	19.52	13.68
ClO_4^-	28.71	20.30	14.01

Correlations between the properties of an electrolyte and a solvent and the extent of association are limited. Generally in the acyclic ureas, association within an alkali metal salt series increases slightly and association within a tetraalkylammonium salt series decreases as the crystallographic radii of the cations increase. Given the same cation[2, 3], association in

[*] S, S_z, E, J, J_1, J_2 = physical constants of the electrolyte and solvent, c = concentration, f = activity coefficient, α, β = physical constants of the solvent, γ = degree of dissociation.

TMU and TEU decreases along the series $NO_3^- > Br^- > SCN^- > I^- > ClO_4^- > BPh_4^-$. The lower dielectric constant of TEU causes much greater association in that solvent than in TMU. In contrast, the cyclic solvents DMEU and DMPU, with their higher dielectric constants, are excellent dissociating media for electrolytes (see Fig. 2).

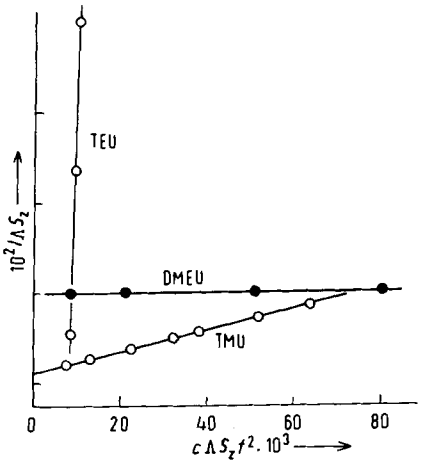


Fig. 2. Conductance behavior of NaSCN in different urea solvents. The slope of the curve is a measure of the association.

5.2. Spectroscopic Studies

Although several ^1H-, ^{13}C-, and ^{23}Na-NMR studies have been undertaken in liquid ureas[23,46-49], few systematic NMR investigations have been reported. TMU has been shown to be a water structure breaker[19] and TEU should have similar properties since the dipole moments and sizes of these molecules are comparable. ^{13}C-NMR data measured by Fourier transform methods[47,48] are listed in Table 3. The

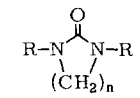
Table 3. ^{13}C-NMR shifts (δ values, TMS as standard) [47].

	C O	CH_3	N CH_2
TMU	165.7	38.6	–
TEU	164.4 [50] 164.1 [48]	13.4 [48]	42.6 [48]
DMEU	161.3	31.3	45.0
DMPU	156.7	35.6	48.1

decreasing order of carbonyl shift for heterocyclic solvents generally appears to be *N*-methyl-2-pyrrolidone > TMU, TEU > DMEU > 3-methyl-2-oxazolidone > DMPU, ethylene carbonate[48]. Such an order suggests a decreasing availability of the carbonyl oxygen for cation interaction. The carbonyl shifts for the acyclic ureas are also close to those for the acyclic amides[50]. ^{23}Na-NMR data for salts dissolved in TMU[49] indicate that ions appear to be "freely solvated" in TMU and that TMU's donor ability approximates that of DMSO. The donor ability of TMU is greater than that of pyridine even though the donor number of the former (28.9 as estimated from ^{23}Na experiments) is less than that of the latter (33.0).

Other spectroscopic investigations have included ultraviolet (UV)[8,51], nuclear quadrupole resonance (NQR)[52], and

Table 4. IR frequencies of cyclic ureas [6]. (The O(C N) band of DPPU has only medium intensity.)



	R	n	νC O [cm^{-1}]	νO(C N) [cm^{-1}]
EU	H	2	1661	1240
DMEU	CH_3	2	1681	1282
DPEU	C_3H_7	2	1690	1280
DBEU	C_4H_9	2	1695	1258
PU	H	3	1664	1304
DMPU	CH_3	3	1623	1311
DEPU	C_2H_5	3	1626	1289
DPPU	C_3H_7	3	1634	1294
DBPU	C_4H_9	3	1639	1304
BU	H	4	1610	1309
DMBU	CH_3	4	1631	1326

infrared (IR)[9,53,54] studies of numerous acyclic and cyclic ureas (see Table 4). Some of these studies have attempted to correlate common functional group shifts with pharmacological activity[9]. Inorganic complexes of the ureas, *e.g.* with lanthanides and the uranyl groups[55,56], also have been synthesized and examined by IR techniques. ^1H-NMR data pertaining to solute-solvent interaction in DMEU[57] support conductivity data[34,35] indicating ion dissociation in DMEU.

6. Summary

In conclusion, it appears likely that the ureas, especially TMU, DMEU and DMPU, will be useful solvents for further chemical investigations. Of the acyclic substances, TMU has a greater dielectric constant than TEU which suggests that it is better suited as an electrolytic solvent; among the cyclic compounds, DMEU has a lower viscosity than DMPU. In both classes of ureas there exist reasonable solubilities for many electrolytes; their solvation behavior varies widely. Of the two groups, the cyclic ureas are clearly the better dissociating media, as expected from consideration of their higher dielectric constants and dipole moments. These physical properties and the wide liquid ranges of about 250 °C indicate much future potential for cyclic ureas.

We can expect more fundamental and applied research into this class of dipolar-aprotic solvents in the future. Many important physical properties, as well as data about long-term toxicities for most of the available liquid ureas, are still needed. The solubilities of many inorganic, organic, and significant biological substances in the ureas have still not been determined. The behavior of electrolytes and nonelectrolytes in solution, as well as solution structure determinations studied by electrochemical, spectroscopic, and kinetic experiments, likewise await investigation. Studies presently in progress in this area include: fast kinetics, ^{13}C-NMR analysis of solute-solvent interaction, and fundamental acid-base studies. Interestingly, the ureas provide a significant addition to

previously studied sets of homologous heterocyclic solvents such as the pyrrolidones, oxazolidones, and carbonates. In order to elucidate the behavior of nonaqueous solvents as media for chemical investigations, there is a need for systematic studies on series of homologous compounds; the liquid ureas are such a series.

Received: June 19, 1978 [A 275 IE]
German version: Angew. Chem. 91, 560 (1979)

[1] *A. Lüttringhaus, H. W. Dirksen*, Angew. Chem. *75*, 1059 (1963); Angew. Chem. Int. Ed. Engl. *3*, 260 (1964).
[2] *B. J. Barker, J. A. Caruso*, J. Am. Chem. Soc. *93*, 1341 (1971).
[3] *B. J. Barker, J. Rosenfarb, E. Z. Riesen*, J. Solution Chem. *4*, 571 (1975).
[4] *J. F. Mulvaney, R. L. Evans*, Ind. Eng. Chem. *40*, 393 (1948).
[5] *M. Sugiura, H. Ota*, Jap. Pat. 70 36893 (1970); Chem. Abstr. *74*, 63583r (1971).
[6] *J. Rosenfarb, H. L. Huffman, Jr., J. A. Caruso*, J. Chem. Eng. Data *21*, 150 (1976).
[7] *A. B. A. Jansen, P. T. Stokes*, J. Chem. Soc. *1962*, 4909.
[8] *E. J. Lien, W. D. Kumler*, J. Med. Chem. *11*, 214 (1968).
[9] *M. H. Hussain, E. J. Lien*, Spectrosc. Lett. *6*, 97 (1973).
[10] *M. H. Hussain, E. J. Lien*, J. Med. Chem. *14*, 138 (1971).
[11] *M. H. Hussain, E. J. Lien*, J. Heterocycl. Chem. *8*, 507 (1971).
[12] *N. A. Puschin, R. U. Mitić*, Justus Liebigs Ann. Chem. *532*, 300 (1937).
[13] *W. R. Boon*, J. Chem. Soc. *1948*, 307.
[14] *S. M. Mistry, P. C. Guha*, J. Indian Chem. Soc. *7*, 793 (1930).
[15] *S. Ozaki, T. Mukaiyama, U. Keikichi*, J. Am. Chem. Soc. *79*, 4358 (1957).
[16] *J. W. Vaughn, P. G. Sears*, J. Phys. Chem. *62*, 183 (1958).
[17] *J. G. Kirkwood*, J. Chem. Phys. *7*, 911 (1939); *H. Fröhlich*: Theory of Dielectrics. Oxford University Press, New York 1949.
[18] *J. C. Davis, R. R. Grinstead*, US-Pat. 3808267 (1974); Chem. Abstr. *81*, 1329w (1974).
[19] *H. E. Zaugg*, J. Am. Chem. Soc. *82*, 2903 (1960); *83*, 837 (1961).
[20] *J. Dazzi*, DOS 1927094 (1969); Chem. Abstr. *72*, 81212g (1970).
[21] *H. J. Stimberg, J. Galinke, E. Schmadel*, DOS 1965640 (1971); Chem. Abstr. *75*, 119417e (1971).
[22] *S. Taira, A. Kuroda*, Brit. Pat. 1206981 (1970); Chem. Abstr. *74*, 6954p (1971).
[23] *D. M. Soignet, G. J. Boudreaux, R. J. Berni, E. J. Gonzoles*, Appl. Spectrosc. *24*, 272 (1970).
[24] *R. J. Berni, M. W. Pilkington, R. R. Benerito*, US Agric. Res. Serv., South Req., 1975, ARS-S-64 8-9 (Eng).; Chem. Abstr. *84*, 106954p (1976); *S. L. Vail, G. B. Bergurg, T. A. Calamari, Jr.*, Text. Chem. Color. *7*, 26 (1975).
[25] *G. A. Petropavlovski, G. G. Vasileva, Zh. D. C. Lernova*, Faserforsch. Textiltech. *25*, 49 (1974); *E. Hofmann, K. Herrle*, DOS 2255263 (1974).
[26] *Ya. A. Serednitskii, V. V. Shibanov, D. K. Tolopko*, Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol. *17*, 397 (1974); Chem. Abstr. *81*, 13060s (1974).
[27] *H. Matschimer, R. Voigtlander, A. Teschach*, J. Organomet. Chem. *70*, 387 (1974).
[28] "M-Pyrol, *N*-methyl-2-pyrrolidone". GAF Corp., New York, N. Y. (USA) 1972.
[29] *P. Rohdewald*, Pharmazie *30*, 460 (1975).
[30] *M. S. Greenberg, B. J. Barker, J. A. Caruso*, Anal. Chim. Acta *54*, 159 (1971).
[31] *S. L. Culp, J. A. Caruso*, Anal. Chem. *41*, 1329 (1969).
[32] *S. L. Culp, J. A. Caruso*, Anal. Chem. *41*, 1876 (1969).
[33] *B. J. Barker, J. A. Caruso*, J. Phys. Chem. *77*, 1884 (1973).
[34] *J. Rosenfarb, J. A. Caruso*, J. Solution Chem. *5*, 345 (1976).
[35] *J. Rosenfarb, J. A. Caruso*, J. Solution Chem. *5*, 355 (1976).
[36] *T. Shedlovsky*, J. Franklin Inst. *255*, 739 (1938); *R. M. Fuoss, T. Shedlovsky*, J. Am. Chem. Soc. *71*, 1496 (1949).
[37] *R. M. Fuoss, F. Accascina*: Electrolytic Conductance. Interscience, New York 1959; *R. M. Fuoss, L. Onsager*, J. Phys. Chem. *61*, 668 (1957).
[38] *R. Fernández-Prini, J. E. Prue*, Z. Phys. Chem. Leipzig *228*, 373 (1965); *R. Fernández-Prini*, Trans. Faraday Soc. *65*, 3311 (1969).
[39] *E. Pitts, B. E. Tabor, J. Daly*, Trans. Faraday Soc. *65*, 894 (1969); *E. Pitts*, Proc. R. Soc. London Ser. A *217*, 43 (1953).
[40] *R. M. Fuoss, K.-L. Hsia*, Proc. Nat. Acad. Sci. USA *57*, 1550 (1967); *K.-L. Hsia, R. M. Fuoss*, J. Am. Chem. Soc. *90*, 3055 (1968).
[41] *E. Pitts, B. E. Tabor, J. Daly*, Trans. Faraday Soc. *66*, 693 (1970).
[42] *G. A. Lester, T. A. Gover, P. G. Sears*, J. Phys. Chem. *60*, 1076 (1956).
[43] *E. D. Wilhoit, P. G. Sears*, Trans. Ky. Acad. Sci. *17*, 123 (1956).
[44] *H. M. Smiley, P. G. Sears*, Trans. Ky. Acad. Sci. *19*, 62 (1958).
[45] *M. D. Dyke, P. G. Sears, A. I. Popov*, J. Phys. Chem. *71*, 4140 (1967).
[46] *G. Barone, C. Giuseppina, C. D. Volpet, E. Vittorio*, J. Solution Chem. *6*, 117 (1977).
[47] *H. O. Kalinowski, H. Kessler*, Org. Magn. Reson. *6*, 305 (1974).
[48] *J. Rosenfarb, T. Baugh*, to be published.
[49] *A. I. Popov* in *J. F. Coetzee, C. D. Ritchie*: Solute-Solvent Interactions. Vol. 2. Chap. 13. Marcel Dekker, New York 1976.
[50] *G. C. Levy, G. L. Nelson*: Carbon-13 Nuclear Magnetic Resonance for Organic Chemists. Wiley Interscience, New York 1972.
[51] *G. C. Crawshaw, H. H. Monks*, J. Macromol. Sci. Chem. *A 9*, 1085 (1975).
[52] *D. Y. Osokia, L. A. Safin, L. A. Nuretdinov*, Izv. Akad. Nauk SSSR Ser. Khim. *1975*, 1422; Chem. Abstr. *83*, 95873n (1975).
[53] *I. D. Kuntz, Jr., C. J. Chen*, J. Am. Chem. Soc. *97*, 4852 (1975).
[54] *C. Lammen et al.*, Teintex *39*, 259 (1974).
[55] *R. J. Berni, R. R. Benerito, H. B. Johassen*, J. Inorg. Nucl. Chem. *31*, 1023 (1969).
[56] *K. W. Bagnal, J. G. Preez, M. C. Gibson*, J. Chem. Soc. *A 1971*, 2124.
[57] *J. Rosenfarb, J. A. Caruso*, Can. J. Chem. *54*, 3492 (1976).

The Chemistry of Iodine Azide

By Kurt Dehnicke[*]

Whereas chlorine azide and, to a lesser extent, bromine azide have long been used as preparative reagents in spite of their explosive nature, little is known about the properties of iodine azide although it was actually discovered before the other two compounds. *Hantzsch*'s warning to beware of this material, uttered in 1900, still seems to be widely observed. Only recently has iodine azide been isolated as a pure substance, thus promoting its more detailed investigation. Proper use of this highly labile reagent opens up new vistas in synthetic chemistry.

1. Mode of Formation and Preparation of Iodine Azide

Iodine azide was first obtained as very unstable ethereal solutions and as crystals contaminated with iodine by *Hantzsch* and *Schümann* on reaction of iodine with silver azide[1]:

$$AgN_3 + I_2 \xrightarrow{\text{Ether}} IN_3 + AgI \qquad (a)$$

Whereas the solutions decompose quickly forming iodine and nitrogen, the crystalline residue left on evaporation of the ether, "would explode regularly and violently on touching with a spatula"[1].

[*] Prof. Dr. K. Dehnicke
Fachbereich Chemie der Universität Marburg
Lahnberge, D-3550 Marburg 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/07 07-0507 $ 02.50/0

Although some of the less sensitive heavy metal azides are also suitable for the production of iodine azide, the first synthesis (a) is still the most effective one even today. However, an important factor affecting the stability of the product is the exclusion of oxygen-containing solvents. Solutions of iodine azide in dichloro- or tetrachloromethane, freon, benzene, *etc.* are by far more stable, and can be handled easily when moisture is excluded; according to our experience they can be handled safely at concentrations below 3%, and can even be dried over diphosphorus pentoxide[2].

As silver azide is safe only when moist, while even traces of water decompose iodine azide the reaction gives best yields if a suspension of silver azide in dichloromethane is treated with a desiccant, *e.g.* sodium sulfate, before adding iodine. This procedure gives a very pure solution of iodine azide, from which golden and needle-shaped crystals (Fig. 1) can be isolated by careful evaporation of the solvent. Larger crystals can be grown by sublimation onto a cold finger in a current of dry nitrogen[2].

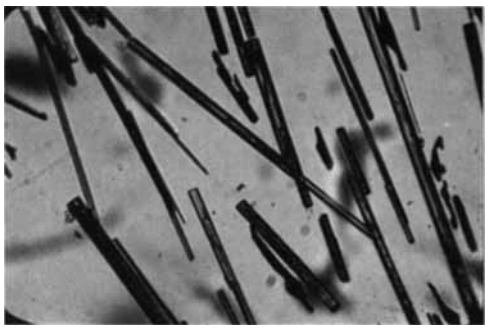


Fig. 1. Crystals of iodine azide. Magnification 25 ×.

Analogous reactions of $Pb(N_3)_2$ and of freshly precipitated TlN_3 with iodine proceed much slower and do not go to completion[3]. Most probably, iodine azide is also formed in the reaction of ICl with NaN_3 in acetonitrile, pyridine, and solvents of comparable polarity. Such solutions are used by *Hassner et al.* for the addition of iodine azide generated *in situ* to olefinic double bonds (cf. Section 3.1)[4].

It is an experimental advantage that the solutions of iodine azide, the concentration of which can be determined iodometrically, can be dosed very exactly: the IN_3 solution is shaken with excess aqueous sodium thiosulfate and the residual $S_2O_3^{2-}$ is back-titrated[3].

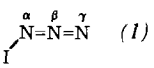
$$IN_3 + 2S_2O_3^{2-} \rightarrow I^- + N_3^- + S_4O_6^{2-} \qquad (b)$$

The smooth course of reaction (b) suggests a redox potential close to that of I_2 (0.535 V).

2. Physical Properties

2.1. Vibrational Spectrum

The IR spectrum of iodine azide is known for the polycrystalline phase, the benzene solution[2], as low-temperature matrix spectrum in CH_2Cl_2[5], and—partly—in the gas phase[6]. The spectra are in accord with the C_s symmetry of molecule *(1)*, bent at the N_α atom.



(1)

This is confirmed by the Raman spectrum which, owing to photochemical cleavage of IN_3 by the laser beam (6741 Å), could not be recorded in solution, but only in the solid state in a dichloromethane matrix[5]. Iodine formed on decomposition affects the band maxima; this is explained in terms of formation of a iodine-iodine azide complex[5].

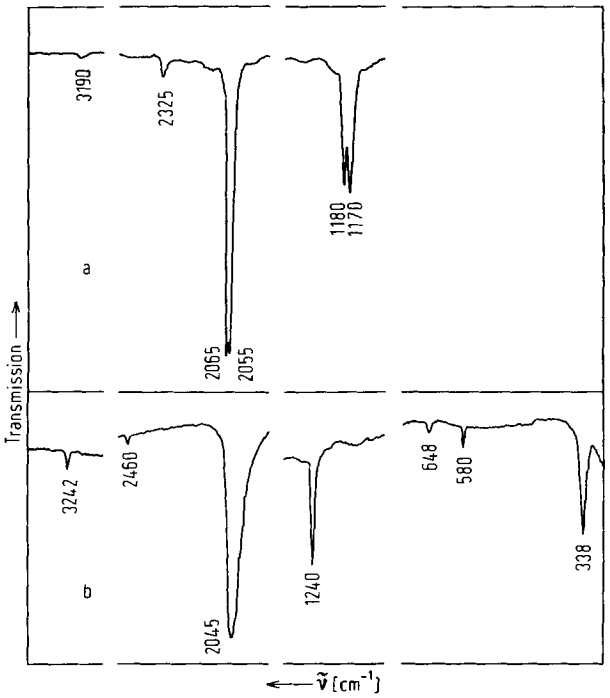
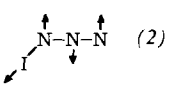


Fig. 2. IR spectrum of iodine azide: a) in the gas phase, 10 torr IN_3/750 torr N_2; b) in nujol.

In the series fluorine azide to iodine azide the nitrogen-halogen stretching vibration shows an anomalous shift to lower wave numbers in iodine azide:

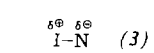
	FN_3[7]	ClN_3[7,8]	BrN_3[7]	IN_3[2]
νN X [cm^{-1}]	869	719	687	338

This effect is certainly due in part to coupling with the A′ in-plane bending vibration of the N_3 group *(2)*. In the homologues FN_3, ClN_3, and BrN_3 this frequency ($\approx$650 cm^{-1}) is lower than the nitrogen-halogen stretching frequency but higher in iodine azide. Thus in the case of IN_3 the whole N_3 group may be treated as a point mass[9].



(2)

On the other hand, the extremely low frequency of the νN I vibration indicates a significant polarity of the iodine-nitrogen bond *(3)*.



(3)

Both the UV data of the halogen azides[10] (cf. Section 2.2) and the reactivity of iodine azide favor this interpretation.

2.2. UV Spectrum

The electronic spectrum of iodine azide recorded in hexane solution[10] shows three maxima (Table 1); one of them lies in the visible range and is thus responsible for the golden yellow color of IN_3 solutions. This band corresponds to an electronic transition of the I component of iodine azide; it is shifted to higher energies compared to that of iodine (517 nm)[11]. This result indicates a positive partial charge of the iodine atom, as is shown by the remarkably low wave number of the νN I vibration (cf. Section 2.1).

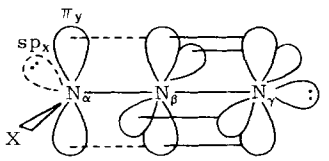
Table 1. UV spectrum of iodine azide in hexane.

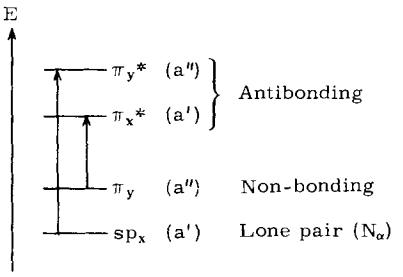
λ_{max} [nm]	ε [l·mol^{-1}·cm^{-1}]	Half width [nm]	Assignment
209	870	11	$sp_x \rightarrow \pi_y^*$
243	615	26	$\pi_y \rightarrow \pi_y^*$
350	40	60	[a]

[a] Compare text for assignment.

Comparison of the corresponding band of chlorine azide (380 nm) with the absorption maximum of chlorine (332 nm)[12] shows that it is shifted bathochromically, indicating a slight negative partial charge on the chlorine atom in ClN_3. This difference correlates well with some chemical properties of the two compounds[13].

In the UV region, IN_3 exhibits two maxima which are approximately equivalent in wavelength and extinction to those of other covalent, monomeric azides[14], *e.g.* alkyl azides, which absorb at about 285 and 215 nm. As in covalent azides of the type XN_3, bonding in the N_3 group can be described by two σ bonds, one localized π bond N_β N_γ, one delocalized π-bond N_α N_β N_γ and two lone pairs at the N_α- and the N_γ atom (symmetry C_s), these bands are assigned to the possible transitions $\pi_y(a'') \rightarrow \pi_y^*(a')$ and $sp_x(a') \rightarrow \pi_y^*(a'')$, by *Closson* and *Gray*[15], *i.e.* transitions from the two highest occupied orbitals to the lowest unoccupied antibonding π orbitals.



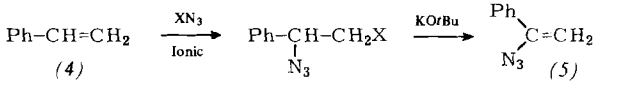


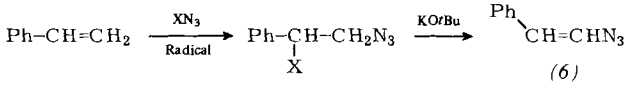
In the more highly symmetrical azide ion ($D_{\infty h}$ symmetry) these transitions become degenerate, so only one band is observed[14]. As in iodine azide the energy difference between the two transitions is significantly smaller (34 nm) than in the alkyl azides ($\approx$70 nm), thus providing more evidence for the polarity of the iodine-nitrogen bond *(3)*.

3. Chemical Properties

3.1. Addition to Olefinic Double Bonds

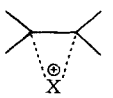
The addition of iodine azide to olefinic double bonds may be used for the synthesis of simple vinyl azides, which are obtained from the iodine- and azido-substituted primary products by elimination of HI with potassium *tert*-butoxide[4]. Iodine azide adds preferentially by an ionic mechanism, whereas chlorine and bromine azide frequently add by a radical mechanism. Thus the regioisomeric vinyl azides *(5)* and *(6)* are accessible from styrene *(4)*.





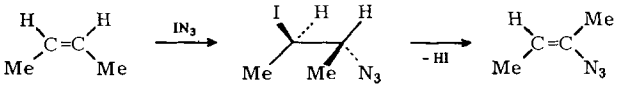
Whether the addition follows an ionic or a radical course depends on the polarity of the solvent. *Hassner et al.*[4] obtained iodine azide in presence of the olefin *in situ* from sodium azide and iodine monochloride and investigated its reactions mostly in highly polar solvents such as acetonitrile, dimethyl formamide, and pyridine. This experimental technique had essentially been applied by *Birckenbach et al.*[16] when they reacted cyclohexene with iodine in the presence of silver salts, such as AgNCO, $AgNO_2$, and $AgClO_4$, and found evidence for the addition of INCO, INO_2, and $IClO_4$ respectively, to the olefinic double bond.

The tendency towards homolytic cleavage increases along the series $IN_3 < BrN_3 < ClN_3$[4]; this is in accordance with the UV[10] and IR spectra[2, 13] of the halogen azides. The same trend is also observed in their reactions with numerous inorganic agents.

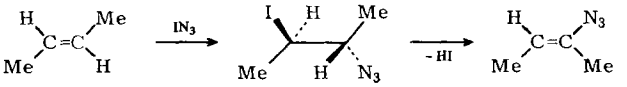


(7)

The ionic addition of iodine azide to olefins involves the intermediacy of a halogenium ion *(7)*. This becomes evident from the stereospecific reaction of *cis*- and *trans*-2-butene to

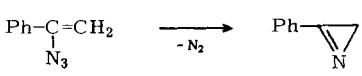


(8), *cis* — *(9)*, *threo* — *(10)*, *trans*



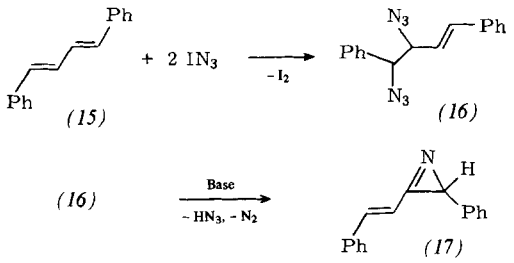
(11), *trans* — *(12)*, *erythro* — *(13)*, *cis*

form *threo- (9)* and *erythro*-2-azido-3-iodobutane *(12)*, respectively, the dehydrohalogenation of which yield *trans- (10)* and *cis*-vinyl azide *(13)*[17, 18].



Vinyl azides are interesting starting materials for pyrolytic or photolytic syntheses of azirines *(14)*[19, 20].

Thus the synthesis of the first 2-vinylazirine *(17)* was accomplished by reaction of iodine azide with diphenylbutadiene and basic cleavage of HN_3 from the primary diazide *(16)*[21].



3.2. Reactions with Metal Iodides

The significant polarity of the $\overset{\delta+}{I}\ \overset{\delta-}{N}$ bond in iodine azide suggests substitution reactions with metal iodides, with charge neutralization between the I^+ and I^- species involved providing the driving force. Such reactions proceed smoothly and very fast in benzene solution[22]; in contrast, chlorine azide reacts much slower with metal chlorides[13].

$$\overset{\delta+}{M}I_3 + \overset{\delta+}{I}\overset{\delta-}{N}_3 \rightarrow I_2MN_3 + I_2 \qquad (c)$$

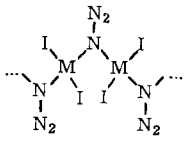
M = B, Al, Ga *(18a—c)*

Whereas aluminum- *(18b)* and gallium azide diiodide *(18c)* were found to be quite stable and resistant to thermal and mechanical stress[22], the boron compound *(18a)*, which is presumably associated like its trimeric homologues $[Cl_2BN_3]_3$[23,24] and $[Br_2BN_3]_3$[23] decomposes slowly *in vacuo* at room temperature:

$$I_2BN_3 \rightarrow BN + I_2 + N_2$$
(18a)

IR spectra show $[IBNI]_n$ to occur as intermediate. The instability of this species, which is isoelectronic with hexaiodobenzene, is attributed to a difference in the polarity of the iodine ligands $B\ \overset{\delta-}{I}\ /\ N\ \overset{\delta+}{I}$. *(18a)* decomposes explosively on contact with water, yielding iodine and nitrogen[22].

Aluminum- *(18b)* and gallium azide diiodide *(18c)* are shown by their solubility and their vibrational spectra to be polymeric species, associated *via* the N_α atoms of the N_3 groups (type *(19)*).



(19)

Titanium azide triiodide I_3TiN_3[25], accessible from titanium tetraiodide and iodine azide, also seems to be associated by way of azido bridges. In contrast to the explosive Cl_3TiN_3, which is easily converted into very pure TiNCl by elimination of N_2 and Cl_2[26], I_3TiN_3 is much less sensitive to mechanical and thermal stress. Striking thermal stability is also found with MoI_2N_3, which is prepared from MoI_3 and iodine azide, and is shown by the absence of the $\nu_s N_3$ mode in the IR spectrum to contain azide ions[25].

Because the iodine ligand is sensitive to oxidation, the metal azide iodides are very easily converted into metal azide bromides by reaction with an excess of bromine[22].

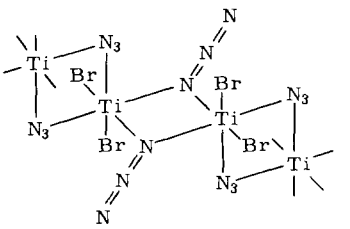
$$I_2AlN_3 + Br_2 \rightarrow Br_2AlN_3 + I_2$$
(18b) *(20)*

3.3. Reactions with Metal Bromides

We recently discovered a direct entry to metal azide bromides by reaction of an iodine azide solution with metal bromides:

$$TiBr_4 + 2IN_3 \rightarrow Br_2Ti(N_3)_2 + 2IBr$$
(21)

Titanium tetrabromide yields exclusively the diazide *(21)*, which according to the vibrational spectrum is associated *via* azide bridges. Titanium has the coordination number six and *cis*-positioned bromine ligands[25]. Thus a structural relationship exists with Cl_3TiN_3, which contains alternating azido- and chloro bridges[27] in keeping with its modified composition.



(21)

Interesting products result from the reaction of iodine azide with molybdenum tetrabromide. Although this reaction again initially forms a molybdenum azide bromide which is highly explosive, it slowly releases nitrogen in solution and thus turns into molybdenum bromide nitride *(22)*[28]:

$$Br_3MoN_3 \rightarrow MoNBr_3 + N_2 \qquad (d)$$
(22)

Monomeric $MoNBr_3$ is observed in the mass spectrum. In the solid state, however, it is most probably associated, containing Mo≡N Mo groups, like $[MoNCl_3]_4$[29,30] which was obtained previously by a different method. Characteristically the Mo≡N stretching frequency in the IR is found at 1025 cm^{-1} (νMoN in $MoNCl_3$: 1045 cm^{-1})[29]. The metal-nitrogen triple bond, which is at the center of current interest owing to its possible role in nitrogen assimilation, is understood as resulting from overlap of unoccupied d_{xy}, d_{x^2} orbitals of molybdenum with the occupied, doubly degenerate π orbital of the nitride ligand.

$WNBr_3$ can be obtained from WBr_5 and iodine azide [cf. eq. (d)][31].

Donor molecules like phosphorus oxide trichloride and tribromide react with $MoNBr_3$ to form the complexes $MoNBr_3 \cdot OPCl_3$ and $MoNBr_3 \cdot OPBr_3$, whereas tetramethylammonium bromide gives compound *(23)*, which contains a terminal triply bonded nitride ligand (symmetry C_{4v})[25]:

$$MoNBr_3 + NMe_4Br \rightarrow NMe_4[Br_4Mo \quad N]$$
(22) *(23)*

Upon heating to 200 °C *in vacuo*, $MoNBr_3$ releases bromine to give $MoNBr_2$ *(24)*, also not reported previously. In a closed system, this procedure gives single crystals of $MoNBr_2$; the transport reaction (e) is probably involved in their formation:

$$MoNBr_{2(s)} + \tfrac{1}{2}Br_2 \rightleftharpoons MoNBr_{3(g)} \qquad (e)$$
(24) *(22)*

The reduction to Mo^V causes a low energy shift of the Mo≡N stetching frequency in $MoNBr_2$ to 953 cm^{-1}[25].

3.4. Reactions with Metal Chlorides

The preparative applications of the reaction of chlorine azide with metal chlorides were reviewed in 1967[13]. Use of iodine azide instead of chlorine azide as a reagent with metal chlorides has a number of advantages. Apart from the exact dosage, it is mainly the higher reactivity of iodine azide which enhances the range of application and also permits some reactions to be carried out at low temperatures. In some reactions of iodine azide with metal chlorides the N I bond is even preserved.

A pertinent example is the reaction of vanadium tetrachloride with iodine azide in tetrachloromethane to give *N*-iodo vanadium trichloride nitride *(25)*[32]:

$$VCl_4 + 2IN_3 \xrightarrow{CCl_4} Cl_3V \quad N \quad I + 2\tfrac{1}{2}N_2 + ICl \qquad (f)$$
(25)

(25) is only slightly soluble in CCl_4 and can be isolated as very dark brown needles which are sensitive to moisture and oxygen. The course of reaction (f) is understood as a primary addition of iodine azide to the Lewis acid VCl_4 followed by spontaneous elimination of N_2 from *(26)*:

$$Cl_4VN \quad \overset{I}{N_2} \xrightarrow[-N_2]{} Cl_3V \quad N \quad I + \tfrac{1}{2}Cl_2$$
(26) *(25)*

Simultaneously a (presumably radical) extrusion of one chlorine ligand occurs, most probably in the *trans* position relative to the VN multiple bond.

With an excess of bromine, *(25)* is converted into the bromide *(27)*[32]:

$$Cl_3VNI + Br_2 \rightarrow Cl_3VNBr + IBr$$
(25) *(27)*

The IR spectra show the three *N*-halo vanadium trichloride nitrides to contain V≡N triple bonds:

	Cl_3VNCl[33]	Cl_3VNBr	Cl_3VNI
νVN [cm^{-1}]	1110	1032	963

The decrease in the wave number of the VN stretching vibration on going from the NCl to the NI compound is caused by the weakening of the coupling with the nitrogen-halogen stretching vibration in the above order.

The reaction of iodine azide with molybdenum pentachloride leads to a surprising result[32]:

$$MoCl_5 + IN_3 \xrightarrow{CCl_4} MoNCl_4 + ICl + N_2$$
(28) *(29)*

According to magnetic measurements, the chloride nitride *(29)* contains molybdenum(v) ($\mu_{eff} = 1.6\,\mu_B$); the IR spectrum reveals no N Cl group, but Mo N multiple bonds are deduced from a doublet of bands at 1005/1023 cm^{-1}. Hence $MoNCl_4$ has to be formulated as a dimeric molecule[32]:

$$Cl_4Mo \quad N \quad N \quad MoCl_4 \leftrightarrow Cl_4Mo \overset{1}{} \quad N \quad N \quad Mo\overset{1}{}Cl_4$$
(29)

From the viewpoint of bonding theory, the group Mo≡≡N N is related to the isodiazene derivatives synthesized by *N. Wiberg et al.*[34] and *Veith*[35], *e.g.* Cp_2V N $N(SiMe_3)_2$, to compounds of the type $[Cl_4W{\equiv\equiv}N \quad C_2Cl_5]_2$[36] or $[Cl_3PO \quad WCl_4{\equiv\equiv}N \quad CCl_3]$[37], and with carbyne complexes containing the M ≡C R group, investigated by *E. O. Fischer et al.*[38,39]. Expulsion of chlorine by boiling in tetrachloromethane converts *(29)* into $MoNCl_3$ *(30)*, the structure of which is known[29,30]:

$$MoNCl_4 \xrightarrow[80\ ^\circ C]{CCl_4} MoNCl_3 + \tfrac{1}{2}Cl_2$$
(29) *(30)*

Tungsten hexachloride, however, reacts with iodine azide to form $WNCl_3$ *(31)* directly:

$$WCl_6 + IN_3 \rightarrow WNCl_3 + ICl + Cl_2 + N_2 \qquad (g)$$
(31)

Reaction (g) gives quantitative yields and is complete within a few minutes. It is therefore preferred over the synthesis of *(31)* with chlorine azide[29].

The pronounced reactivity of iodine azide even permits the preparation of $CrCl_2N_3$ from the kinetically very stable chromium trichloride[58].

3.5. Reaction with Halometalates

The tetraphenylarsonium hexahalometalates $AsPh_4[MX_6]$ of niobium and tantalum with X = Cl, Br, I, also react with iodine azide in dichloromethane, undergoing substitution and forming azidopentahalometalates *(32)*[6]:

$$[MX_6]^{(-)} + IN_3 \rightarrow [X_5MN_3]^{(-)} + IX$$
M = Nb, Ta *(32)*

On the other hand, $[WSCl_5]^{(-)}$ causes exclusive spontaneous catalytic decomposition of iodine azide[31] (cf. Section 3.7).

The anions *(32)* can be decomposed photochemically in the presence of $AsPh_4X$ in the molar ratio 1:1 in acetonitrile, to form the tetrahalonitridometalates *(33)*, the first compounds to contain a terminal Nb≡N and Ta≡N triple bond respectively[6]:

$$[X_5MN_3]^{(-)} + X^{(-)} \xrightarrow{h\nu} [X_4M \quad N]^{(-)} + N_2 + X_2$$
(32) *(33)*

3.6. Oxidative Additions

The oxidative addition of iodine azide to tin(II) chloride yields tin(IV) diazide dichloride *(34)*[40], also obtained by substitution from $SnCl_4$ and Me_3SiN_3[41]:

$$2\,SnCl_2 + 2\,IN_3 \rightarrow \underset{(34)}{SnCl_2(N_3)_2} + \text{"}SnCl_2I_2\text{"} \qquad (h)$$

Reaction (h) is assumed to involve primary formation of $SnCl_2IN_3$ which however reacts further *via* ligand exchange, favored by azido bridge formation. This is supported by the fact that in the presence of chloride ions, reaction (h) gives the mixed ligand complex *(35)*[42]:

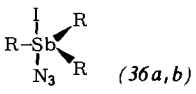
$$2\,NMe_4Cl + SnCl_2 + IN_3 \rightarrow \underset{(35)}{[NMe_4]_2[SnCl_4IN_3]}$$

The octahedral shielding of the tin atoms by complexation prevents intermolecular bridging and thus rules out the possibility of ligand transfer. In an analogous way antimony trichloride reacts with iodine azide to form the highly explosive $SbCl_3(N_3)_2$.

Trimethyl- and triphenylantimony also undergo oxidative addition with iodine azide[43]:

$$\underset{R = CH_3,\ C_6H_5}{R_3Sb + IN_3} \rightarrow \underset{(36a,\ b)}{R_2SbIN_3} \qquad (i)$$

Determination of the molecular weight and vibrational spectra show both antimony compounds *(36a, b)* to be monomeric in solution as well as in the solid, the coordination number of antimony being five. The ligand arrangement was determined by ^{121}Sb Mössbauer spectroscopy[43]:



(36a,b)

Eq. (i) demonstrates the pseudohalogen character of iodine azide: chlorine, bromine, and iodine also react with triorganoantimony compounds *via* oxidative addition[44,45].

3.7. Halo- and Pseudohalo Complexes of Iodine Azide

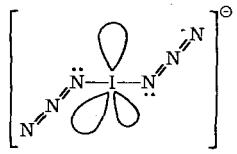
The distinct polarity of the I–N bond in iodine azide [see *(3)*] suggested the iodine atom to exhibit Lewis acidity. This was verified by the behavior of IN_3 in reactions with halide and pseudohalide ions, which, on account of their negative charge might serve as Lewis bases.

Tetramethylammonium azide, suspended in dichloromethane, reacts smoothly with stoichiometric quantities of iodine azide, forming diazidoiodate(I) *(37)*[46], which is readily soluble in CH_2Cl_2 (orange solution):

$$NMe_4N_3 + IN_3 \xrightarrow{CH_2Cl_2} \underset{(37)}{NMe_4[I(N_3)_2]} \qquad (k)$$

(37) forms red, hygroscopic, and highly explosive crystals. In laser light (5145 Å) their solution decomposes with evolution of nitrogen. The anion $[I(N_3)_2]^{\ominus}$ is isoelectronic with the hypothetical xenon diazide $Xe(N_3)_2$. As an example of a xenon-nitrogen compound is already known, *viz.* $XeN(SO_2F)_2$[47], it is conceivable that $Xe(N_3)_2$ might also be capable of existence.

Interaction of the lone pairs at the iodine atom with those of the N_α atoms should lead to a dihedral angle of 120° for the N_3 groups [cf. *(38)*].



(38)

The resulting low symmetry C_2 is confirmed by the appearance of in-phase and out-of-phase vibrations in the IR spectra[46].

Reactions analogous to (k) are also observed with tetramethylammonium halides, -cyanides, -cyanates, and -selenocyanates. The results are compiled in Table 2.

Table 2. Pseudohalo complexes $NMe_4[X–I–N_3]$.

Compound	Symmetry of anion	Color
$NMe_4[F–I–N_3]$	C_s	yellow
$NMe_4[Cl–I–N_3]$	C_s	orange
$NMe_4[Br–I–N_3]$	C_s	orange red
$NMe_4[I–I–N_3]$ *(39)*	C_s	deep purple
$NMe_4[N_3–I–N_3]$ *(37)*	C_2	orange red
$NMe_4[OCN–I–N_3]$	C_1	ocher
$NMe_4[NCSe–I–N_3]$	C_1	orange red
$NMe_4[NC–I–N_3]$	C_s	orange
$NMe_4[N_3–I–NC–I–N_3]$ *(40)*	C_1	orange

On the other hand, tetramethylammonium thiocyanate spontaneously eliminates nitrogen from iodine azide even at −60 °C in CH_2Cl_2. This is reminiscent of the well known "iodine azide reaction", in which iodine in the presence of traces of $S_2O_3^{2-}$, CS_2, H_2S, $S_nO_6^{2-}$ ($n = 4, 5, 6$), cysteine, and related compounds, effects spontaneous evolution of nitrogen from aqueous solutions of hydrazoic acid. This is a very sensitive test for the above sulfur compounds[48,49]:

$$2\,HN_3 + I_2 \rightarrow 3\,N_2 + 2\,HI \qquad (l)$$

The kinetics of reaction (l) have also been thoroughly investigated[49–51].

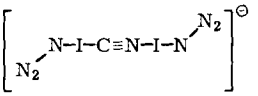
The pseudohalo complexes $NMe_4[X–I–N_3]$ (Table 2) crystallize readily, yet are sensitive to laser light (5145 Å); thus Raman spectra could not be recorded. In the solid state the compounds are explosive, but can still be handled with comparative safety. The complex $NMe_4[I_2N_3]$ *(39)*, obtained from NMe_4I and IN_3, was also prepared from iodine and tetramethylammonium azide[46]:

$$NMe_4N_3 + I_2 \rightarrow \underset{(39)}{NMe_4[I_2N_3]}$$

Being able to form linear bridges, *e.g.* between metal atoms, the cyanide ion can also act as a bridge between iodine azide molecules[46]:

$$NMe_4CN + 2\,IN_3 \rightarrow \underset{(40)}{NMe_4[CN(IN_3)_2]}$$

The structure of the complex anion of *(40)* is remarkable because of its linear axis of six atoms. As indicated in *(41)*, this anion is assumed to be bent at the N_α-atoms [cf. *(38)*].



(41)

3.8. Reactions with Carbonylmetal Complexes

Iodine azide reacts with carbonylmetal complexes at even -40 to $-20\,^{\circ}C$ to form various products. Decacarbonyldimanganese or octacarbonyldicobalt yield the metal diazides[54], which are also accessible in other ways[52,53]:

$$Mn_2(CO)_{10} + 4IN_3 \rightarrow 2Mn(N_3)_2 + 10CO + 2I_2$$
(42)

With tetracarbonylnickel an equimolar mixture of nickel diazide and nickel diiodide is formed[54]:

$$2Ni(CO)_4 + 2IN_3 \rightarrow Ni(N_3)_2 + NiI_2 + 8CO$$
(43)

Presumably, these reactions initially yield azide iodides, which subsequently react to form the diazides by substitution with more iodine azide or by elimination of the iodine ligand. In the case of pentacarbonyliron, such an intermediate was isolated at $-20\,^{\circ}C$; being stable in the absence of solvent it could be characterized[54]:

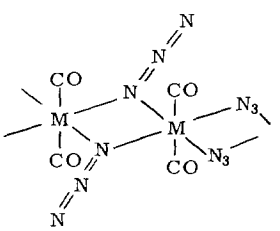
$$Fe(CO)_5 + IN_3 \rightarrow Fe(CO)_2IN_3 + 3CO$$
(44)

The iron atoms are linked by azido bridges, whereas the iodine ligands are of ionic character.

A new group of carbonylmetal derivatives, *viz.* carbonylmetal azides not containing iodine, result from the reaction of hexacarbonylmolybdenum or -tungsten with iodine azide[54]:

$$M(CO)_6 + 2IN_3 \rightarrow M(CO)_2(N_3)_2 + I_2 + 4CO$$
$M = Mo, W$ *(45a, b)*

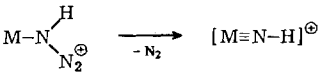
The compounds *(45a, b)* are hygroscopic and extremely sensitive solids, which explode upon application of the least mechanical stress. This immensely complicates their handling. Yet their characterization by IR spectroscopy has been accomplished. They form polymeric structures of type *(46)*, bridged by the N_α atoms of the N_3 groups. The extremely high frequency of $\nu_{as}N_3$ [*(45a)*: 2200 cm^{-1}, *(45b)*: 2220



(46)

cm^{-1}] indicates a distinct diazonium character of the N_3 groups.

It is interesting to note that the azides *(45a, b)* also explode violently on contact with traces of water. After brief exposure to moist air samples show a strong IR absorption band at $\approx 1000\ cm^{-1}$, which is characteristic for M≡N triple bonds. Both observations can be interpreted by assuming primary protonation at the N_α atom; formation of the diazonium group *(47)* initiates the secondary elimination of N_2 which leads to the metal-nitrogen triple bond in *(48)*[54]:



(47) *(48)*

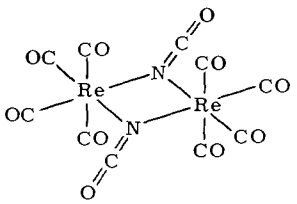
The protonation of covalent azides is known; for instance, protonated hydrazoic acid can be isolated as hexachloroantimonate[55].

An entirely different mode of reaction with iodine azide is found for the carbonyl compounds of rhenium and osmium. Primary formation of an azide actually occurs, but this cannot be isolated because it eliminates nitrogen spontaneously and transforms into cyanate by migration of CO[54]:

$$Re_2(CO)_{10} + 2IN_3 \rightarrow [(CO)_4ReNCO]_2 + 2N_2 + I_2$$
(49)

$$Os_3(CO)_{12} + 3IN_3 \rightarrow Os_3(CO)_6(NCO)_3 + 3N_2 + 1\tfrac{1}{2}I_2 + 3CO$$
(50)

The formation of cyanates has occasionally been observed in the reaction of alkali metal azides with carbonylmetal compounds[56,57]. According to mass- and vibrational spectroscopic investigations the cyanate *(49)* is associated *via* the N



(51)

atoms of the cyanate groups [see *(51)*], which means octahedral coordination of the rhenium atoms. The structure of the osmium compound *(50)* has not yet been determined.

4. Summary

This paper has considered the chemistry of iodine azide, taking into account some representative groups of materials. Undoubtedly the types of reactions investigated can be varied in numerous ways; also new, hitherto unexplored reactions of iodine azide appear in outline. Its pronounced reactivity and its comparative stability are consequences of the polarity of the I N bond; the iodine atom has acceptor properties, and the N_α atom of the N_3 group can act as donor. The N_3 group introduced on substitution with iodine azide, can undergo frequently surprising secondary reactions on account of its high energy content.

The example of iodine azide was chosen to demonstrate how prejudice can be overcome by appropriate handling of a

compound known to be highly explosive, and how one can do preparative chemistry of a kind which has existed in oblivion for almost 80 years.

I am very much indebted to my daring and imaginative coworkers for their dedicated and thorough research in this field: Rainer Dübgen, Werner-M. Dyck, Kurt Fleck, Norbert Krüger, Wolfgang Liebelt, Werner Liese, Peter Ruschke. The Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie generously supported our experimental work reported here.

Received: August 9, 1978;
supplemented: April 20, 1979 [A 277 IE]
German version: Angew. Chem. *91*, 527 (1979)
Translated by Dr. *Frank Weller*, Marburg

[1] *A. Hantzsch, M. Schümann*, Ber. Dtsch. Chem. Ges. *33*, 522 (1900).
[2] *K. Dehnicke*, Angew. Chem. *88*, 612 (1976); Angew. Chem. Int. Ed. Engl. *15*, 553 (1976).
[3] *K. Dehnicke*, unpublished.
[4] *G. L'abbé, A. Hassner*, Angew. Chem. *83*, 103 (1971); Angew. Chem. Int. Ed. Engl. *10*, 98 (1971).
[5] *U. Engelhardt, M. Feuerhahn, R. Minkwitz*, Z. Anorg. Allg. Chem. *440*, 210 (1978).
[6] *R. Dübgen, K. Dehnicke*, unpublished.
[7] *D. E. Milligan, M. E. Jacox*, J. Chem. Phys. *40*, 2461 (1964).
[8] *W. Kolitsch*, Dissertation, Universität Marburg 1974.
[9] *H. J. Becher*, personal communication.
[10] *K. Dehnicke, P. Ruschke*, Z. Naturforsch. *B 33*, 750 (1978).
[11] *R. Buckles, J. Mills*, J. Am. Chem. Soc. *75*, 552 (1953).
[12] *A. Popov, J. Mannion*, J. Am. Chem. Soc. *74*, 222 (1952).
[13] *K. Dehnicke*, Angew. Chem. *79*, 253 (1967); Angew. Chem. Int. Ed. Engl. *6*, 240 (1967).
[14] *A. Treinin* in *S. Patai*: The Chemistry of the Azido Group, Interscience, London 1971, pp. 11 ff.
[15] *W. D. Closson, H. B. Gray*, J. Am. Chem. Soc. *85*, 290 (1963).
[16] *L. Birckenbach, J. Goubeau, H. G. Krall*, Ber. Dtsch. Chem. Ges. *69*, 476 (1936).
[17] *A. Hassner, L. A. Levy*, J. Am. Chem. Soc. *87*, 4203 (1965).
[18] *F. W. Fowler, A. Hassner, L. A. Levy*, J. Am. Chem. Soc. *89*, 2077 (1967).
[19] *G. Smolinsky, C. A. Pryde*, J. Org. Chem. *33*, 2411 (1968).
[20] *L. Horner, A. Christmann, A. Gross*, Chem. Ber. *96*, 399 (1963); *K. Isomura, M. Okada, H. Taniguchi*, Tetrahedron Lett. *1969*, 4073.
[21] *A. Hassner, J. Keogh*, Tetrahedron Lett. *1975*, 1575.
[22] *K. Dehnicke, N. Krüger*, Z. Anorg. Allg. Chem. *444*, 71 (1978).
[23] *P. I. Paetzold, M. Gayoso, K. Dehnicke*, Chem. Ber. *98*, 1173 (1965).
[24] *U. Müller*, Z. Anorg. Allg. Chem. *382*, 110 (1971).
[25] *N. Krüger, K. Dehnicke*, unpublished.
[26] *K. Dehnicke*, J. Inorg. Nucl. Chem. *27*, 809 (1965).
[27] *H.-O. Wellern, U. Müller*, Chem. Ber. *109*, 3039 (1976).
[28] *K. Dehnicke, N. Krüger*, Z. Naturforsch. *B 33*, 1242 (1978).
[29] *K. Dehnicke, J. Strähle*, Z. Anorg. Allg. Chem. *339*, 171 (1965).
[30] *J. Strähle*, Z. Anorg. Allg. Chem. *375*, 238 (1970); *380*, 96 (1971).
[31] *P. Ruschke, K. Dehnicke*, unpublished.
[32] *W. Liebelt, K. Dehnicke*, Z. Anorg. Allg. Chem., in press.
[33] *J. Strähle, K. Dehnicke*, Z. Anorg. Allg. Chem. *338*, 287 (1965).
[34] *N. Wiberg, H. W. Häring, O. Schieda*, Angew. Chem. *88*, 383 (1976); Angew. Chem. Int. Ed. Engl. *15*, 386 (1976).
[35] *M. Veith*, Angew. Chem. *88*, 384 (1976); Angew. Chem. Int. Ed. Engl. *15*, 387 (1976).
[36] *M. G. B. Drew, G. W. A. Fowles, D. A. Rice, N. Rolfe*, Chem. Commun. *1971*, 231.
[37] *U. Weiher, K. Dehnicke, D. Fenske*, Z. Anorg. Allg. Chem., in press.
[38] *E. O. Fischer, U. Schubert*, J. Organomet. Chem. *100*, 59 (1975).
[39] *E. O. Fischer, Nguyen Quy Dao, W. R. Wagner*, Angew. Chem. *90*, 51 (1978); Angew. Chem. Int. Ed. Engl. *17*, 50 (1978).
[40] *K. Dehnicke, P. Ruschke*, Z. Anorg. Allg. Chem. *444*, 54 (1978).
[41] *N. Wiberg, K. H. Schmid*, Chem. Ber. *100*, 748 (1967).
[42] *K. Fleck, K. Dehnicke*, unpublished.
[43] *J. Pebler, K. Schmidt, K. Fleck, K. Dehnicke*, Z. Anorg. Allg. Chem. *451*, 109 (1979).
[44] *H. Hibbert*, Ber. Dtsch. Chem. Ges. *39*, 160 (1906).
[45] *G. O. Doak, C. G. Long, L. D. Freedman*, J. Organomet. Chem. *4*, 82 (1965).
[46] *R. Dübgen, K. Dehnicke*, Naturwissenschaften *65*, 535 (1978).
[47] *R. D. LeBlond, D. D. Desmarteau*, J. Chem. Soc. Chem. Commun. *1974*, 555.
[48] Supplement to Mellor's Comprehensive Treatise on Inorganic and Theoretical Chemistry, Supplement II, Part I, Longmans, Green & Co., London 1965.
[49] Gmelins Handbuch der anorganischen Chemie, 8th Edit. System-Nr. 8 "Iod", Verlag Chemie, Berlin 1933; *R. C. Brasted* in *M. C. Sneed, J. L. Maynard, R. C. Brasted:* Comprehensive Inorganic Chemistry, Vol. 3, Van Nostrand, New York 1954.
[50] *J. Weiss*, Trans. Faraday Soc. *43*, 119 (1947).
[51] *G. Dodd, R. O. Griffith*, Trans. Faraday Soc. *45*, 546 (1949).
[52] *L. Wöhler, G. Martin*, Ber. Dtsch. Chem. Ges. *50*, 586 (1917).
[53] *V. Gutmann*, Coord. Chem. Rev. *2*, 239 (1967).
[54] *K. Dehnicke, R. Dübgen*, Z. Anorg. Allg. Chem. *444*, 61 (1978).
[55] *A. Schmidt*, Chem. Ber. *99*, 2976 (1966).
[56] *W. Beck, H. Werner, H. Engelmann, H. S. Smedal*, Chem. Ber. *101*, 2143 (1968).
[57] *D. A. Brown, F. M. Hussein, C. L. Arora*, Inorg. Chim. Acta *29*, L215 (1978).
[58] *W.-M. Dyck, K. Dehnicke*, unpublished.

Pyrolysis of Sulfones as a Synthetic Method[1]

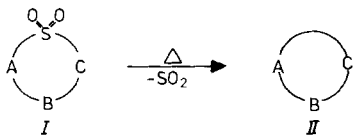
By Fritz Vögtle and Ludovica Rossa[*]

New synthetic methods (28)

Cyclic sulfones containing structural elements such as aromatic rings, heteroatoms, functional groups, and further SO_2-groups as ring members decompose on heating with cleavage of SO_2 and formation of a new C C bond. In the last decade this "sulfone pyrolysis" has been expanded into a generally applicable method even allowing the synthesis of sterically strained medium-membered and multi-membered cyclic and polycyclic systems containing aromatic rings. By the pyrolysis of sulfones which are only unilaterally activated by benzyl moieties, aromatic systems can be bridged by $(CH_2)_n$ chains of any desired length. In addition, $(CH_2)_n$ chains can be split off together with two SO_2 molecules, with recombination of the remaining centers, resulting in ring contraction by four to n atoms. However, sulfone pyrolysis is of importance not only as a ring-contraction method but also as a crucial final step in the synthesis of multi-membered hydrocarbon cycles, *e.g.* of the phane type.

1. Introduction

This review concerns primarily the preparation of multi-membered, particularly angularly-strained and sterically overloaded ring compounds by thermal elimination of SO_2 from sulfones of the general type *I*[1]. A new C C bond is formed in the course of this reaction. A, B, and C are structural elements in the ring system, *e.g.* aromatic rings, heteroatoms, functional groups, and further SO_2-groups.

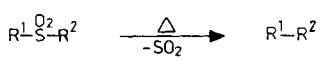


I *II*

Thermolyses had already been carried out with acyclic and three- to seven-membered cyclic sulfones[2-6], but the method acquired no general preparative significance.

2. Pyrolysis of Acyclic and Three- to Seven-Membered Cyclic Sulfones

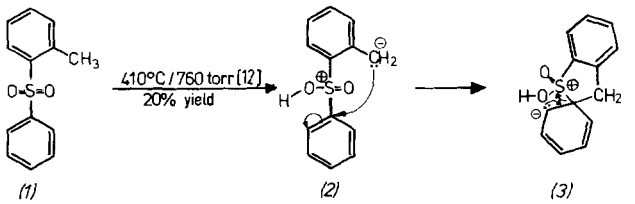
The sulfones *III*, R^1, R^2 = alkyl, aryl, count among the most well-known organic compounds[7]. They are characterized, *inter alia*, by their generally simple synthesis, thermal stability, and chemical inertness. Simple sulfones can as a rule be distilled without decomposition, are stable to acids and bases even at higher temperatures, and other functional groups in the molecule can normally be oxidized without cleavage of the C S bond, since the sulfur is present in its highest oxidation state[7]. Nevertheless, it was observed at an early date that sulfones lose SO_2 on heating, and that depending on the reaction conditions the C-fragments may recombine with the formation of new C C bonds:



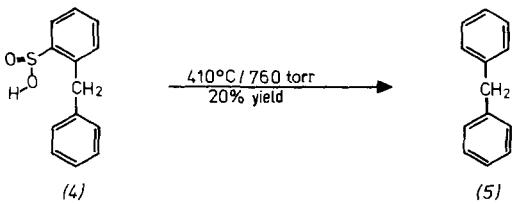
III *IV*

Studies on the thermal stability of acyclic dialkyl sulfones showed that the decomposition temperature increases in the sequence *tert-* < *sec-* < *prim*-alkyl[8,9]. Aryl alkyl sulfones are more stable than dialkyl sulfones; diaryl sulfones as a rule only decompose above 800 °C[10], though at lower temperatures in the presence of Al_2O_3/SiO_2 catalysts[10]. It is assumed that the basicity of the sulfones is sufficient to coordinate them in the transition state on the catalyst.

An ionic mechanism has also been suggested for the pyrolysis of *o*-alkyl-substituted diaryl sulfones such as *(1)*[11]: no recombination to biphenyl derivatives in accordance with the pattern *III*→*IV* is observed; but diphenylmethanes such as *(5)* are formed. A thermally generated carbanion could substitute the SO_2-group nucleophilically in a five-membered ring as an intermediate stage *(3)*.



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



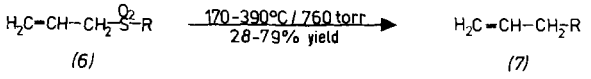
(4) *(5)*

A radical mechanism is assumed for the elimination of SO_2 from diaryl sulfones without an *o*-methyl group[11].

Allyl and benzyl sulfones decompose at substantially lower temperatures than the purely aromatic sulfones: thus, allyl sulfones are pyrolyzed at 150—400 °C with rearrangement and loss of SO_2[13,14], any CN-, keto-, halogen and ester groups remaining unchanged. A systematic connection between the pyrolysis temperature and the structure of the sulfone was established here for the first time. The pyrolysis temperatures have been optimized for sulfones of the type *(6)* (R = *n*-alkyl, *tert*-alkyl, phenyl, benzyl).

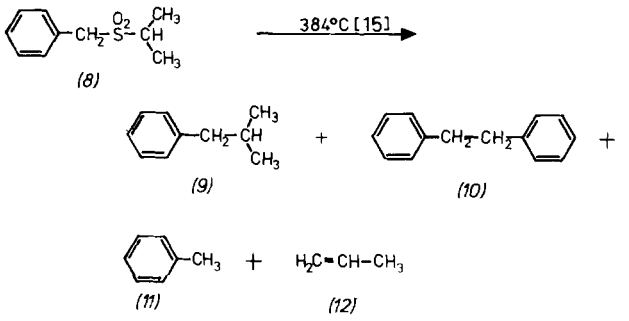
[*] Prof. Dr. F. Vögtle, Dipl.-Chem. L. Rossa
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/07 07-0515 $ 02.50/0*



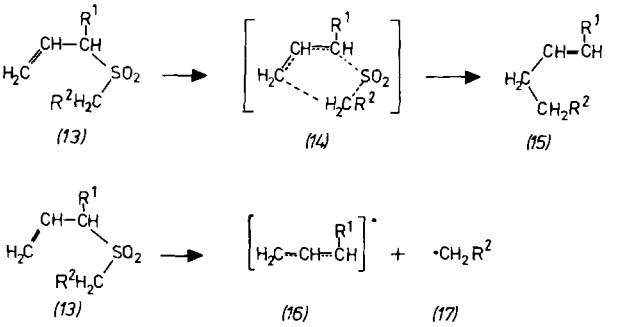
(6) (7)

The likewise unsymmetrically substituted benzyl isopropyl sulfone *(8)* has been pyrolyzed at 384 °C with the formation of isobutylbenzene, bibenzyl, toluene, and propene.



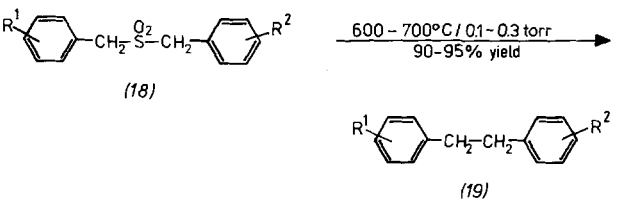
(8) (9) (10) (11) (12)

The mechanism of these pyrolysis reactions has also been assumed to be temperature-dependent. At lower temperatures[14] a cyclic transition state of the type *(14)* should appear; at higher temperatures radicals [*(16)* and *(17)*] seem to be involved.



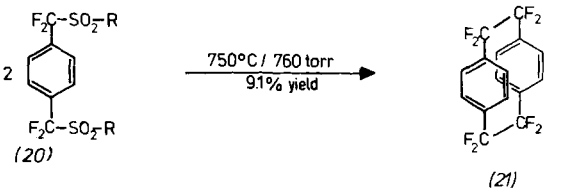
(13) (14) (15) (13) (16) (17)

In 1903 *Fromm et al.*[16] did not obtain bibenzyl but stilbene and toluene[17] in the pyrolysis of dibenzyl sulfone at 290 °C[15]. *Leonard*[18] was able to pyrolyze dibenzyl sulfones of the type *(18)* for the first time in preparative amounts practically exclusively to bibenzyls. He assumed that at higher temperatures benzyl radicals are formed, which by means of H-abstraction give rise to toluene and stilbene. This secondary reaction can be circumvented by the use of low pressure (0.1—0.3 torr)[18] and by arranging a short residence time in the zone of pyrolysis (cf. Section 5.3.3).



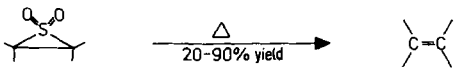
(18) (19)

The acyclic bis-sulfone *(20)*, R = C_2H_5, C_3H_7, or C_4H_9, forms the octafluorinated [2.2]paracyclophane *(21)*, with cleavage of SO_2[19]. The synthesis of strained hydrocarbon rings from acyclic bis-sulfones is so far restricted to this single example.



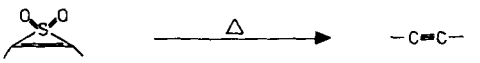
(20) (21)

The thermolysis of cyclic sulfones can lead to ring contraction, ring expansion, and fragmentation of the ring system, besides extrusion of SO_2: thiirane 1,1-dioxides *(22)*[20] are as a rule already split into alkenes and SO_2 at room temperature, with the result that their isolation often presents problems. Starting from pure *cis*- or *trans*-thiirane 1,1-dioxides *Z*- and *E*-alkenes are obtained; the thermodynamically more stable *E*-alkene is usually in excess[20].



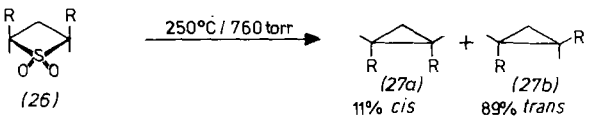
(22) (23)

Thiirene 1,1-dioxides *(24)*[20] are more stable than the saturated three-ring sulfones. On pyrolysis they give alkynes with the elimination of SO_2.



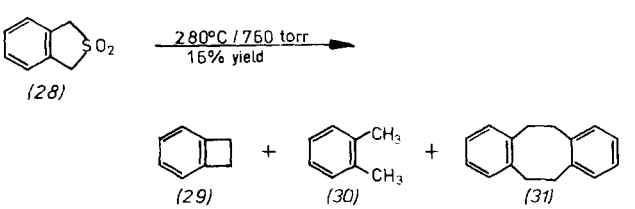
(24) (25)

Thietane 1,1-dioxide *(26)*[21] also loses SO_2 thermally, the stereochemistry of the four-ring sulfone again exerting no pronounced influence on the configuration of the resulting cyclopropane.



(26) (27a) (27b)

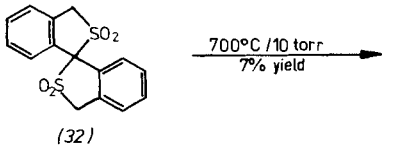
Pyrolysis of benzylic five-membered ring sulfones has been studied in detail by *Cava et al.*[22-26], who in 1959 used an apparatus[22] in which it was possible to decompose the sulfones under vacuum[27]. In the attempts to synthesize dihydrocyclobutabenzene *(29)*[22] and dihydrocyclobutanaphthalene[23] different products were obtained, depending on the reaction conditions[22]. Pyrolysis of *(28)* at 280 °C in the melt gave a liquid with an overall yield of 16%, containing 80% of *(29)* and 20% of *o*-xylene *(30)*. The dimer *(31)* could also be isolated (4%) from the polymeric residue (84%). If *(28)* is pyrolyzed in diethyl phthalate solution at 300 °C, *(31)* is produced in 48% yield. The best yields (59–63%) of dihydrocyclobutabenzene *(29)* were obtained by thermolysis at 460–670 °C/2 torr in the gas phase (cf. Section 5.3.2)[28,29].



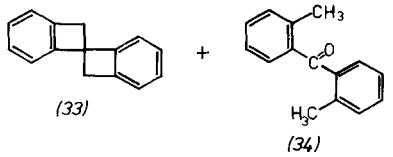
(28) (29) (30) (31)

This example shows the influence of apparatus factors and the pyrolysis conditions on the nature and yield of the products.

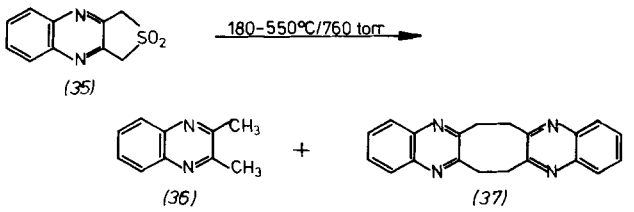
Sulfone pyrolysis has also proved successful as a general synthesis method in the production of the spiro-compound *(33)* by pyrolysis of the bis-sulfone *(32)*[25].



(32)

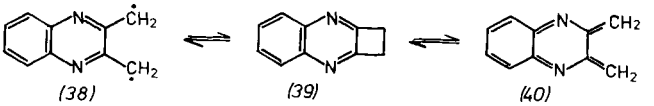


(33) *(34)*



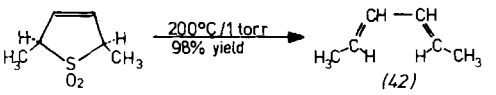
(35) *(36)* *(37)*

Moriconi et al.[30] investigated the thermal behavior of five-ring sulfones of the type *(35)* with an annelated quinoxaline system. *Inter alia* two SO_2-free compounds *(36)* (14%) and *(37)* (27%) containing the quinoxaline system were formed during the pyrolysis. The yield ratios were again strongly dependent on the pyrolysis temperature and on the solvent. A diradical *(38)* or a 1,3-diene *(40)* formed by concerted ring opening are possible intermediate stages, in equilibrium with the cyclobutane derivative *(39)*.



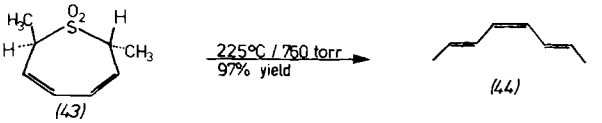
(38) *(39)* *(40)*

The elimination of SO_2 is a stereochemically uniform process in five-ring sulfones without an annelated aromatic system. The retro-Diels-Alder reaction[31,32] of 2,5-dimethyl-2,5-dihydrothiophene 1,1-dioxide *(41)* affords (*E,E*)-2,4-hexadiene *(42)*[33,34] in 98% yield.



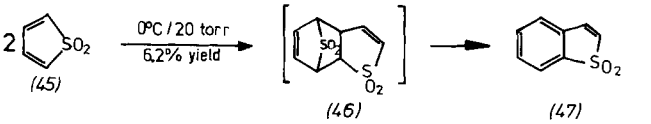
(41) *(42)*

The ring of 2,7-dimethyl-2,7-dihydrothiepine 1,1-dioxide *(43)* opens in the same way with elimination of SO_2 and with 97% stereospecifity[35].



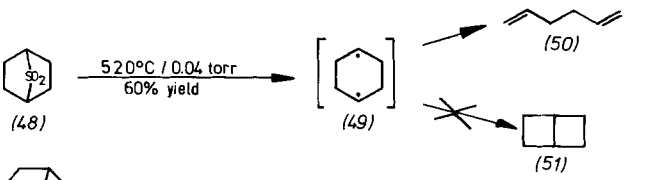
(43) *(44)*

Strained bicyclic five-ring sulfones are said to occur during the Diels-Alder dimerization of two thiophene 1,1-dioxide molecules *(45)*[36,37] conducted under very mild conditions with subsequent elimination of one SO_2 molecule.

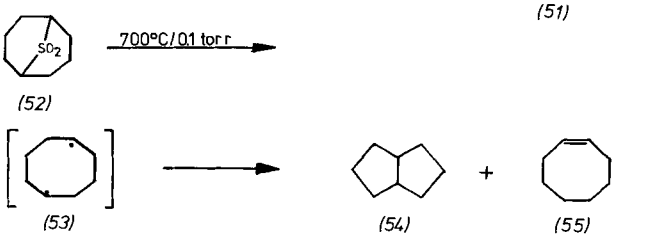


(45) *(46)* *(47)*

However, the thermal extrusion of SO_2 from the bicyclic sulfone *(48)*[38] requires a substantially higher temperature. The diradical *(49)* has been postulated as an intermediate stage. No recombination to the strongly strained bicyclo[2.2.0]hexane *(51)* has been observed.



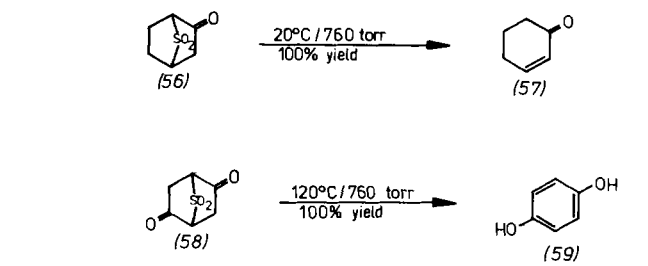
(48) *(49)* *(50)* *(51)*



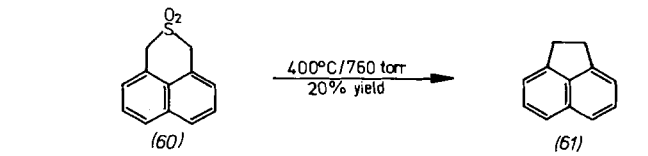
(52) *(53)* *(54)* *(55)*

Still higher temperatures are necessary for the pyrolysis of 9-thia-bicyclo[3.3.1]nonane 9,9-dioxide *(52)*[38]. At 700 °C/0.1 torr, 40—50% of bicyclo[3.3.0]octane *(54)* and 10% of cyclooctene *(55)* are formed.

At 20 and 120 °C the bicyclic oxo-sulfones *(56)* and *(58)* lose SO_2 with formation of 2-cyclohexenone *(57)* and hydroquinone *(59)*, respectively. It is assumed that the SO_2 elimination proceeds *via* the enol form: a concerted mechanism appears possible[39]. The six-ring sulfone *(60)* fragments to acenaphthene *(61)*[40] with ring contraction and loss of SO_2.

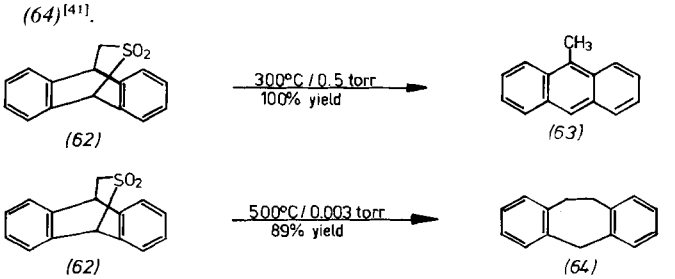


(56) *(57)* *(58)* *(59)*



(60) *(61)*

In contrast to this, the strongly pressure- and temperature-dependent SO_2 elimination from the bicyclic sulfone *(62)* can proceed with rearrangement to *(63)* and ring expansion to *(64)*[41].



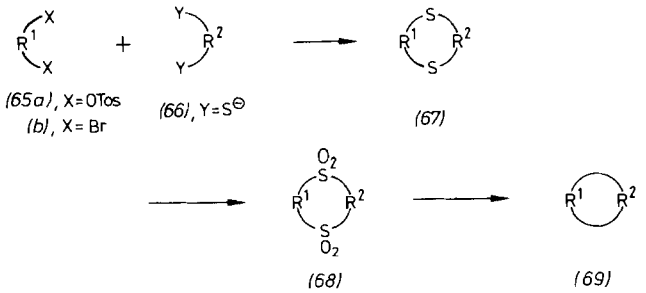
(62) *(63)* *(62)* *(64)*

3. Pyrolysis of Medium- and Multi-Membered Cyclic Sulfones

3.1. Principle of the Method, Special Features

In recent years interest has focussed on the pyrolysis of sulfones that, unlike the three- to seven-membered rings, lead to new medium-membered and multi-membered hydrocarbon cycles[42-45]. The known methods of synthesis were too awkward for such mixed aromatic/aliphatic mediocycles[46] or they required difficultly accessible starting substances.

The preparative pyrolysis of medium-membered and multi-membered cyclic mono- and oligosulfones discovered in 1969[17,42,47] opened up a novel, simple, and general entry to the cyclophane hydrocarbons. Sulfone pyrolyses in multi-membered systems are to be regarded as steps in ring-synthesis reactions in which, starting from acyclic educts *(65)* and *(66)*, the cyclic oligosulfide stage *(67)* is passed through as an intermediate; after its oxidation to the oligosulfone *(68)*, the desired multi-membered hydrocarbon *(69)* is obtained by pyrolysis.



(65a), X=OTos
(b), X=Br

(66), $Y=S^{\ominus}$

(67)

(68)

(69)

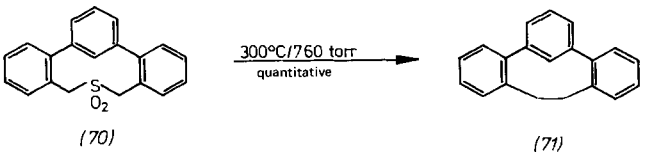
The sulfone pyrolysis is here the final step in a reaction sequence that also includes the important ring closure to the cyclic sulfide. Syntheses of this kind, with the use of sulfone pyrolysis, have given rise to many new ring systems enabling, *inter alia*, the investigation of steric[48] and electronic interactions[49,50].

3.2. Double Benzyl Sulfones

The pyrolysis of mediocyclic and macrocyclic sulfones opens a direct route to substituted, unsymmetrical, angularly-strained hydrocarbon rings. At first the method was restricted to sulfones with a bilaterally benzyl-bonded sulfur atom.

3.2.1. Monosulfones

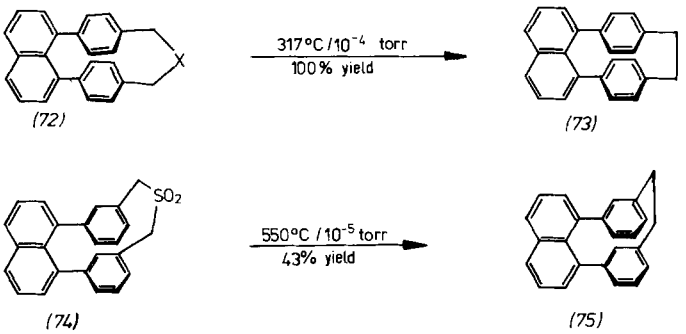
Thermal desulfurization by sulfone pyrolysis was first performed on the ten-membered *m*-terphenyl ring system *(70)*[51] in diphenyl ether as solvent or in the melt at 300 °C (see Sections 5.1 and 5.2). The unexpected quantitative yield of the sterically strained nine-membered ring *(71)* stimulated further studies on pyrolysis in other ring systems.



(70)

(71)

The bridging of naphthalene in the 1,8-position by a 1,2-diphenylethane unit to give the likewise strained compound *(73)* was first achieved at a much later date by pyrolysis of the monosulfone *(72a)*, X=SO_2[52]. The reaction can also be carried out with the bis-sulfone *(72b)*, X=$O_2S(CH_2)_2SO_2$[97] (see Section 5.3.6).



(72)

(73)

(74)

(75)

The ethano-bracket can also be fixed to other positions[53].

3.2.2. Bis-Sulfones

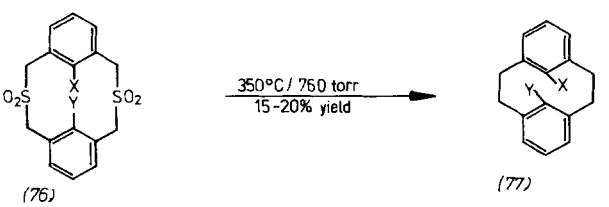
Many hydrocarbons with medium-membered to multi-membered rings can be synthesized by the pyrolysis of the appropriate bis-sulfones [cf. *(68)*→*(69)*]. Bis-sulfones *(68)* are obtained from bis-sulfides which can be prepared by cyclizing dibromides or ditosylates with dithiolates under dilution-principle conditions. Aromatic/aliphatic bis-sulfones with two SO_2-groups in the same monocycle were apparently unknown before 1965. Since then a large number of bis-sulfones have been described, whose pyrolysis products have been classified in this review according to ring structure.

[2.2]Phanes: According to the first experiments in 1969 with the ten-membered *m*-terphenyl system [*(70)*→*(71)*], the [2.2]metacyclophanes *(77)*[117] could be synthesized from the bis-sulfones *(76)* by extrusion of two SO_2 molecules.

Not only [2.2]metacyclophane *(77a)* itself, but also derivatives such as *(77b)*—*(77d)*, additionally sterically strained by intraannular substituents, can be obtained under very simple pyrolysis conditions[42]. The yields of the products are surprisingly high, particularly in comparison with the yields of the organometallic syntheses[46].

The rapid and simple preparation of such variously substituted [2.2]metacyclophanes made possible detailed studies into the steric interactions[54] of atoms not directly bound to one another[48,55].

With only simple apparatus, the pyrolysis of *(78)* leads to *(79)* with opening of the ring[42]; it is assumed that if the pyrolysis technique is improved (see Section 5), it will be possible to obtain the desired dichloro[2.2]metacyclophane.

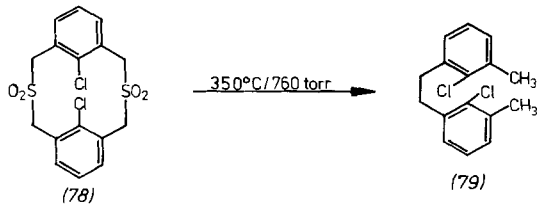


(76)

(77)

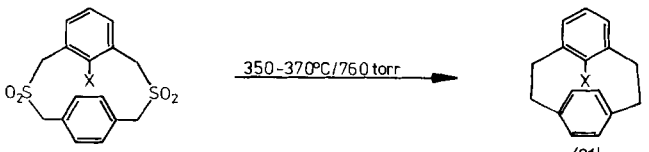
(a), X=H, Y=H; (b), X=H, Y=F;
(c), X=F, Y=F; (d), X=H, Y=Cl

The observation that no crossover products are formed from *(76b)* and *(76d)* indicates a strictly intramolecular course of the C C bonding[42]. The sulfone-pyrolysis step is thus suitable for the directed syntheses of unsymmetrical polynuclear phanes. A mono-sulfone with a C C bond already coupled on one side could be detected mass-spectrometrically as early as this stage[47].



(78) *(79)*

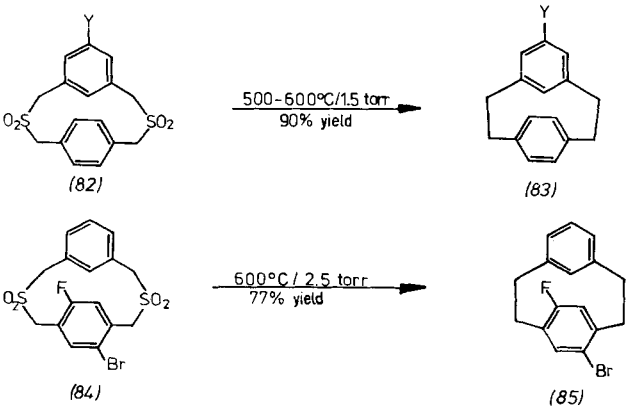
[2.2]Metacyclophane *(77a)* was later obtained in the same way in a higher yield (64%)[56]. This may be ascribed to the improved pyrolysis conditions (cf. Section 5). In 1969 the [2.2]metaparacyclophane *(81a)* previously prepared in other ways[57,58] was produced from the sulfone *(80a)* by thermal elimination of SO_2 in a simple pyrolysis apparatus[17] (see Section 5.3.1). The advantage of this ring-contraction method over conventional synthesis methods lies in the fact that preparative (gram) quantities of [2.2]metaparacyclophane *(81a)* can be obtained quickly and comparatively easily from readily available starting substances. When larger amounts of *(81a)* became available, the temperature-dependence of the ^{1}H-NMR-spectrum was observed and the mechanism of the conformational changes was hence derived[17,59,60].



(80) *(81)*

(a), X = H; (b), X = F; (c), X = CH_3

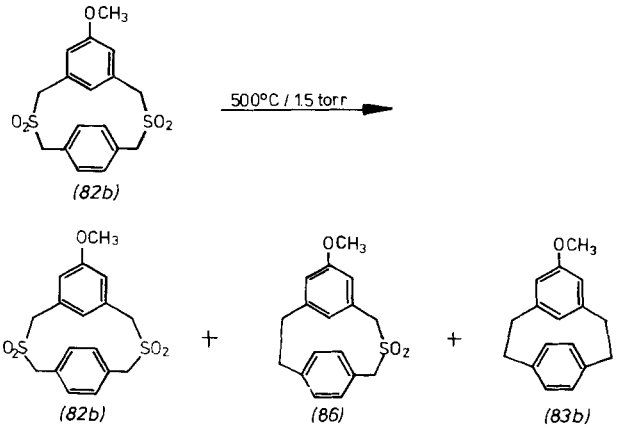
The advantage of the sulfone pyrolysis method was clearly demonstrated in attempts at the synthesis of the intraannularly methyl-substituted phane *(81c)*[61]: all earlier attempts had been unsuccessful or had given unsatisfactory yields, whereas the thermal decomposition of *(80c)* at 500 °C[15] afforded *(81c)* in a yield of 90%; large quantities are thus accessible. Further substituted [2.2]metaparacyclophanes, interesting because of the steric interactions within the eleven-membered ring[48], were synthesized by an analogous method[62].



(82) *(83)* *(84)* *(85)*

(a), Y = F; (b), Y = OCH_3; (c), Y = NO_2; (d), Y = Br

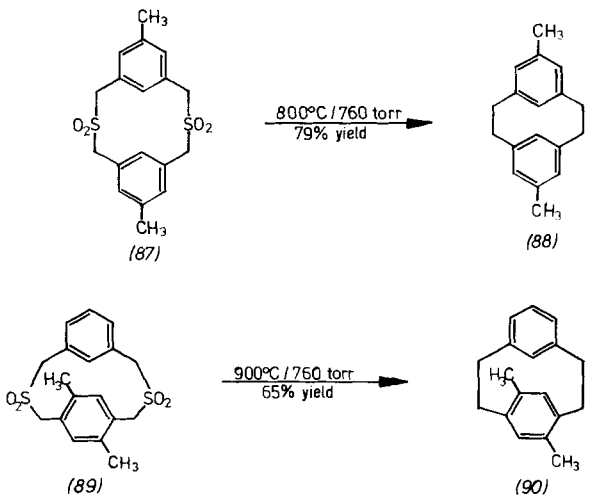
The general applicability of the sulfone pyrolysis method is clearly demonstrated by the conversions of *(82)* into *(83)* and of *(84)* into *(85)*: as a rule good yields with a high selectivity are obtained (without crossover products), even in the presence of various substituents and functional groups that interfere in other methods of synthesis (*e.g.* halogens and esters in reactions with organometallic compounds), provided that a suitable temperature and pressure have been selected.



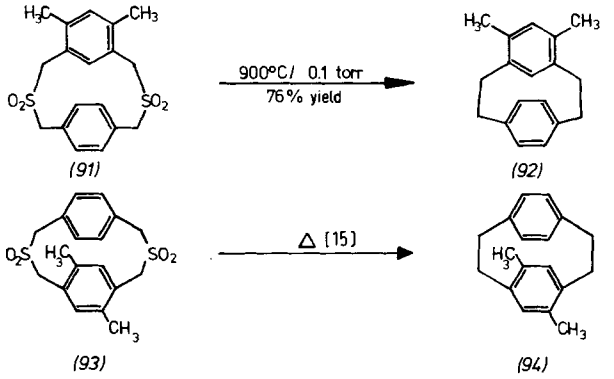
(82b) *(82b)* *(86)* *(83b)*

The ratio of the pyrolysis products of *(82b)* is clearly temperature-dependent[58]: pyrolysis at 600 °C/1.5 torr leads exclusively to *(83b)*, while at 500 °C in addition to considerable quantities of the initial sulfone *(82b)* and the desired phane *(83b)* traces of the cyclic monosulfone *(86)* are also detectable. From this it is concluded[62] that the loss of one SO_2 molecule from the monosulfone *(86)* to *(83b)* occurs more rapidly than the loss of the two SO_2 molecules from the bis-sulfone *(82b)*. The authors interpret this as a consequence of the higher strain energy of the monosulfone *(86)* in comparison with that of the bis-sulfone *(82b)*. An alternative plausible explanation is the formation of the already previously claimed diradicals[2] (see Section 2), whose C C recombination to the monosulfone is so strongly exothermic that the latter ends up in a state of high oscillation, resulting in spontaneous deactivation with loss of the second SO_2 group.

The synthesis of multilayered phanes[45,63-65] requires preparative quantities of methyl-substituted [2.2]phanes. Sulfone pyrolysis often proves to be the best method.



(87) *(88)* *(89)* *(90)*



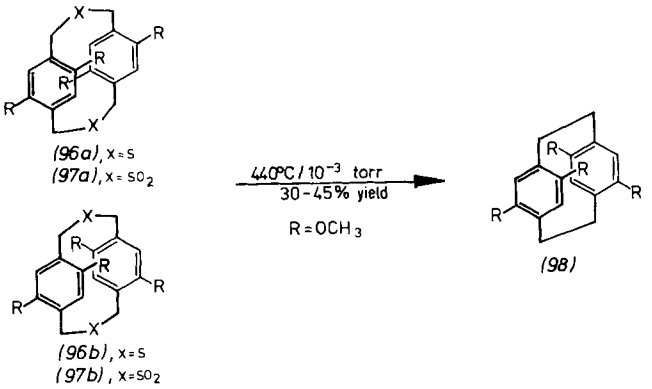
(91) (92) (93) (94)

In the study of intramolecular charge-transfer interactions in [2.2]phanes the pyrolysis of sulfones was often an essential step *en route* to the intramolecularly bracketed quinhydrones such as *(95a)* and *(95b)*[49, 65, 67]:



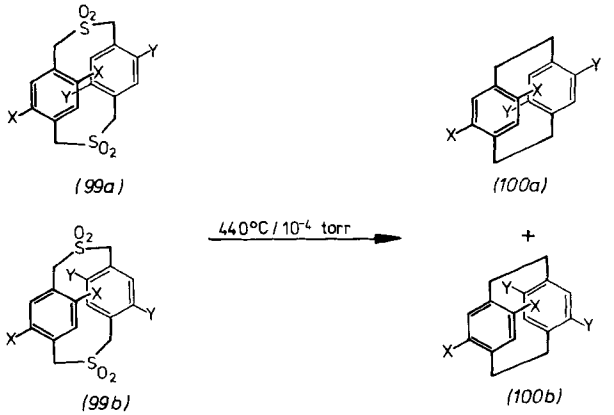
(95a) (95b)

Starting from the methoxy-protected dithia-compounds *(96a, b)*, the synthesis of the quinhydrone precursors *(98)* was possible in two ways: by photolysis of *(96a, b)* and by pyrolysis of the sulfones *(97a, b)*. Photolysis[68] proved to be the more suitable method. An important resolving factor for the mechanism of the pyrolysis is the observation that always only the (chiral) phane *(98)* is produced, irrespective of whether pure *(97a)* or *(97b)* or a mixture of these two sulfones is used as the starting substance[67].



(96a), X = S
(97a), X = SO2
(96b), X = S
(97b), X = SO2
(98)

The pyrolysis of *(99a, b)* gives other results[49a]: a mixture of *(100a, b)* is isolated, regardless of whether *(99a)* or *(99b)* or



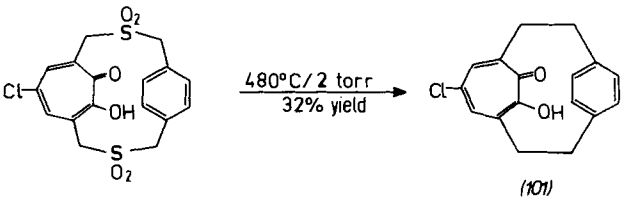
(99a) (100a) (99b) (100b)

X = NO2, Y = OCH3

their mixture is pyrolyzed. The yields of *(100a)* and *(100b)* are respectively 1–2 and 4.5—9%.

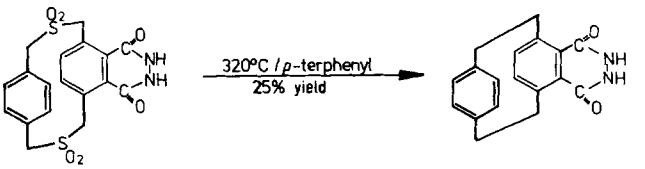
The results obtained in the synthesis of *(98)* and *(100)* have certain consequences for the mechanism of the sulfone pyrolysis (see Section 4).

In a similar connection — investigation of intramolecular charge-transfer interactions — non-benzoid [2.2]phanes[69] such as the tropolone derivative *(101)* were also synthesized by sulfone pyrolysis.



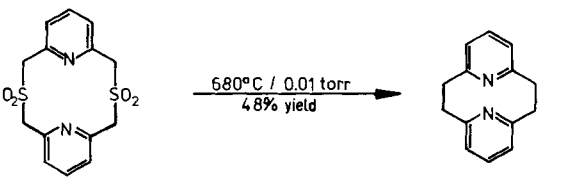
(101)

The phane *(103)* was prepared in a 12-fold amount of *p*-terphenyl as high-boiling solvent[70, 71] (see Section 5.1). In the absence of the terphenyl only a complex product mixture was obtained. This is explained by a matrix-like close-ordering effect of the *p*-terphenyl (b.p. = 383 °C).

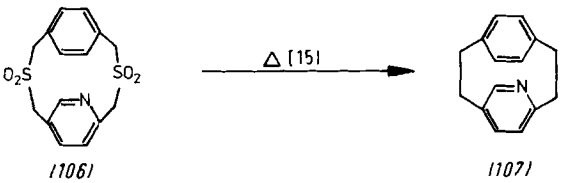


(102) (103)

Pyrolyses of pyridinophanes sometimes yielded poorer results. The bis-sulfone *(104)* can be converted, with ring contraction, into [2.2](2,6)pyridinophane *(105)*[72] under the conditions used for open-chain dibenzyl sulfones by *Leonard*[18].

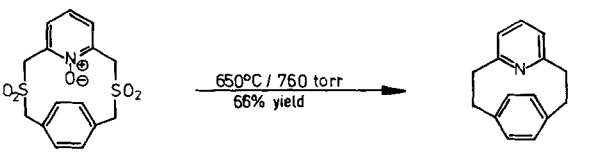


(104) (105)



(106) (107)

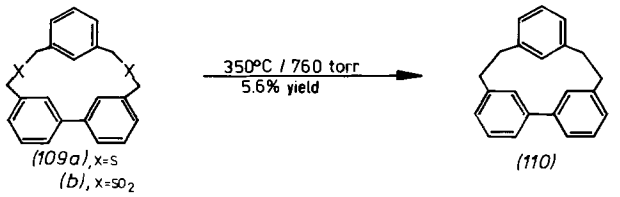
Difficulties were encountered in the preparative scale application of the Curie-point pyrolysis of pyridinophane *(106)* to *(107)*, which was detected by GC/MS coupling[73].



(108)

Pyridine *N*-oxides such as *(108)* not only lose two SO_2 molecules during pyrolysis but also the oxygen atom on the nitrogen[74].

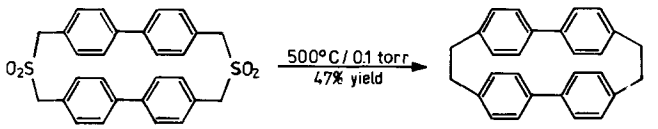
[2.2.n...]- and [2.n...]phanes; pyrolysis of multi-membered cyclic sulfones with more than two (non-annelated) aromatic rings: In addition to the bridging of two aromatic (non-annelated) rings, sulfone pyrolysis has also been used for synthesizing bi-, ter-, quater-, and quinquephenylophanes. The dimethylbiphenyl bridged with 1,3-benzene-bis(methanethiol) *(109a)*[47] could be oxidized to the bis-sulfone *(109b)*, which was pyrolyzed at 350 °C. The only product of this reaction was the strained hydrocarbon *(110)*, even though the (symmetrical) crossover products would be less strongly strained. Therefore, here too it is hardly likely that a synchronous elimination of two SO_2 molecules with the formation of two



(109a), X=S
(b), X=SO_2
(110)

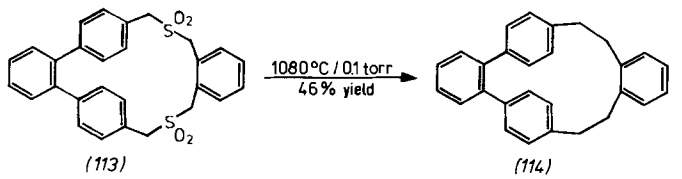
diradicals had taken place. The yield would probably be higher under the experimental conditions used nowadays[43].

[2.2](4,4')biphenylophane *(112)* was synthesized[43] by pyrolysis of the bis-sulfone *(111)*.

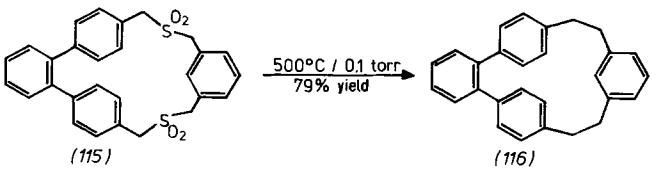


(111) *(112)*

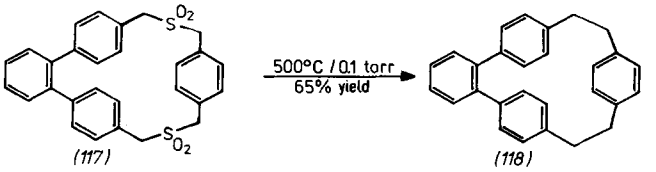
In 1975 it became possible for the first time to carry out the directed pyrolysis of multi-membered sulfones such as *(113)* containing *o*-xylylene-units. At very high temperatures (around 1000 °C) the darkening and carbonization of *(113)* frequently observed under other conditions is suppressed in favor of hydrocarbon formation[75]. The corresponding sulfones with *m*- and *p*-xylylene groups can be pyrolyzed at the usual temperatures.



(113) *(114)*

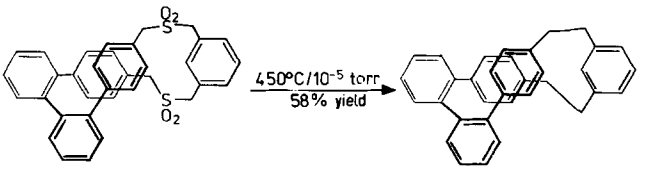


(115) *(116)*

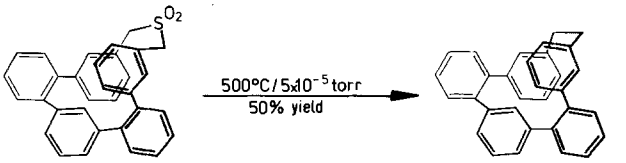


(117) *(118)*

Pyrolysis of the double benzylic quaterphenyl system *(119)* proceeds analogously[76], as does also the pyrolysis of the quinquephenyl system *(121)*[77].

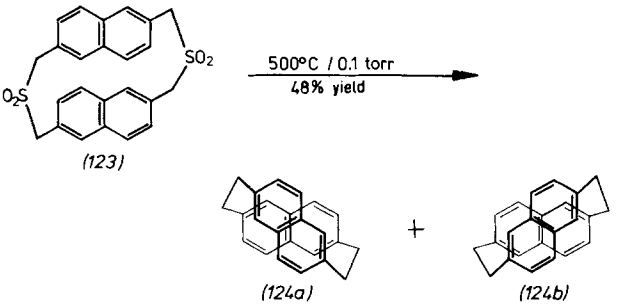


(119) *(120)*



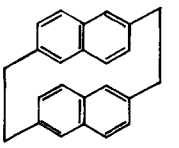
(121) *(122)*

Pyrolysis of multi-membered cyclic sulfones with annelated aromatic rings: Sulfone pyrolysis has proved invaluable in the field of bridged annelated aromatic hydrocarbons. Thus, after other attempts at its synthesis had failed, [2.2]naphthalenophane *(124)*[43,44] was made accessible by sulfone pyrolysis. Of the two possible isomers only the (chiral) product *(124a, b)* [cf. *(97a, b)→(98)*] is formed. This is evidently due



(123) *(124a)* *(124b)*

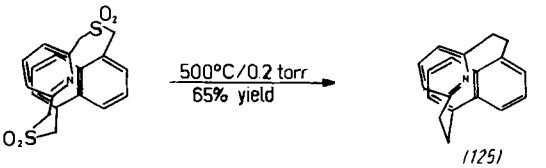
to the fact that the strain energy of the chiral *(124a, b)* is lower than that of the symmetric (achiral) product. In *(124a, b)* the $-(CH_2)_2-$ bridges are oriented at an angle to the plane of the naphthalene rings:



(124)

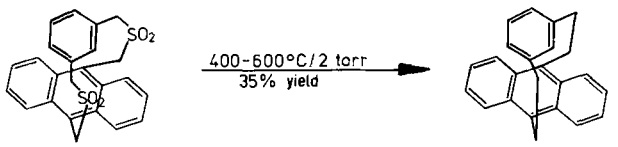
For the mechanism of the pyrolysis it must be assumed that at least on one side of the bis-sulfone a diradical with such long lifetime arises that rapid rotation of the naphthalene system is possible, whereby the preferred chiral phane is formed.

For the investigation of *n*-π interactions[78] (amine-aromatic exciplexes) the naphthalene system was bridged at the 1,5 position with a pyridine ring at the 2,6 position. Pyrolysis of this bis-sulfone gave the desired phane *(125)* in 65% yield.



(125)

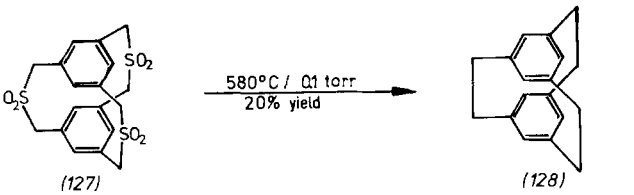
More highly condensed phane systems, *e.g.* anthracenophanes[74,79] and phenanthrenophanes[43a], have likewise been synthesized by pyrolysis.



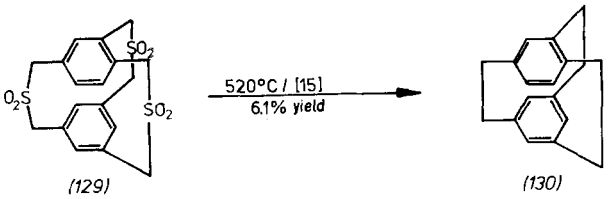
(126)

3.2.3. Tris-Sulfones

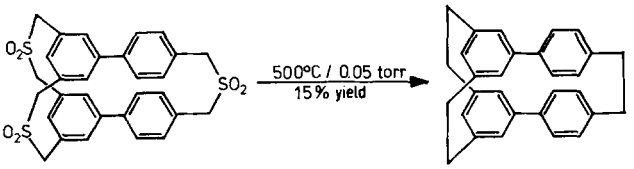
The most important triply-bridged benzenophanes have been synthesized by the pyrolysis of tris-sulfones. Thus, [2.2.2](1,3,5)benzenophane *(128)*[81] could be obtained from the tris-sulfone *(127)*[80]. The constitutionally isomeric cyclophane *(130)* was later synthesized in the same way[82]. The triply-bridged [2.2.2]biphenylophane *(132)*[83] has also been produced by pyrolysis of the corresponding tris-sulfone.



(127) *(128)*

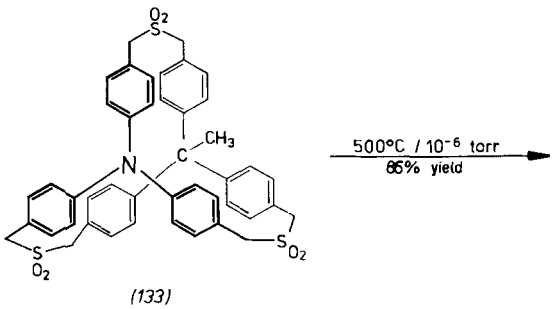


(129) *(130)*



(131) *(132)*

The tris-sulfone *(133)*[84], composed of one triphenylamine unit and one triphenylmethane unit, forms on pyrolysis the triply-bracketed propeller molecule *(134)*[85].

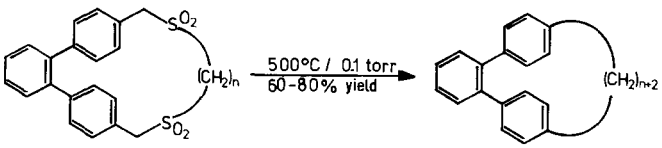


(133) *(134)*

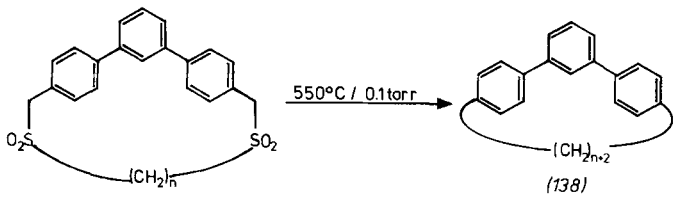
3.3. Unilateral Benzyl Sulfones

Whereas until a few years ago it had been assumed that a benzyl group is necessary on both sides of the SO_2-group in cyclic sulfones for the thermal elimination of SO_2 with C C-recombination, recently it was shown that the benzyl group is dispensable at least on one side, and that such "unilateral non-benzylic sulfones" split off SO_2 thermally in equally good yields with C C bond formation[75]. Pyrolysis of such sulfones allows the synthesis of hydrocarbon cycles bridged by longer chains.

Sulfone pyrolyses of this type were first tested on the terphenyl system; in *(136a-h)* n is 2 to 9, in *(138)* it is 10 or 11 (yields 67 and 77%)[75].

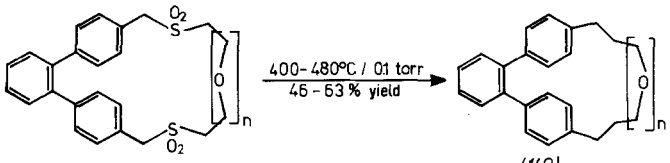


(135a-h) *(136a-h)*



(137) *(138)*

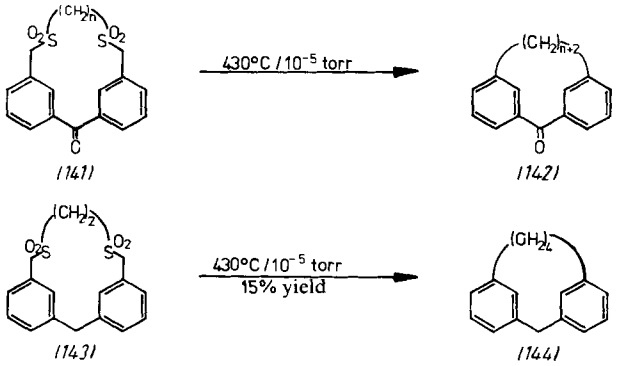
Oligoether structures in the aliphatic chain[75] remain unchanged in the course of thermolysis; this makes possible the



(139) *(140)*

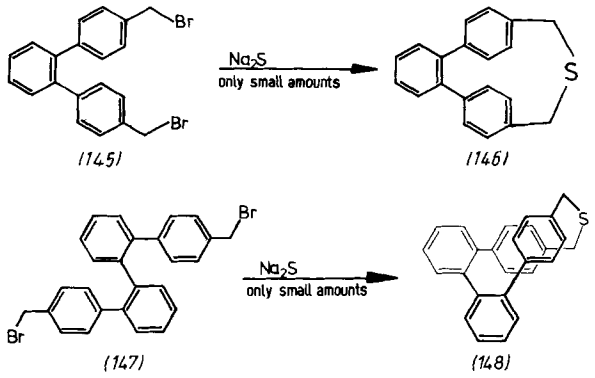
syntheses of new lipophilic/polarophilic neutral ligands such as *(140)*, $n = 1$ to 3.

The bridged benzophenone and diphenylmethane systems[86b] *(142)* $n = 2$ and 3 (yields 7 and 47%) and *(144)*, necessary for studies on the conformative mobility of two-bladed molecular propellers, are also obtained by the pyrolysis of unilaterally benzyl-activated sulfones[86a].



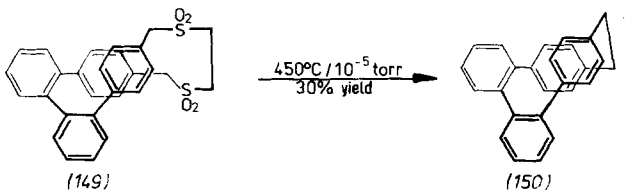
(141) (142) (143) (144)

The cyclization of benzyl halides with Na_2S (or thioacetamide[87]) to monothiaphanes is often impossible, or only possible in unsatisfactory yield, if highly strained ring systems such as *(146)* and *(148)* are to be formed.



(145) (146) (147) (148)

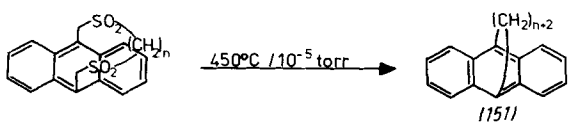
Cyclizations with short-chain alkanedithiols to dithiaphanes often provide the answer. By means of bridging *(147)* with 1,2-ethanedithiol and oxidation the unilateral benzyl bis-sulfone *(149)* is formed; on pyrolysis this gave, after elimination of two SO_2 molecules *and* the C_2H_4 unit, the quaterphenylophane *(150)*[76], which would also be expected in the pyrolysis of the—so far unknown—double benzyl monosulfone.



(149) (150)

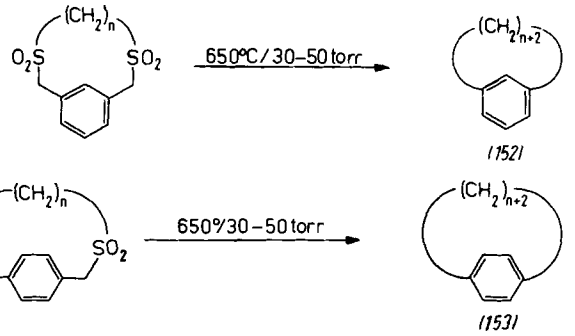
Elimination of the C_2H_4 unit has also been observed in other ethano-bridged bis-sulfones of this type[53a,77,88].

Longer alkane bridges, however, were neither cleaved from anthracene-bis-sulfone[79,89] nor from the benzene-bis-sulfones[90]; the products were formed in high yields [*(151)*,



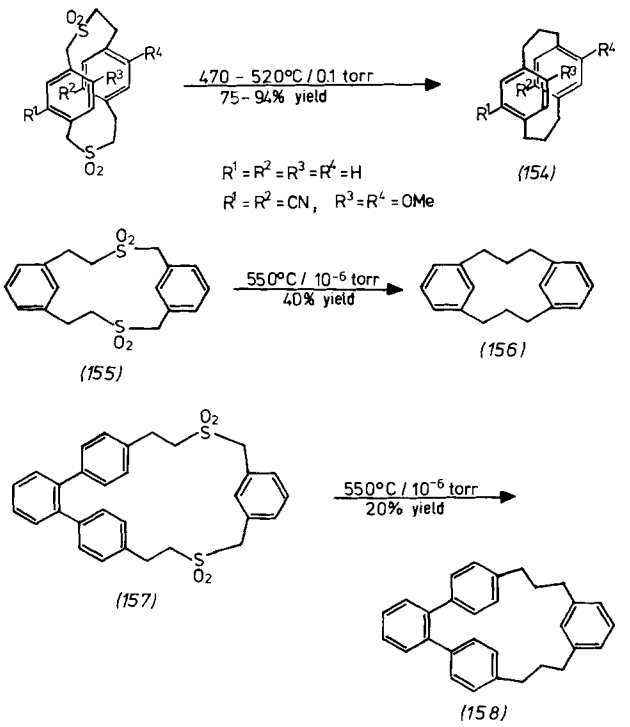
(151)

$n = 8$ and 12 (52 and 10%); *(152)*, $n = 7$ and 10 (53 and 56%); *(153)*, $n = 8$, 9, 10, 11, 12, or 14 (55, 65, 66, 67, 56, and 48%)]. The pyrolysis of unilateral benzyl sulfones was used at prac-



(152) (153)

tically the same time around 1977 by four teams for the synthesis of [3.3]phanes such as *(154)*, *(156)*, and *(158)*[90-94].

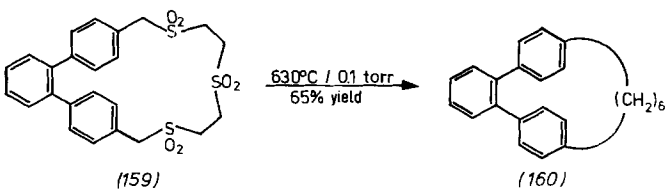


(154) (155) (156) (157) (158)

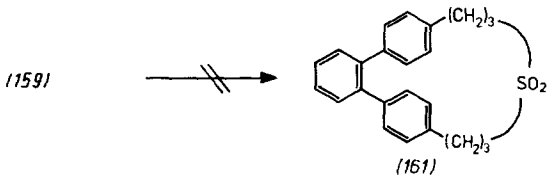
This type of sulfone pyrolysis was also used for the synthesis of multi-layered phanes[95]; the yields were occasionally very high[96].

3.4. Bilateral Non-Benzyl Sulfones

After the pyrolysis of the unilaterally benzylic sulfones had been achieved, the question arose whether bilaterally non-benzylic multimembered sulfones could also be pyrolyzed with the formation of C C bonds. Two observations, made in another context, provided the impetus for systematic studies[75,79]. The surprisingly smooth pyrolysis of the trissulfone *(159)*[75] which contains two unilaterally benzylic SO_2-groups and one bilaterally non-benzylic SO_2-group, with the loss of all three SO_2-groups and recombination of all C-fragments to give the hydrocarbon *(160)* [≡ *(136c)*], was at first regarded as a special case.

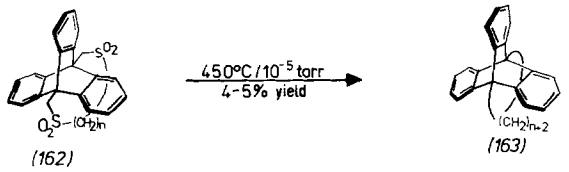


(159) (160)



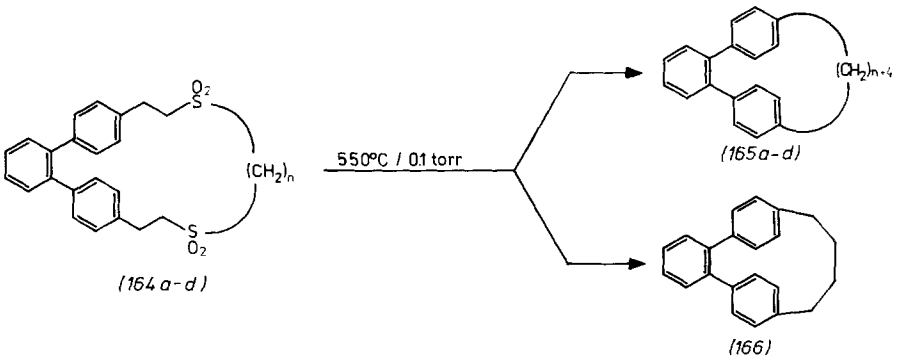
(159) (161)

In spite of the apparently unfavorable steric relationships, the double non-benzyl sulfone pyrolysis of triptycene *(162)* was also successful, with the formation of *(163)*, $n=8$ and 12[79].



(162) (163)

Systematic investigations of the pyrolysis of bilateral non-benzyl sulfones were undertaken on the *o*-terphenyl skeleton[88], which proved to be a highly suitable model system for pyrolysis studies.



(164a-d) (165a-d) (166)

Educt	Products (Yield [%])			
(164a), n = 2	*(165a)* [a]	5	*(166)* [d]	15
(164b), n = 3	*(165b)* [b]	10	*(166)*	7
(164c), n = 6	*(165c)* [c]	15	*(166)*	5
(164d), n = 10	*(165d)*	10	*(166)*	5

[a] *(165a)* ≡ *(160)* ≡ *(136c)*. [b] *(165b)* ≡ *(136d)*. [c] *(165c)* ≡ *(136g)*. [d] *(166)* ≡ *(136a)*.

Cleavage of the alkane chain was also observed in some pyrolyses[53,76,77]. In every case a mixture of phanes with incorporated *(165)* and eliminated *(166)* alkane chains was formed. The ratio of the products depends, *inter alia*, on the lengths of the alkane chains. Further studies on the temperature dependence are still needed[97] (see Section 5.3.6[114]).

4. The Mechanism of Sulfone Pyrolysis

The mechanisms of thermal elimination of SO_2 are still far from completely understood. The most essential experimental findings are summarized in the following.

The majority of sulfone pyrolyses are regarded today as radical processes, though multicenter transition states and ionic intermediates have also been formulated[2,11,98,99]. A sharp delimitation of the mechanisms is difficult, since the outcome of the pyrolysis depends on the substrate structure, the pressure, the solvent, and in particular on the temperature.

4.1. Radical Mechanisms

4.1.1. Acyclic Sulfones

Radicals have long been assumed to be intermediates in pyrolysis reactions and numerous attempts have been made to detect them[14,18,98,99]. The thermal elimination of SO_2 from some acyclic *monosulfones* can be subdivided schematically into the following individual reactions:

$$R^1-SO_2-R^2 \rightarrow R^1-SO_2\cdot + R^2\cdot$$
$$R^1-SO_2\cdot \rightarrow R^1\cdot + SO_2$$
$$R^1\cdot + R^2\cdot \rightarrow R^1-R^2$$
$$2R^1\cdot \rightarrow R^1-R^1$$
$$2R^2\cdot \rightarrow R^2-R^2$$

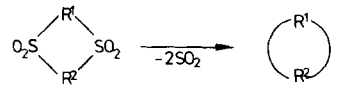
Recombination of the C-radicals which are formed leads to a mixture of products, indicating the production of radicals[98].

4.1.2. Cyclic Monosulfones

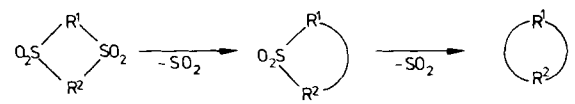
Although no radicals have yet been detected as reactive intermediates in the pyrolyses of cyclic monosulfones[42], it nevertheless seems likely that they do occur as intermediates at the temperatures used.

4.1.3. Cyclic Bis-Sulfones

Two radical mechanisms are conceivable in the thermolysis of cyclic bis-sulfones[43,44]: The two SO_2 molecules could be eliminated at approximately the same time in one step ("one-step mechanism")[43,44],



or the process could take place in two steps. After the first SO_2 molecule has been eliminated, the "diradical" could recombine before the other SO_2 group leaves the molecule ("two-step mechanism")[43,44].



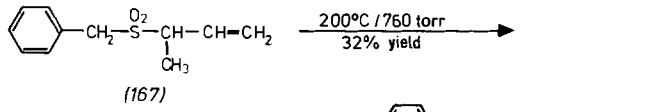
This intramolecular process was postulated as early as 1969 as an explanation for the absence of crossover products[17,42,47]. A good indication that some bis-sulfones eliminate SO_2 by this two-step mechanism is the fact that monosulfones are isolated, even if only in small quantities[47,62] [cf. Section 3.2.2, compound *(86)*].

However, the two-step mechanism cannot account for all the experimental findings. For example, it cannot explain the elimination of alkane residues from unilaterally benzyl-activated bis-sulfones such as *(149)*[53a,76,77,88]. This observation is rather attributed to the one-step mechanism.

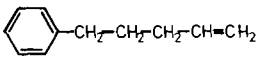
4.2. Reactions with Multicenter Transition States

4.2.1. Acyclic Monosulfones

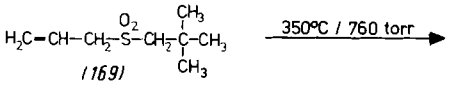
LaCombe and *Steward*[14] assumed that acyclic allyl sulfones eliminate SO_2 at temperatures above 150 °C in a multicenter reaction. This hypothesis is supported by two experimental findings: in the first place, benzyl-(1-methylallyl)sulfone *(167)* eliminates SO_2 with the formation of 32% of 5-phenylpentene *(168)*. No symmetric products have yet been detected that would indicate a radical mechanism. Secondly, the composition of the product mixture in the pyrolysis of



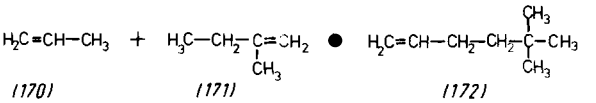
(167)



(168)



(169)



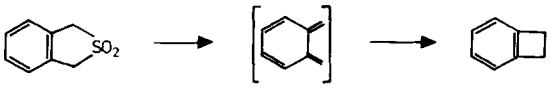
(170) *(171)* *(172)*

allyl neopentyl sulfones, *e.g.* the parent substance *(169)*, is temperature-dependent. At 350 °C, in addition to 5,5-dimethyl-1-hexene *(172)* larger amounts of propene *(170)* and 2-methyl-1-butene *(171)* are also produced. The formation of these substances, which can be interpreted as due to radicals, may possibly be suppressed by lowering the temperature.

4.2.2. Cyclic Sulfones

The thermal elimination of SO_2 from *cyclic monosulfones* such as *(41)* and *(43)* to give compounds with conjugated π-systems can be interpreted in terms of an electrocyclic ring opening. This type of sulfone pyrolysis is thus a special case of cheletropic reactions. In a concerted process the elimination of SO_2 follows the Woodward-Hoffmann rules[31,32]. The characteristic features—distinct stereospecific course of the reaction and mild conditions—suggest a mechanism of this kind.

The mechanism of the thermal elimination of SO_2 from *cyclic aromatic-aliphatic sulfones* is uncertain. As an example we may cite the synthesis of dihydrocyclobutabenzene *(29)* by *Cava*'s method[22] (cf. Section 2).



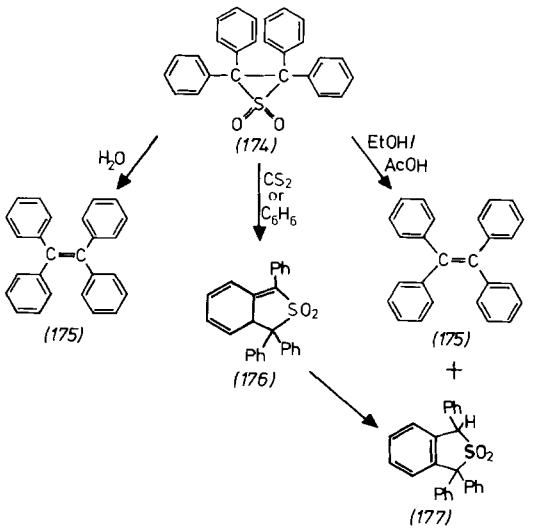
(28) *(173)* *(29)*

The intermediate *(173)* could be intercepted by a Diels-Alder reaction, but its existence gives no indication of the course of the actual cleavage of SO_2. It is quite possible that a radical mechanism and a reaction with a multicenter transition state are competing. Although the high pyrolysis temperature would suggest the formation of radicals, it could also be regarded as necessary to break up the aromatic system in a concerted mechanism.

4.3. Ionic Mechanisms

The pyrolysis of sulfones in which the SO_2-group is part of a three-membered ring can be interpreted as probably ionic, without the influence of bases or acids as catalysts[20,100]. Definite proof is difficult, because most of the thiirane 1,1-dioxides cannot be isolated but appear as intermediates in base-induced nucleophilic substitutions from α-halogenosulfones[20]. An SO_2 elimination starting from an isolated thiirane 1,1-dioxide was possible in the case of the tetraphenyl derivative *(174)*[100a].

Two types of reaction compete with each other in dependence on the solvent used: elimination of SO_2 to give the alkene and rearrangement without loss of SO_2. An ionic mechanism is suggested by the finding that in polar, ionizing solvents the formation of tetraphenylethene *(175)* takes precedence over rearrangement to *(177)*. In the same way, the pyrolyses of *o*-alkyl-substituted diaryl sulfones *(1)* to diphenylmethanes *(5)*[11] quoted in Section 2 can also be regarded as ionic. However, so far none of the necessary intermediates have been detected.



(174) *(175)* *(176)* *(175)* *(177)*

5. Experimental Description of Selected Sulfone Pyrolyses

In this section an account is given of some typical sulfone pyrolysis methods and apparatus. These methods and the apparatus used are suitable not only for the pyrolysis of these and other sulfones under similar conditions, but in principle also for the pyrolysis reactions such as the thermal elimination of CO_2[101,104], CO[101,105,107], and N_2[101,108].

5.1. Pyrolysis of Dissolved Sulfones

[2](2,2'')-m-terphenylophane (71)[51]: 2.6 g (8.10 mmol) of *(70)* was heated in 7 ml of diphenyl ether for 45 min to 290—

300 °C (oil bath temperature). The diphenyl ether was distilled off at 12 torr. The yield of the crystalline crude product (m.p. 148—150 °C) was quantitative. Recrystallization from ethanol gave practically colorless flakes (m.p. 153 °C), readily sublimable under vacuum.

[2.2]Paracyclophane-4,5-dicarboxylic acid dihydrazide (103)[71]: The sulfone *(102)* was mixed with a 12-fold amount of *p*-terphenyl and pyrolyzed at 325 °C. The *p*-terphenyl evidently exerts here a matrix-like short-range order effect, since the yield increases from a few percent of *(103)* in the absence of *p*-terphenyl to 25% in its presence.

5.2. Pyrolysis in the Melt

[2](2,2'')-m-terphenylophane (71)[51]: 1.0 mg (3×10^{-3} mmol) of *(70)* was heated in a melting-point tube to 290 °C, the substance melting and evolving gas. After about 5 min the melt was allowed to cool and crystallization was induced by rubbing with florists' wire at about 145 °C. The material was then reheated; it now melted at 150 °C, even on repetition of the melting point determination.

5.3. Pyrolysis Apparatus

5.3.1. Simple Apparatus

[2.2]Metaparacyclophane (81a)[17]: 1—3 g of *(80a)* was placed in a horizontally clamped modified bulb-tube and heated in an electrically heated aluminum block (Fig. 1) to a temperature of 350—370 °C, the pyrolysis products being distilled off and solidifying in the bulb. Re-crystallization from a mixture of chloroform and methanol followed by sublimation gave pure *(81a)*.

If we take into account the simplicity of the method and the strained ring system, the yield (18%) is astonishingly high. It may be possible to increase the yield with present-day apparatus[109], by the application of vacuum[18,22,43a] (the bulb-tubes used could be fitted to normal vacuum tubes), and division of the metal block into mobile ring furnaces[75]. However, this reaction has been selected to demonstrate the utter simplicity of the pyrolysis; smaller quantities of [2.2]phanes can be obtained readily and rapidly with means available in all laboratories and without ring furnace arrangements. The temperature of the metal block is adjusted as desired to the sublimation or decomposition temperature of the sulfone, so that the latter is pyrolyzed while still in the furnace during or shortly after the sublimation.

5.3.2. Pyrolysis Apparatus for Liquid Sulfones or Sulfones Melting without Decomposition

1,2-Dihydrocyclobutabenzene (29)[22]: The sulfone *(28)* is transferred to a 125 ml round-bottom flask fitted with a sleeve containing a nichrome heating coil and a cold finger cooled with acetone and dry ice located above the heating coil (Fig. 2). The apparatus is flushed out with N_2 and evacuated to 2 torr. The sulfone is slowly sublimed through the electrically heated coil ("gas-phase-vacuum" apparatus) and the product condenses on the cold finger. After warming the solid condensate to room temperature, slow equalization of pressure, and distillation under normal pressure, *(29)* is obtained as a colorless liquid (b.p. 149—150 °C) in a yield of 60%.

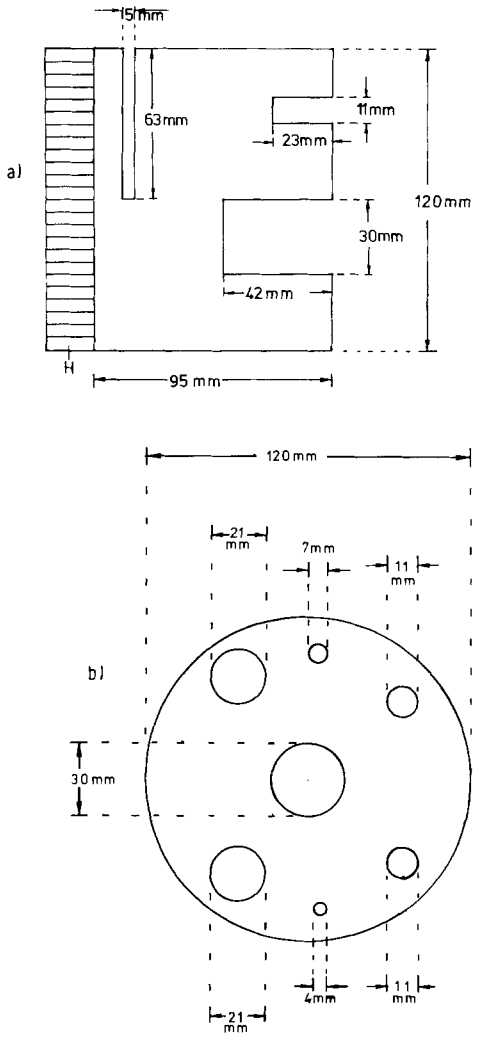


Fig. 1. Simple apparatus for sulfone pyrolysis (after [47]), with the original dimensions. a) Longitudinal section: the electric hot plate H is fitted with removable clamps. b) Top view of a similar pyrolysis furnace with drilled holes of various diameters for several bulb tubes of various diameters and for melting-point tubes, test tubes, and thermometers.

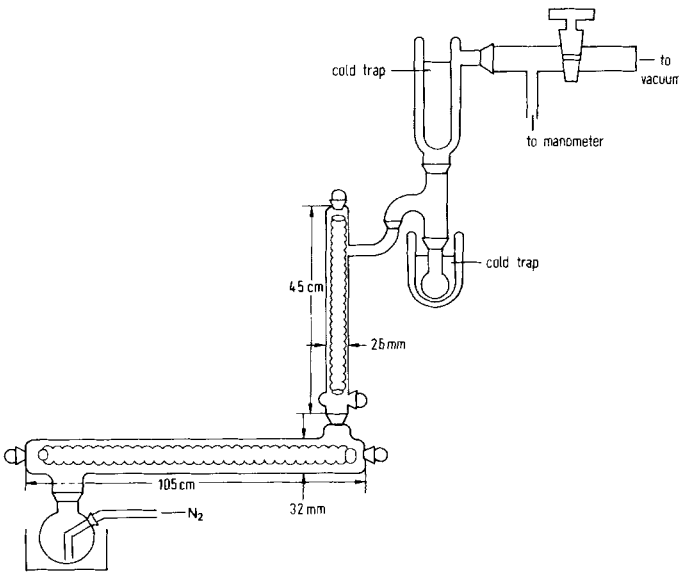


Fig. 2. Pyrolysis apparatus (with dimensions) after *Oliver* and *Ongley* [28].

5.3.3. Pyrolysis Apparatus with Stationary Ring Furnaces

Bibenzyl (19), $R^1=R^2=H$[18]: The pyrolysis apparatus consists of a tube about 700 mm in length and 25 mm in diameter, closed at one end. The open end is connected to a cold finger followed by two cold traps connected in series. The tube is enclosed by three electrically heated furnaces. The purpose of the first furnace is to distill the sulfone (temperature 50 °C above the melting point of the sulfone), while the second and third furnaces constitute the pyrolysis unit proper. 1.00 g (6.40 mmol) of dibenzyl sulfone *(18)*, $R^1=R^2=H$, was placed in a refractory boat which was pushed near the closed end of the tube. At 650 °C/0.1 torr it took 30 min for all the sulfone to be pyrolyzed to *(19)*, $R^1=R^2=H$ in a yield of 90%.

[2.2](4,4')Biphenylophane (112)[43,44]: After charging the boat with a total of 2.40 g (4.92 mmol) of *(111)* in portions of 300—500 mg, the apparatus (cf. Fig. 3) was evacuated with oil and mercury diffusion pumps to 0.1 torr; a current of argon was passed in through a capillary tube to maintain this pressure. The temperature of the pyrolysis furnace was raised to 500 °C and the evaporator furnace was quickly heated to 300 °C and in 2—3 h to 400 °C. 1.05 g (59%) of light yellow pyrolyzate condensed on the cold finger, leaving a brown, amorphous residue in the boat. Purification gave colorless needles (m.p. 247—249 °C).

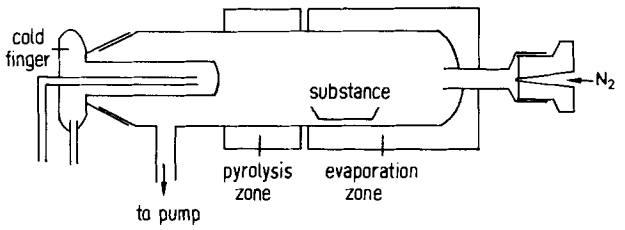


Fig. 3. Gas-phase-vacuum pyrolysis apparatus after *Staab* and *Haenel* [43, 44].

5.3.4. Apparatus with Freely Mobile Ring Furnaces

[4]-[11](4,4'')-o-Terphenylophanes (136a—h), n=2—9[75b]: The pyrolysis apparatus shown in Figure 4 was used for small quantities (50—100 mg) of the sulfone *(135a—h)*. The 250-mm long quartz pyrolysis tube had an internal diameter of 4 mm and was fused at one end. It opened *via* a screw connection with silicone seal into a further glass tube, into which a cold finger protruded from the other side, the cold finger providing the connection to the vacuum pump. Four ring furnaces served as the source of heat, mounted independently of one another and adjustable horizontally on a light metal support. Each furnace could be adjusted independently to the desired temperature.

After charging with 50—80 mg of *(135a—h)*, the ring furnaces were heated to about 500 °C. As a rule the first ring

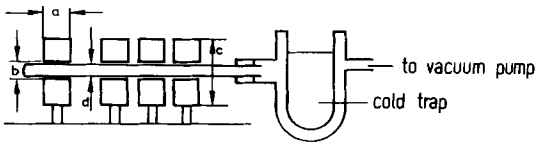


Fig. 4. Small pyrolysis apparatus, schematic [75]. Furnace: a = 10, b = 6, c = 18 mm; quartz tube: d = 4 mm.

furnace was used to sublime the sulfone while the other three ring furnaces, pushed closely together, jointly acted as a pyrolysis zone 40 mm in length. The pyrolysis product *(136a—h)* was deposited on the cold finger in a yield of 60—80%.

The pyrolysis furnace shown in Figure 5 was in principle no different from the furnaces of the micro-apparatus (Fig. 4). Apart from mechanical improvements[110], the only difference was that it was larger and thus particularly well suited for "medium" quantities (0.1—1 g) of the sulfone; the ring furnaces were controlled electronically and could be quickly adjusted to preselected temperatures without the risk of overheating[110].

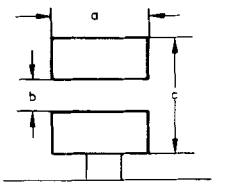


Fig. 5. Furnace of the medium-sized pyrolysis apparatus, schematic. a = 50, b = 12, c = 42 mm [110].

[2](2,4'''')-1,1';2',1'';3'',1''';2''',1''''-Quinquephenylophane[77]: 2,5-Dithia[6](2,4'''')-1,1';2',1'';3'',1''';2''',1''''-quinquephenylophane 2,2,5,5-tetroxide (735 mg, 1.30 mmol) was placed in the 40 mm-long quartz tube (diameter 8 mm) of the medium pyrolysis apparatus (Fig. 5). After evacuation of the tube to 5×10^{-5} torr with a diffusion pump, the 50-mm long mobile furnace was set at 600 °C. The sulfone pyrolyzed to the phane in a yield of 46%, with loss of SO_2 and C_2H_4.

[2.2]Paracyclophane[112]: The "macro-pyrolysis apparatus" shown in Figure 6 is suitable for larger amounts of sulfone. In this apparatus too the four ring furnaces can be moved in a longitudinal direction on ball-bearings[111]; their temperatures can be adjusted independently of one another.

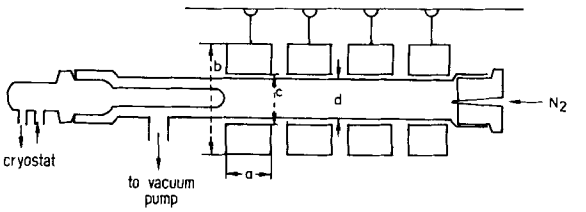


Fig. 6. Pyrolysis apparatus for larger quantities of the substance, schematic [111]. Furnace: a = 105, b = 117, c = 27 mm; quartz tube: d = 25 mm.

1.00 g (2.98 mmol) of *2,9-Dithia[3.3]paracyclophane 2,2,9,9-tetroxide (99a)*, X=Y=H, was mixed with 10 g of dried sea sand (p.a.) and the mixture placed in the 140 cm long quartz tube (diameter 25 mm). The ring furnaces were set as follows: evaporator furnace 380 °C, pyrolysis furnaces 450 °C. The pyrolysis was carried out under inert gas at a pressure of 0.1 torr. The (nonoptimized) yield was 18%.

5.3.5. Continuous Sulfone Pyrolysis for Larger Quantities of Substance[112]

Up to now in the pyrolysis of larger quantities of the substance it was usually necessary to open the apparatus after it had cooled and to recharge it. We have developed an apparatus in which additional sulfone can be added during the pyrolysis[112]. The principle is illustrated in Figure 7. The basic

components are inlet and outlet tubes fused perpendicularly into the pyrolysis tube, through which the starting material can be introduced and the residues can be removed without breaking the vacuum, together with a vacuum-tight solids-metering device.

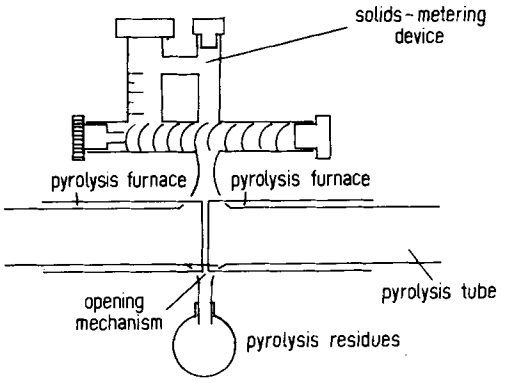


Fig. 7. Sulfone-pyrolysis apparatus for continuous operation (schematic) [112].

5.3.6. Coupling of Sulfone Pyrolysis with Gas Chromatography

The pyrolysis of mg amounts of a sulfone is required for a systematic study of the elimination-incorporation equilibrium in sulfones bridged with paraffin chains [cf. *e.g. (164)* → *(165)* + *(166)*]. A combination of pyrolysis apparatus and gas chromatograph is suitable for this purpose[113].

[2.0.0](1,4)Benzeno(1,8)naphthaleno(1,4)benzenophane (73) (see [52]): The apparatus used for the pyrolysis of the sulfone *(72b)*, $X = O_2S(CH_2)_2SO_2$[97, 114]— commercial Curie point[115] and Pyroprobe®-190 pyrolyzers[116]— was in each case connected directly to the injector of a gas chromatograph[117]. With a constant injector temperature of 450—900 °C (at intervals of 50 °C) the sulfone was injected into the injector space through the membrane. Pyrolysis occurred within about 10 msec, and the elimination of C_2H_4 increased with increasing temperature. The retention times of the products were compared with those of authentic samples. Some of the pyrolyses were repeated in the apparatus shown in Figure 4 so as to keep a check on the preparative scale performance; the temperature dependence of the product distribution proved to be comparable. The pyrolysis of multimembered sulfides with the elimination of sulfur and the formation of C C bonds was first discovered using this combination of equipment[113].

6. Outlook

The described examples of SO_2 elimination from sulfones allow an appraisal of the conditions for pyrolyses still untried. Given comparable mechanisms, it may be possible to cleave other fragments similarly to the elimination of SO_2 (*e.g.* CO_2[101-104], CO[101,105-107], N_2[101,108], SO[118,119], and S[113]. The ease with which the pyrolysis conditions may be varied, the solvent-free operations and the rapidity of the preparations make this technique a basically attractive one.

For our own results quoted in this article we are especially grateful to all co-workers cited in the accompanying references. We are also grateful to the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for their invaluable support and to Dipl.-Chem. R. Wingen for reading the manuscript.

Received: July 25, 1978
supplemented: May 2, 1979 [A 278 IE]
German version: Angew. Chem. *91*, 534 (1979)
Translated by AD-EX (Translations) Ltd., London

[1] We shall deal here only with those sulfones whose sulfur atoms are directly bonded to two C atoms.
[2] *J. L. Kice* in *N. Kharasch, C. Y. Meyer:* The Chemistry of Organic Sulfur Compounds. Pergamon Press, London 1966, p. 115.
[3] *J. D. London* in *N. Kharasch, C. Y. Meyer:* The Chemistry of Organic Sulfur Compounds. Pergamon Press, London 1966, p. 99.
[4] *L. Field*, Synthesis *1972*, 101.
[5] *R. L. Olsen, J. O. Currie*, Jr., in *S. Patai:* The Chemistry of the Thiol Group. Wiley, New York 1974, Vol. 2, p. 566.
[6] *W. E. Truce, T. C. Klingler, W. W. Brand* in *S. Oae:* Organic Chemistry of Sulfur. Plenum Press, New York 1977, p. 577.
[7] *Houben-Weyl-Müller:* Methoden der organischen Chemie. Thieme, Stuttgart 1955, 4th Edit. Vol. IX.
[8] *E. Gibstein, E. Wellisch, O. J. Sweeting*, J. Appl. Polym. Sci. *8*, 1623 (1964).
[9] *E. Gibstein, E. Wellisch, O. J. Sweeting*, J. Org. Chem. *29*, 207 (1964).
[10] *W. Z. Heldt*, J. Org. Chem. *30*, 3897 (1965).
[11] *H. Drews, E. K. Fields, S. Meyerson*, Chem. Ind. (London) *1961*, 1403.
[12] Conversion factor 1 torr = 133 pascal.
[13] *J. B. Hendrickson, R. Bergeron*, Tetrahedron Lett. *1973*, 3609.
[14] *E. M. LaCombe, B. Steward*, J. Am. Chem. Soc. *83*, 3457 (1961).
[15] The work does not contain further data on the conditions of pyrolysis.
[16] *E. Fromm, O. Achert*, Ber. Dtsch. Chem. Ges. *36*, 534 (1903).
[17] Cf. *F. Vögtle*, Chem. Ber. *102*, 3077 (1969).
[18] *E. C. Leonard, Jr.*, J. Org. Chem. *27*, 1921 (1962).
[19] *S. W. Chow, L. A. Pilato, W. L. Wheelwright*, J. Org. Chem. *35*, 20 (1970).
[20] *N. H. Fischer*, Synthesis *1970*, 393; and references cited therein.
[21] a) *R. M. Dodson, G. Klose*, Chem. Ind. (London) *1963*, 450; b) *B. M. Trost, W. L. Schinski, F. Chen, J. B. Mantz*, J. Am. Chem. Soc. *93*, 676 (1971).
[22] *M. P. Cava, A. A. Deana*, J. Am. Chem. Soc. *81*, 4266 (1959).
[23] *M. P. Cava, R. L. Shirley*, J. Am. Chem. Soc. *82*, 654 (1960).
[24] *M. P. Cava, R. L. Shirley, B. W. Erickson*, J. Org. Chem. *27*, 755 (1962).
[25] *M. P. Cava, J. A. Kuczkowski*, J. Am. Chem. Soc. *92*, 5800 (1970).
[26] *M. P. Cava, R. H. Schlessinger*, Tetrahedron Lett. *1965*, 3065.
[27] Pyrolysis apparatus are described in Section 5.
[28] *J. A. Oliver, P. A. Ongley*, Chem. Ind. (London) *1965*, 1024.
[29] *E. Giovanni, H. Vuilleumier*, Helv. Chim. Acta *60*, 1452 (1977).
[30] *E. J. Moriconi, R. E. Misner, T. E. Brady*, J. Org. Chem. *34*, 1651 (1969).
[31] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[32] *M. J. S. Dewar*, Angew. Chem. *83*, 859 (1971); Angew. Chem. Int. Ed. Engl. *10*, 761 (1971).
[33] *W. L. Mock*, J. Am. Chem. Soc. *88*, 2857 (1966).
[34] *S. D. McGregor, P. M. Lemal*, J. Am. Chem. Soc. *88*, 2858 (1966).
[35] *W. L. Mock*, J. Am. Chem. Soc. *91*, 5682 (1969).
[36] *F. G. Bordwell, W. H. McKellin, D. Bablock*, J. Am. Chem. Soc. *73*, 5566 (1951).
[37] *W. J. Bailey, E. W. Cummins*, J. Am. Chem. Soc. *76*, 1936 (1954).
[38] *E. J. Corey, E. Block*, J. Org. Chem. *34*, 1233 (1969).
[39] *I. Tabushi, Y. Tamaru, Z. Yoshida*, Tetrahedron Lett. *1976*, 3957.
[40] *D. H. Hunter, J. B. Stothers*, Can. J. Chem. *51*, 2884 (1973).
[41] *N. J. Hales, D. J. H. Smith, M. E. Swindles*, J. Chem. Soc. Chem. Commun. *1976*, 981.
[42] *F. Vögtle*, Angew. Chem. *81*, 258 (1969); Angew. Chem. Int. Ed. Engl. *8*, 274 (1969).
[43] Cf. a) *H. A. Staab, M. Haenel*, Chem. Ber. *106*, 2190 (1973); b) *M. Haenel, H. A. Staab, ibid. 106*, 2203 (1973).
[44] *M. Haenel*, Tetrahedron Lett. *1977*, 4191.
[45] a) *N. Kannen, T. Otsubo, Y. Sakata, S. Misumi*, Bull. Chem. Soc. Jpn. *49*, 3203 (1976); b) *ibid. 49*, 3208 (1976).
[46] *F. Vögtle, P. Neumann*, Synthesis *1973*, 85, and references cited therein.
[47] *F. Vögtle*, Justus Liebigs Ann. Chem. *728*, 17 (1969).
[48] Review: *F. Vögtle, H. Förster*, Angew. Chem. *89*, 443 (1977); Angew. Chem. Int. Ed. Engl. *16*, 429 (1977).
[49] Cf. a) *H. A. Staab, H. Haffner*, Tetrahedron Lett. *1974*, 4397; b) *H. A. Staab, C. Herz, H.-E. Henke, ibid. 1974*, 4393.
[50] Review: *F. Vögtle, G. Hohner*, Top. Curr. Chem. *74*, 1 (1978).
[51] *F. Vögtle*, Chem. Ber. *102*, 1449 (1969).
[52] *W. Bieber, F. Vögtle*, Angew. Chem. *89*, 199 (1977); Angew. Chem. Int. Ed. Engl. *16*, 175 (1977).
[53] a) *F. Vögtle, R. Wingen*, Tetrahedron Lett. *1978*, 1459; b) analogous bridging in 3',4''-position: *W. Bieber, F. Vögtle*, Chem. Ber. *112*, 1919 (1979).

[54] *F. Vögtle, L. Schunder*, Chem. Ber. *102*, 2677 (1969).
[55] *F. Vögtle, R. Lichtenthaler*, Z. Naturforsch. *26*, 872 (1971).
[56] *V. Boekelheide, P. H. Anderson*, J. Org. Chem. *38*, 3928 (1973).
[57] *D. J. Cram, R. C. Helgeson, D. Lock, R. A. Singer*, J. Am. Chem. Soc. *88*, 1324 (1966).
[58] *T. Hylton, V. Boekelheide*, J. Am. Chem. Soc. *90*, 6887 (1968).
[59] *F. Vögtle, P. Neumann*, Chimia *26*, 64 (1972).
[60] a) *P. Neumann*, Dissertation, Universität Heidelberg 1973; b) *F. Vögtle, P. Neumann*, Top. Curr. Chem. *48*, 69 (1974).
[61] *V. Boekelheide, Ch. H. Tsai*, J. Org. Chem. *38*, 3933 (1973).
[62] *S. A. Sherrod, R. L. DaCosta, R. A. Barnes, V. Boekelheide*, J. Am. Chem. Soc. *96*, 1565 (1974).
[63] a) *D. T. Longone, H. S. Chow*, J. Am. Chem. Soc. *86*, 3898 (1964); b) *ibid. 92*, 994 (1970).
[64] a) *T. Umemoto, S. Satani, Y. Sakata, S. Misumi*, Tetrahedron Lett. *1975*, 3159; b) *N. Kannen, T. Umemoto, T. Otsubo, S. Misumi, ibid. 1973*, 4537.
[65] a) *H. A. Staab, M. Zapf, A. Gurke*, Angew. Chem. *89*, 841 (1977); Angew. Chem. Int. Ed. Engl. *16*, 801 (1977); b) *H. A. Staab, C. Herz, ibid. 89*, 839 (1977) and *16*, 799 (1977).
[66] a) *W. Rebafka, H. A. Staab*, Angew. Chem. *85*, 831 (1973); Angew. Chem. Int. Ed. Engl. *12*, 776 (1973); b) *ibid. 86*, 234 (1974) and *13*, 203 (1974).
[67] *H. A. Staab, W. Rebafka*, Chem. Ber. *110*, 3333 (1977).
[68] Cf. *J. Bruhin, W. Jenny*, Tetrahedron Lett. *1973*, 1215. For further desulfuration methods see *R. H. Mitchell*, Heterocycles *11*, 563 (1978).
[69] *N. Kato, Y. Fukazawa, S. Ito*, Tetrahedron Lett. *1979*, 1113.
[70] *K.-D. Gundermann, K.-D. Röker*, Justus Liebigs Ann. Chem. *1976*, 140.
[71] *K.-D. Gundermann, K.-D. Röker*, Angew. Chem. *85*, 451 (1973); Angew. Chem. Int. Ed. Engl. *12*, 425 (1973).
[72] *H. J. J.-B. Martell, M. Rasmussen*, Tetrahedron Lett. *1971*, 3843.
[73] *J. Bruhin, W. Jenny*, Chimia *26*, 420 (1972); cf. [115].
[74] *V. Boekelheide, K. Galuszko, K. S. Szeto*, J. Am. Chem. Soc. *96*, 1578 (1974).
[75] a) *F. Vögtle, J. Grütze*, Angew. Chem. *87*, 453 (1975); Angew. Chem. Int. Ed. Engl. *14*, 559 (1975); b) *J. Grütze, F. Vögtle*, Chem. Ber. *110*, 1978 (1977).
[76] *F. Vögtle, M. Atzmüller, W. Wehner, J. Grütze*, Angew. Chem. *89*, 338 (1977); Angew. Chem. Int. Ed. Engl. *16*, 325 (1977).
[77] *F. Vögtle, E. Hammerschmidt*, Angew. Chem. *90*, 293 (1978); Angew. Chem. Int. Ed. Engl. *17*, 268 (1978); *E. Hammerschmidt, F. Vögtle*, Chem. Ber. *112*, 1785 (1979).
[78] *M. W. Haenel*, Tetrahedron Lett. *1978*, 4007.
[79] *F. Vögtle, P. Koo Tze Mew*, Angew. Chem. *90*, 58 (1978); Angew. Chem. Int. Ed. Engl. *17*, 60 (1978).
[80] *F. Vögtle*, Justus Liebigs Ann. Chem. *735*, 193 (1970).
[81] *V. Boekelheide, R. A. Hollins*, J. Am. Chem. Soc. *95*, 3201 (1973).
[82] a) *M. Nakazaki, K. Yamamoto, Y. Miura*, J. Chem. Soc. Chem. Commun. *1977*, 206; b) J. Org. Chem. *43*, 1041 (1978).
[83] *F. Vögtle, G. Steinhagen*, Chem. Ber. *111*, 205 (1978).
[84] *J. Winkel*, Diplomarbeit, Universität Bonn 1977; *F. Vögtle, J. Winkel*, Tetrahedron Lett. *1979*, 1561.
[85] *G. Hohner, F. Vögtle*, Chem. Ber. *110*, 3052 (1977).
[86] a) [*n*.1]Paracyclophanes by sulfone pyrolysis cf.: *A. Ruland, H. A. Staab*, Chem. Ber. *111*, 2997 (1978). We thank Prof. *Staab* for sending a copy of the manuscript prior to publication; b) *F. Vögtle, M. Atzmüller, ibid. 111*, 2547 (1978).
[87] *E. Hammerschmidt, W. Bieber, F. Vögtle*, Chem. Ber. *111*, 2445 (1978).
[88] *F. Vögtle, L. Rossa*, Tetrahedron Lett. *1977*, 3577.
[89] *T. Otsubo, M. Kitasawa, S. Misumi*, Chem. Lett. *8*, 977 (1977).
[90] *T. Otsubo, S. Misumi*, Synth. Commun. *1978*, 285.
[91] *D. T. Longone, S. H. Küsefoglu, J. A. Gladysz*, J. Org. Chem. *42*, 2787 (1977).
[92] *M. W. Haenel, A. Flatow, V. Taglieber, H. A. Staab*, Tetrahedron Lett. *1977*, 1733.
[93] *L. Rossa, F. Vögtle*, J. Chem. Res. (S) *1977*, 264; (M) *1977*, 3010.
[94] Here, [3.3]phanes were prepared *via* another route: *T. Shimnyozu, T. Inazu, T. Yoshino*, Chem. Lett. *7*, 1405 (1976).
[95] *T. Otsubo, T. Kohda, S. Misumi*, Tetrahedron Lett. *1978*, 2507.
[96] *M. W. Haenel, A. Flatow*, Chem. Ber. *112*, 249 (1979).
[97] *W. Bieber*, Dissertation, Universität Würzburg 1979.
[98] The pyrolyses products of methyl sulfones have been accurately analyzed: a) *W. K. Busfield, K. J. Ivin*, Trans. Faraday Soc. *57*, 1044 (1961); b) *W. K. Busfield, K. J. Ivin, H. Mackle, P. A. G. O'Hare, ibid. 57*, 1064 (1961); c) *W. K. Busfield, H. Mackle, P. A. G. O'Hare, ibid. 57*, 1054 (1961).
[99] *A. Henglein, H. Url, W. Hoffmeister*, Z. Phys. Chem. (Frankfurt) *18*, 26 (1958).
[100] a) *H. Kloosterziel, H. J. Backer*, Rec. Trav. Chim. Pays-Bas *71*, 1235 (1952); b) *H. Staudinger, F. Pfenninger*, Ber. Dtsch. Chem. Ges. *49*, 1941 (1916).
[101] *G. Seybold*, Angew. Chem. *89*, 377 (1977); Angew. Chem. Int. Ed. Engl. *16*, 365 (1977); and references cited therein. Flash thermolysis is a gas-phase thermolysis with the substance having a brief residence time in the heating zone (1×10^{-3} to 1 s) and with subsequent cooling to very low temperatures (−196 °C). It is suitable for the detection of thermolabile compounds and short-lived intermediates.
[102] *E. A. Truesdale*, Tetrahedron Lett. *1978*, 3777.
[103] *F. Messier, D. C. De Jongh*, Can. J. Chem. *55*, 2734 (1977).
[104] *D. Horton, C. G. Tindall, Jr.*, J. Org. Chem. *35*, 3558 (1970).
[105] *F. W. Eastwood*, private communication 1979.
[106] *L. Carlson, J. P. Snyder*, Tetrahedron Lett. *1977*, 2044.
[107] *G. Schaden*, Angew. Chem. *89*, 50 (1977); Angew. Chem. Int. Ed. Engl. *16*, 50 (1977).
[108] a) *G. Seybold, C. Heibl*, Angew. Chem. *87*, 171 (1975); Angew. Chem. Int. Ed. Engl. *14*, 248 (1975); b) *H. Bock, W. Kaim, A. Semkow, H. Nöth, ibid. 90*, 308 (1978) and *17*, 286 (1978); c) *H. Bock, B. Solouki, J. Wittmann, ibid. 90*, 985 (1978) and *17*, 932 (1978). Cf. *C. Wentrup, B. Gerecht, H. Briehl*, Angew. Chem. *91*, 503 (1979); Angew. Chem. Int. Ed. Engl. *18*, 467 (1979).
[109] This simple apparatus was used for the synthesis of the [2.2.2](1,3,5)benzenophane *(128)* [80]; since the yields were low at 400—420 °C and normal pressure a water-flow vacuum was employed during pyrolysis, whereby the ratio of pyrolyzate collected in the receiver to remaining charred products could be considerably increased. Besides the [2.2.2]phane, 5,13-dimethyl[2.2]metacyclophane *(88)* could also be detected mass spectrometrically.
[110] We thank the electronics and instruments department of our institute, and in particular Ing. *W. Löhr, E. Obst* and *L. Kreymborg*, for development work and improvements.—Circuit diagrams, the novel ring furnace construction (heating wire wound parallel to the axis of the porcelain tube) and mechanical units cf. [112].
[111] We thank Dr. *P. Neumann* for his help in the design and construction of the apparatus.
[112] Detailed description of the longitudinally wound ring furnace and its electronic temperature control: *F. Vögtle, P. Fornell, W. Löhr*, Chem. Ind. (London) *1979*, in press.
[113] *W. Bieber, F. Vögtle*, Chem. Ber. *111*, 1653 (1978). Cf. *R. W. May, E. F. Pearson, D. Scothern*, Pyrolysis-Gas Chromatography, Analytical Sciences Monograph 3, The Chemical Society, Heffers, Cambridge 1977.
[114] Further investigations are presently being carried out on elimination-incorporation equilibria with this combination of apparatus.
[115] Fischer, D-5309 Meckenheim. Such pyrolyses, which exploit the Curie point—a material constant—are called Curie point pyrolyses. A ferromagnetic rod serves as sample carrier. The sudden loss of magnetic properties on reaching the Curie temperature permits the carrier rod to be heated with higher power within milliseconds without overshooting the temperature.
[116] Chemical Data Systems, Inc., Oxford, Pennsylvania (USA). The heating rod consists of a platinum wire, which can heat a quartz tube containing the substance to be pyrolyzed in 600—1000 ms.
[117] F-22, Perkin Elmer & Co., GmbH, D-7770 Überlingen. Column: silicone oil OV 17/Chromosorb G, AW-DMCS, 80—100 mesh.
[118] *F. A. Davis, S. G. Yocklovich, G. S. Baker*, Tetrahedron Lett. *1978*, 97.
[119] *P. Chao, D. M. Lemal*, J. Am. Chem. Soc. *95*, 920 (1973).

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

Generation of the *triangulo*-Group Mo^{V}-η-S_2 in the "Condensation" of $[Mo^{VI}O_2S_2]^{2-}$ to $[Mo^{V}_2O_2S_2(S_2)_2]^{2-}$

By *Walter Rittner* (deceased), *Achim Müller*, *Axel Neumann*, *Wolfgang Bäther*, and *Ramesh Chandra Sharma*[*]

In aqueous medium Mo^{VI} is reduced by S^{2-} and S_n^{2-} with formation of sulfur-rich polynuclear η-disulfido complexes such as $[Mo^{V}_2(S_2)_6]^{2-}$ and $[Mo^{IV}_3S(S_2)_6]^{2-}$ [1,2]. We have now found that the Mo^{V}-η-S_2 group is also formed from $[Mo^{VI}O_2S_2]^{2-}$ in H_2O by *a novel intramolecular redox process* (oxidation of ligands by the metal coordination center). This finding is of interest regarding the catalytic action of molybdenum in electron transfer processes in polynuclear metal-enzymes and in view of a possible key function of the S_2^{2-} group bound to molybdenum in various redox-enzymes[3]. A binuclear complex containing two η-S_2^{2-} ligands was hitherto unknown.

$[Mo^{VI}O_2S_2]^{2-}$ *(1)* (as NH_4^+ salt) "condenses" within a short period of time under physiological conditions to give polynuclear sulfur-bridged complexes with η-S_2^{2-} ligands ("polythiooxoanions" such as $[Mo^{V}_2O_2S_2(S_2)_2]^{2-}$ *(2)*)[4,5]. The reaction conditions would indicate participation of the following redox processes.

$$Mo^{VI} \xrightarrow{red} Mo^{IV} \qquad (Mo^{VI} + Mo^{IV} \rightarrow 2\,Mo^{V})$$

$$2\,S^{2-} \xrightarrow{ox} S_2^{2-}$$

The anion *(2)* can readily be isolated as the tetramethylammonium salt. The compound was characterized by elemental analysis, IR, Raman, UV/VIS, and ESCA spectra and by a complete single-crystal structure analysis[6] (cf. Fig. 1 and Table 1).

[*] Prof. Dr. A. Müller, W. Bäther, Dr. R. C. Sharma [**]
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld 1 (Germany)
Dr. W. Rittner (deceased), Dipl.-Chem. A. Neumann
Anorganisch-Chemisches Institut der Universität
Tammannstrasse 4, D-3400 Göttingen (Germany)
[**] Alexander-von-Humboldt Fellow.

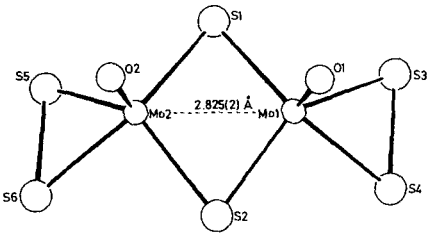


Fig. 1. Structure of the $[Mo_2O_2S_2(S_2)_2]^{2-}$ anion *(2)* in its tetramethylammonium salt [6].

Table 1. Characteristic data of the Mo^{V}-η-S_2 group in $[(CH_3)_4N]_2[Mo_2O_2S_2(S_2)_2]$.

Vibrational frequency	ν(SS) [cm^{-1}]	Raman [a]	515 (s)
		IR [b]	510 (s)
Electronic transition [c]	$\pi^*(S_2^{2-}) \rightarrow d(Mo)$ [cm^{-1}]		$21.7 \cdot 10^3$
	ε [l mol^{-1} cm^{-1}]		$1.8 \cdot 10^3$
Bonding energy [d]	E_B (Mo $3d_{5/2}$) [eV]		230.5
Bond lengths [6]	d(S—S) [Å]		2.090(6)
			2.075(7)

[a] Solid. [b] Solid (Nujol). [c] Solution in *N,N*-dimethylacetamide; first assignment of the transition of S_2^{2-} complexes being responsible for the color. [d] Referred to C_{1s} standard (285.0 eV).

The initial step in the reaction of *(1)* is protonation at the oxygen, which favors both the condensation as well as the intramolecular redox reaction (the effective electron density at the Mo center decreases with decreasing Mo O π-bond order, and consequently the oxidizing action and tendency of the central atom to coordinate increases). The formation of the η-disulfidomolybdenum(V) group in pure aqueous dithiomolybdate(VI) solutions under physiological conditions was detected spectroscopically, using the data for the tetramethylammonium salt of *(2)* (see [4]).

Experimental

A solution of $(NH_4)_2MoO_2S_2$ (1.8 g) in H_2O (25 ml) was heated to boiling for about 10 min. After addition of 0.5 g NaOH and 0.8 g $[(CH_3)_4N]Cl$ in 75 ml H_2O, cooling of the resulting reaction mixture led to precipitation of $[(CH_3)_4N]_2[Mo_2O_2S_2(S_2)_2]$, which was recrystallized from the mother liquor and washed with a small amount each of H_2O, methanol, and ether; yield: 0.5 g of orange-red crystals. – The salt can also be isolated at lower temperature and in higher yield by addition of H_2S-water [*(2)* has a higher S-content than *(1)*] to a saturated aqueous solution of $(NH_4)_2MoO_2S_2$ at *ca.* 50 °C and precipitation with $[(CH_3)_4N]Cl$ (but not pure).

Received: March 21, 1979 [Z 235 IE]
German version: Angew. Chem. 91, 565 (1979)

CAS Registry numbers:
(1)-$(NH_4)_2$, 16150-60-0; *(3)*, 70355-58-7

[1] *A. Müller, W. O. Nolte, B. Krebs*, Angew. Chem. 90, 286 (1978); Angew. Chem. Int. Ed. Engl. 17, 279 (1978).
[2] *A. Müller, R. G. Bhattacharyya, B. Pfefferkorn*, Chem. Ber. 112, 778 (1979); cf. also *A. Müller, S. Sarkar, R. G. Bhattacharyya, S. Pohl, M. Dartmann*, Angew. Chem. 90, 564 (1978); Angew. Chem. Int. Ed. Engl. 17, 535 (1978).
[3] *E. I. Stiefel*, Prog. Inorg. Chem. 22, 1 (1977).
[4] The decomposition of *(1)* was monitored by measurement of the pH value and the UV/VIS, Raman, and IR spectra [precipitation of Me_4N^+ salts]. The "condensation reaction" is strongly dependent upon temperature. Whereas a substantial amount of unreacted *(1)* is still present after *ca.* 10 min at 40 °C, at 60 °C the reaction mixture consists almost exclusively of reduced products (investigations on saturated solutions of $(NH_4)_2MoO_2S_2$).

[5] Older data given in the literature on the formation of "polythioanions" [cf. *E. Diemann, A. Müller*, Coord. Chem. Rev. *10*, 79 (1973)], which we intend investigating systematically, are in need of revision since the possibility of redox processes (strongly temperature dependent owing to the high activation energy [4]) taking place simultaneously has not been taken into consideration.

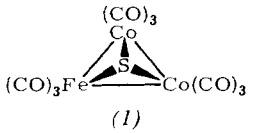
[6] Space group $Pca2_1$; $a = 29.202$ (5), $b = 6.546$ (1), $c = 10.875$ (2) Å; see *G. M. Sheldrick, A. Müller, et al.*, Inorg. Chem., in press.

$FeCoMoWS(AsMe_2)Cp_2(CO)_7$: The First Cluster to Contain Four Different Metal Atoms[**]

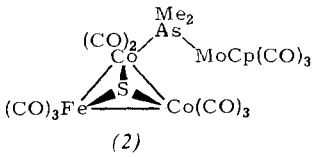
By *Felix Richter* and *Heinrich Vahrenkamp*[*]

The directed synthesis of clusters is still in its infancy[1], and especially in the case of heteroclusters there are but few preparative pathways which owe their success more to strategy than to chance[2]. We discovered such a pathway in the replacement of carbonylcobalt groups by other organometallic fragments[3]. A detailed study of this reaction has provided an entry to a new class of compounds by leading to the synthesis of the first cluster to contain four different metal atoms.

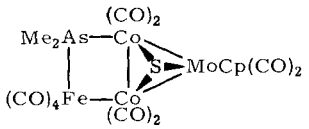
On transformation[3] of the μ_3-bridged complex *(1)* into *(4)* the straightforward substitution product *(2)* previously described was found to be converted into a further isolable intermediate *(3)*[4]. This intermediate under mild conditions underwent not only elimination to give the trinuclear FeCoMo cluster *(4)* but also aggregation to form the tetranuclear $FeCo_2Mo$ cluster having the skeleton *(5)*[5]. A corresponding reaction sequence starting from *(4)* and the organometallic base $Cp(CO)_3W\quad AsMe_2$[6] led—as planned—to the tetranuclear cluster named in the title to which we assign the tetrahedral FeCoMoW skeleton *(6)*[7].



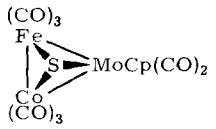
(1)



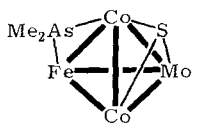
(2)



(3)

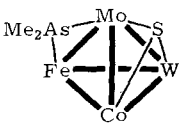


(4)



$FeCo_2MoS(AsMe_2)Cp(CO)_8$

(5)



$FeCoMoWS(AsMe_2)Cp_2(CO)_7$

(6)

The composition of compound *(6)* has been established by complete elemental analysis and FD mass spectrometry. Its ^{1}H-NMR spectrum reveals the nonequivalence of the two $AsCH_3$ groups by the appearance of two signals at $\delta = 1.72$ and 1.74, as well as the two distinct cyclopentadienyl ligands by the occurrence of two broad signals at $\delta = 4.36$ and 4.86 (benzene, TMS int. std.). The CO stretching bands (in cyclohexane 2003 m, 1987 vs, 1946 m, 1888 w, 1811 w, 1779 w, 1769 cm^{-1} w) indicate the presence of terminal and bridging carbonyl ligands. Owing to the different nature of each corner of the tetrahedral skeleton, compound *(6)* is chiral, like the starting compound *(4)*.

The bridging ligands $AsMe_2$ and S which permit the directed synthesis of *(6)* may prove obstructive in studies of the chemical properties of this novel tetranuclear cluster since they tend to "shield" the metal atoms. The versatility of *(6)* (each metal atom coordinated in a different way, six different metal-metal bonds) nevertheless makes it a stimulating object of study.

Procedure

Compound *(4)* (0.52 g, 0.98 mmol) and $Cp(CO)_3W\quad AsMe_2$ (0.43 g, 0.98 mmol) are heated under reflux for 1 d in benzene (20 ml). After evaporation to dryness the product is crystallized from a small volume of benzene/hexane (1:1) at −35 °C; yield 0.35 g (42%) of *(6)*, black crystals, m.p. 135 °C.

Received: February 26, 1979 [Z 220 IE]
German version: Angew. Chem. *91*, 566 (1979)

CAS Registry numbers:
(1), 22364-22-3; *(2)*, 68185-54-6; *(3)*, 70576-10-2; *(4)*, 68185-55-7; *(5)*, 70576-33-9; *(6)*, 70623-72-2; $Cp(CO)_3W\quad AsMe_2$, 52456-36-7

[1] *H. Vahrenkamp*, Struct. Bonding (Berlin) *32*, 1 (1977).
[2] *W. L. Gladfelter, G. L. Geoffroy*, Adv. Organomet. Chem. *18*, in press.
[3] *F. Richter, H. Beurich, H. Vahrenkamp*, Angew. Chem. *90*, 915, 916 (1978); Angew. Chem. Int. Ed. Engl. *17*, 863, 864 (1978); J. Organomet. Chem. *166*, C5 (1979).
[4] *(3)* was characterized by crystallography: monoclinic, $P2_1/c$, $a = 1576.1(7)$, $b = 1136.9(2)$, $c = 1346.0(4)$ pm, $\beta = 93.91(3)°$, 3137 independent reflections, $R = 0.041$.
[5] In the crystalline state, the molecules of *(5)* have three CO bridges: triclinic, $P\bar{1}$, $a = 908.5(3)$, $b = 1464.2(5)$, $c = 862.0(4)$ pm, $\alpha = 90.47(3)°$, $\beta = 101.45(3)°$, $\gamma = 72.70(3)°$, 3015 independent reflections, $R = 0.069$.
[6] *W. Malisch, M. Kuhn*, Angew. Chem. *86*, 51 (1974); Angew. Chem. Int. Ed. Engl. *13*, 84 (1974).
[7] Structure assigned by analogy with *(5)*. Crystal structure determination of *(6)* precluded by the crystals' turning amorphous (apparently without decomposition) in the X-ray beam.

(Diazomethyl)cyclopropenes—Synthesis, Isomerization, and Carbene Reactions[**]

By *Manfred Regitz, Annemarie Heydt*, and *Berndt Weber*[*]

Individual cases of electrophilic substitution at carbon of diazomethyl compounds, such as acylation with acyl chlorides, have been known for a long time[1]; however, generalization of this reaction (halogenation, nitration, metalation, and alkylation) was accomplished only recently[2]. Introduction of Hückel-aromatic cations as electrophiles opens up new vistas.

Model reactions between the diazomethylphosphoryl compounds *(3a)* and *(3b)*[3] in dichloromethane/triethylamine (route *B*), or preferably their silver derivatives *(2a)* and

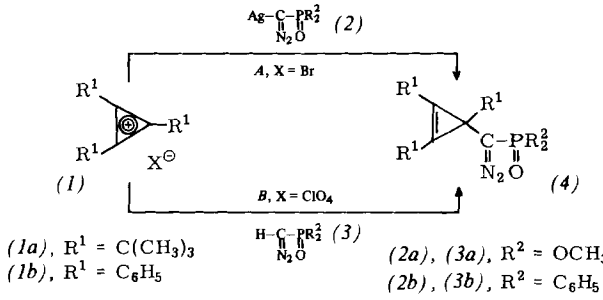
[*] Prof. Dr. H. Vahrenkamp, Dipl.-Chem. F. Richter
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Dr. *K. Steinbach*, Marburg, for the mass spectrum.

[*] Prof. Dr. M. Regitz, Dipl.-Chem. A. Heydt, Dr. B. Weber
Fachbereich Chemie der Universität
Paul-Ehrlich-Strasse, D-6750 Kaiserslautern (Germany)

[**] Studies of Diazo Compounds and Azides, Part 34. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. —Part 33: *M. Regitz, A. M. Tawfik, H. Heydt*, Synthesis, in press.

(2b)[3] in acetonitrile (route *A*), and the cyclopropenylium salts *(1a)*[4] and *(1b)*[5] give good yields of the fairly stable (diazomethyl)cyclopropenes *(4a)*—*(4d)*[6] whose structures were confirmed by IR and ^{1}H-NMR spectroscopic data (see Table 1).



(1a), R^1 = $C(CH_3)_3$
(1b), R^1 = C_6H_5

(2a), *(3a)*, R^2 = OCH_3
(2b), *(3b)*, R^2 = C_6H_5

(from toluene); IR (KBr), 2080 (C N_2), 1190 cm^{-1} (PO); ^{1}H-NMR ($CDCl_3$), δ = 3.50—4.20 (m, 4H), 6.25 (d, 1H, $^3J_{P,H}$ = 6 Hz)].

On heating in toluene, the (diazomethyl)cyclopropenes *(4b)* and *(4d)* undergo a novel isomerization to the pyridazines *(10a)* and *(10b)*, respectively (see Table 2). The cycloadduct *(9)* might function as intermediate; a synchronous transformation *(4)*→*(10)* cannot be ruled out.

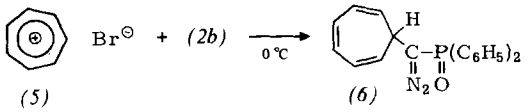
Reaction of tris(dimethylamino)cyclopropenylium perchlorate *(11)*[7] and the diazo compounds *(3a)* and *(3b)* in the presence of 1,5-diazabicyclo[4.3.0]non-5-ene (CH_2Cl_2, 25 °C) also gives pyridazines [*(10c)* and *(10d)*] (see Table 2). The corresponding (diazomethyl)cyclopropenes are apparently so labile that they isomerize at room temperature[8].

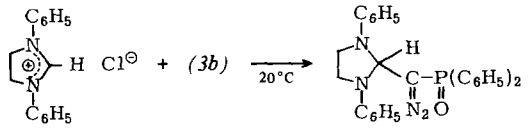
Irradiation of *(4d)* in benzene generates the carbene *(12)* which reacts, partly in a kind of cheletropic reaction to give the acetylenes *(13)* (yield 52%; m.p. 58 °C) and *(14)* (yield

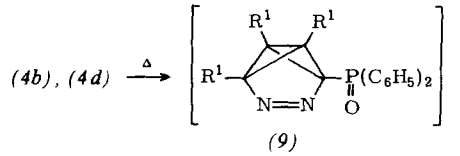
Table 1. Yields, melting points, IR and ^{1}H-NMR data of the (diazomethyl)cyclopropenes *(4a)*—*(4d)*.

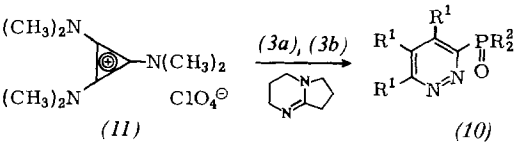
Cpd.	R^1	R^2	Yield [%] *A*	Yield [%] *B*	M.p. [°C] (Solvent)	IR (KBr) C N_2 [cm^{-1}]	^{1}H-NMR ($CDCl_3$, TMS int., δ values)
(4a)	$C(CH_3)_3$	OCH_3	93	43	Oil	2060	0.97 (s, 9H), 1.25 (s, 18H), 3.70 (d, 6H, $^3J_{P,H}$ = 12 Hz)
(4b)	$C(CH_3)_3$	C_6H_5	68	90	114 (Ether)	2050	0.96 (s, 9H), 1.20 (s, 18H), 7.3–7.8 (m, 10H)
(4c)	C_6H_5	OCH_3	75	– –	88 (Ether)	2070	3.48 (d, 6H, $^3J_{P,H}$ = 12 Hz), 7.1–7.8 (m, 15H)
(4d)	C_6H_5	C_6H_5	62	47	131 (Ethyl acetate)	2050	7.2–7.9 (m)

The possibility of extending this substitution to other stable carbocations is recognized. Thus tropylium bromide *(5)* reacts with *(2b)* in dichloromethane to give 7-[diazo(diphenylphosphoryl)methyl]cycloheptatriene *(6)* [yield 70%; m.p. 94 °C (from ether); IR (KBr), 2070 (C N_2), 1190 cm^{-1} (PO); ^{1}H-NMR ($CDCl_3$), δ = 2.60 (q by superposition of 2t, 1H, $^3J_{H^1,H^7} = {}^3J_{H^7,P} = 6$ Hz)]. 1,3-Diphenylimidazolium chloride *(7)* can be transformed similarly with *(3b)* in acetonitrile/triethylamine into 2-[diazo(diphenylphosphoryl)methyl]1,3-diphenylimidazolidine *(8)* [yield 43%; m.p. 169 °C









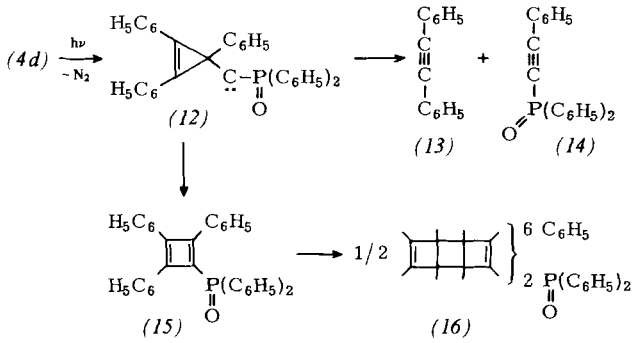
49%; m.p. 101 °C), and partly *via* ring enlargement to form the phosphorylated cyclobutadiene *(15)*[9], which dimerizes to *(16)* [yield 8%; m.p. 349 °C (from benzene/ether 2:1); MS (70 eV), m/e = 961 (M^+, 5%), 760 ($M^+ - PO(C_6H_5)_2$, 12%), 559 ($M^+ - 2PO(C_6H_5)_2$, 50%)][10]. The location of the substituents is still unknown.

Table 2. Yields, melting points, and ^{1}H-NMR data of the pyridazines *(10a)*—*(10d)*.

Cpd.	R^1	R^2	Yield [%]	M.p. [°C] (Solvent)	^{1}H-NMR ($CDCl_3$, TMS int., δ values)
(10a)	$C(CH_3)_3$	C_6H_5	78	161 (Ether)	1.32, 1.47, 1.58 (each s, 9H), 7.2–7.8 (m, 10H)
(10b)	C_6H_5	C_6H_5	49	226 (Benzene/ether)	6.8–8.0 (m)
(10c)	$N(CH_3)_2$	OCH_3	55	69 (Hexane)	2.80, 2.87, 2.95 (each s, 6H), 3.90 (d, 6H, $^3J_{P,H}$ = 12 Hz)
(10d)	$N(CH_3)_2$	C_6H_5	48	169 [a]	2.50, 2.80, 2.90 (each s, 6H), 7.3–7.9 (m, 10H)

[a] After column chromatography.

© Verlag Chemie, GmbH, 6940 Weinheim, 1979
0570-0833/79/0707-0532 $ 02.50/0



Experimental

Synthesis of *(4b)*, route *A*[11]: Compound *(1a)*, X = Br[5] (1.5 g, 5 mmol) in acetonitrile (10 ml) is added dropwise to a stirred suspension of *(2b)* (1.0 g, 3 mmol)[3] in acetonitrile (10 ml) at 0 °C under nitrogen. After 3 h at 20 °C and addition of ether (30 ml), the mixture is filtered and evaporated down *in vacuo*. Chromatography of the crude product (1.3 g, m.p. 96 °C) over Woelm 0.05—0.2 mm silica gel (100 g, column dimensions 50 × 3 cm) with ethyl acetate (200 ml) gives *(4b)* (0.9 g, 68%) as yellow crystals of m.p. 114 °C.

Synthesis of *(10a)*[11]: A solution of *(4b)* (700 mg) in toluene (30 ml) is heated under reflux for 30 min (decoloration) and evaporated. Digestion of the residue with a small volume of ether and cooling gives compound *(10a)* (550 mg, 78%) of m.p. 161 °C (from ether).

Received: March 22, 1979;
supplemented: April 5, 1979 [Z 238 IE]
German version: Angew. Chem. *91*, 566 (1979)

CAS Registry numbers:

(1a) (X = Br$^-$), 70562-64-0; *(1a)* (X = ClO_4^-), 64685-98-9; *(1b)* (X = Br$^-$), 12190-18-0; *(1b)* (X = ClO_4^-), 51778-20-2; *(2a)*, 70550-75-3; *(2b)*, 70550-76-4; *(3a)*, 27491-70-9; *(3b)*, 5353-66-2; *(4a)*, 70550-77-5; *(4b)*, 70550-78-6; *(4c)*, 70550-79-7; *(4d)*, 70550-80-0; *(5)*, 5376-03-4; *(6)*, 70550-81-1; *(7)*, 2522-21-6; *(8)*, 27006-49-1; *(10a)*, 70550-82-2; *(10b)*, 70550-83-3; *(10c)*, 70550-84-4; *(10d)*, 70550-85-5; *(11)*, 36509-73-6; *(12)*, 70550-86-6; *(13)*, 501-65-5; *(14)*, 7608-18-6; *(15)*, 70550-87-7; *(16)*, 70550-74-2

[1] *F. Arndt, B. Eistert, W. Partale*, Ber. Dtsch. Chem. Ges. *60*, 1364 (1927).
[2] Review: *M. Regitz*: Diazoalkane. Thieme, Stuttgart 1977, pp. 235 ff.
[3] *(2a), (3a): D. Seyferth, R. S. Marmor, P. Hilbert*, J. Org. Chem. *36*, 1379 (1971); *(2b), (3b): M. Regitz, A. Liedhegener, U. Eckstein, M. Martin, W. Anschütz*, Justus Liebigs Ann. Chem. *748*, 207 (1971).
[4] *J. Ciabattoni, E. C. Nathan*, J. Am. Chem. Soc. *91*, 4766 (1969).
[5] *R. Breslow, L. J. Altman, A. Krebs, E. Mohacsi, I. Murata, R. A. Peterson, J. Posner*, J. Am. Chem. Soc. *87*, 1326 (1965).
[6] Hitherto, methyl (tri-*tert*-butylcyclopropenyl)diazoacetate was the only known representative of this class; it was prepared from *(1a)* and methyl (diazolithiomethyl)acetate: *S. Masamune, N. Nakamura, M. Suda, H. Ona*, J. Am. Chem. Soc. *95*, 8481 (1973). The reaction can be greatly improved by alkylation of the Hg derivative.
[7] *Z. Yoshida, Y. Tawara*, J. Am. Chem. Soc. *93*, 2574 (1971).
[8] *E. Konrath*, Fortgeschrittenenarbeit, Universität Kaiserslautern 1979.
[9] Such a rearrangement has been mentioned for (tri-*tert*-butylcyclopropenyl)methoxycarbonylcarbene [6]; we found that acetylenes are also formed (*A. Kud*, Fortgeschrittenenarbeit, Universität Kaiserslautern 1979).
[10] *G. Weise*, Fortgeschrittenenarbeit, Universität Kaiserslautern 1979.
[11] Anhydrous solvents must be used.

Homogeneous Catalytic Vinylation of Cyclic Imides and Lactams for the Synthesis of *N*-Vinyl Monomers

By *Ernst Bayer* and *Kurt Geckeler*[*]

N-Vinyl compounds are starting substances for the synthesis of important polymers, *e.g.* poly(vinylpyrrolidinone)[1]. Convenient and general methods for the synthesis of *N*-vinyl compounds, however, were hitherto unknown.

There are two important methods for the synthesis of cycloaliphatic *N*-vinylimides and -lactams: Reaction of imides and lactams according to *Reppe*'s method[1] with acetylene at high pressure and elimination of alcohol from the *N*-(1-alkoxyethyl) derivatives[2]. Procedures involving high pressures and elevated temperatures lead to formation of byproducts, and necessitate special safety precautions; the elimination process has the particular disadvantage that the starting compounds are accessible only by multistep synthesis.

The transvinylation of nitrogen-containing heterocycles with vinyl acetate in the presence of mercury salts has been described[3-5]; in this method addition of oleum is essential. Moreover, this procedure has the disadvantage that the product must be isolated by column chromatography[3, 5].

Attempts by *Hopff et al.* to synthesize *N*-vinylimides by transvinylation with vinyl acetate at room temperature[3] or at 72 °C[4] gave negative results in the case of phthalimide and some other imides.

We have now found that cyclic *N*-vinyl compounds *(2)* are formed in one step and in high yields on reaction of imides and lactams with vinyl acetate in the homogeneous phase if

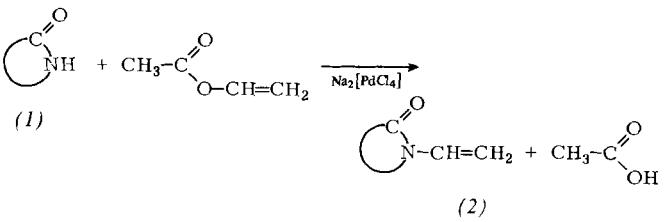
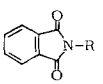
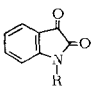
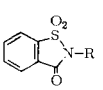


Table 1. Data for *N*-vinyl monomers *(2)*.

R = CH CH$_2$		Yield [%]	Reaction time [h]	M.p. [°C] (obs.)	B.p. [°C/torr] (lit.)
(2a)		82	20	46	47–48 [6]
(2b)		75	12	84	84 [2]
(2c)		85	20	128/21	111/10 [7]
(2d)		81	12	117	
(2e)		79	7	131	131–132 [3]

sodium tetrachloropalladate is employed as catalyst (Table 1). The compounds *(2)* thus prepared were identified by NMR and IR spectroscopy and by thin-layer chromatography.

General procedure

To a stirred solution of the imide or lactam *(1)* (20 mmol) in vinyl acetate (50 ml) is added 50 mg of $Na_2[PdCl_4]$ and the mixture heated under reflux for 4—20 h with exclusion of moisture. After addition of 200 mg of activated charcoal the solution is shaken for 10 min, filtered free of solids, and the

[*] Prof. Dr. E. Bayer, Dr. K. Geckeler
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

solvent removed by distillation in a high vacuum. The same amount of catalyst and reagent is then added again and the procedure repeated. For isolation of the vinyl compound, the solid is extracted with ether or petroleum ether, the solvent removed in a vacuum and the product recrystallized or distilled.

Received: March 5, 1979 [Z 239 IE]
German version: Angew. Chem. 91, 568 (1979)

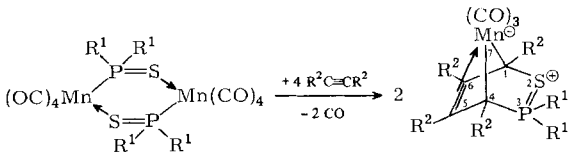
CAS Registry numbers:
(1a), 123-56-8; *(1b)*, 85-41-6; *(1c)*, 105-60-2; *(1d)*, 91-56-5; *(1e)*, 81-07-3; *(2a)*, 2372-96-5; *(2b)*, 3485-84-5; *(2c)*, 2235-00-9; *(2d)*, 69564-74-5; *(2e)*, 20583-38-4; vinyl acetate, 108-05-4; sodium tetrachloropalladate, 13820-53-6

[1] *W. Reppe et al.*, Justus Liebigs Ann. Chem. *601*, 135 (1956).
[2] *J. Furukawa, A. Onishi, T. Tsuruta*, J. Org. Chem. *23*, 672 (1958).
[3] *H. Hopff, U. Wyss, H. Lüssi*, Helv. Chim. Acta *43*, 135 (1960).
[4] *H. Hopff, G. Becker*, Makromol. Chem. *133*, 1 (1970).
[5] *G. Manecke, C. Rühl*, Makromol. Chem. *180*, 103 (1979).
[6] *W. E. Hanford, H. B. Stevenson*, US-Pat. 2231905 (1941), du Pont.
[7] *W. Reppe, H. Krizkalla, O. Dornheim, R. Sauerbier*, US-Pat. 2317804 (1943); Chem. Abstr. *37*, 6057 (1943); *O. F. Salomon, D. S. Vasilescu, V. Tararescu*, J. Appl. Polymer Sci. *12*, 1843 (1968).

Manganese-Containing Heterocycles Having a λ^4-Thia-λ^5-phosphanorbornadiene Skeleton[1]

By *Ekkehard Lindner, Axel Rau*, and *Sigurd Hoehne*[*]

Metal-containing heterocycles are of interest in connection with organic syntheses, and especially with catalytic processes[2]. While looking for new pathways leading to metallacycles containing metal-carbon σ bonds, we obtained the manganacycles *(2)* having a thiaphosphanorbornadiene skeleton for the first time by reaction of the inorganic heterocycles *(1)*[3] with acetylene derivatives.



(1)

(2a), $R^1 = CH_3$, $R^2 = CO_2CH_3$
(2b), $R^1 = CH_3$, $R^2 = CO_2C_2H_5$
(2c), $R^1 = C_6H_5$, $R^2 = CO_2CH_3$
(2d), $R^1 = C_6H_5$, $R^2 = CO_2C_2H_5$

The yellow compounds *(2)* are readily soluble in polar solvents and melt with decomposition above 125 °C. They were characterized by complete elemental analysis, IR [each with three intense bands at *ca.* 2025, 1955, 1948 cm^{-1} (in CCl_4)], ^{31}P-NMR, and mass spectra [*m/e* (M^+): *(2a)* 516, *(2b)* 572, *(2c)* 640, *(2d)* 696]; *(2a)* was further characterized by X-ray crystal structure determination[4] (Fig. 1) and by its $^{13}C\{^1H\}$-NMR spectrum [$CDCl_3$, rel. to TMS: $\delta = 44.9$ (d, $J = 72$ Hz; C-4), 53.6 (s; C-1), 101.6, 103.1 (s; C-5, C-6)][5].

The angle between the planes through the atoms C1, C4, C5, C6 and C1, S, P, C4 is 46.9°. The ester groups (R^2) attached to C1 and C4 are twisted by 10 and 13°, respectively, out of the plane, and those attached to C5 and C6 by 3.5 and 2°, respectively; in a limiting structure the manganese is therefore linked by two σ bonds and one π bond to C1 and C4 and to C5 and C6, respectively[6]. In accord with the IR band ν(P S) at 530 cm^{-1} (in polyethylene), the P S distance corresponds to a value lying between that for a single

[*] Prof. Dr. E. Lindner, Dipl.-Chem. A. Rau, Dipl.-Chem. S. Hoehne
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

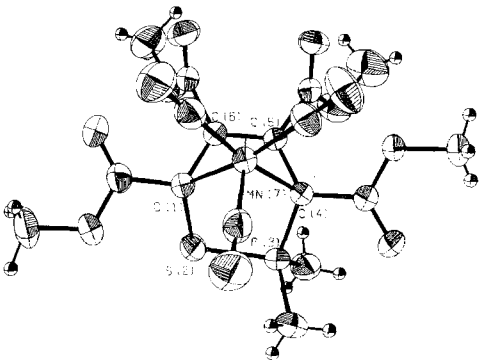
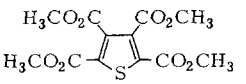


Fig. 1. ORTEP drawing of *(2a)* (vibrational ellipsoids correspond to 50% probability density).

Bond lengths [pm]		Angles [°]	
Mn—C1	213.1(2)	S—C1—Mn	122.3(1)
Mn—C4	215.0(3)	C6—C1—Mn	67.7(1)
Mn—C5	208.1(2)	C6—C1—S	118.0(2)
Mn—C6	207.2(2)	R^2—C1—Mn	116.4(2)
C1—C6	145.0(3)	R^2—C1—S	110.0(2)
C6—C5	141.0(3)	R^2—C1—C6	117.1(2)
C5—C4	146.1(3)	C1—S—P	97.7(1)
C4—P	179.1(2)	S—P—C4	104.1(1)
P—S	203.8(1)	C4—C5—C6	119.0(2)
S—C1	183.2(3)	C5—C6—C1	116.0(2)
		C1—Mn—C4	80.1(1)

(214 pm) and that for a double bond (194 pm). The positive charge in the PS part of *(2)* is manifested in a strong downfield shift (≈ 74 ppm) of the ^{31}P-NMR signal (in CH_2Cl_2, rel. to 85% H_3PO_4 ext.).

Heating of *(2a)* in tetrahydrofuran (THF) to 100 °C under a CO pressure of 200 bar leads to elimination of the $Mn(CO)_3$ and the $P(CH_3)_2$ group, yielding the thiophene derivative *(3)*.



(3)

Procedure

Compound *(1)* (0.5 mmol) and $R^2C{\equiv}CR^2$ (4 mmol) are heated with stirring in THF (100 ml) within 1 h to 66 °C. The reflux temperature is maintained for 30 min. After stripping off the solvent, chromatography with benzene/ethyl acetate on Al_2O_3 (activity V) or silica gel (activity II) gives the organometallic compounds *(2a)* and *(2b)* and *(2c)* and *(2d)*, respectively in yields of 10 to 60% as oils which crystallize at −30 °C or on addition of diethyl ether.

A solution of *(2a)* (0.2 mmol) in THF (50 ml) is subjected to a CO pressure of 200 bar at 100 °C in an autoclave. After 12 h the solvent is stripped off and the residue chromatographed with benzene/ethyl acetate on silica gel. The thiophene *(3)* is obtained in *ca.* 80% yield.

Received: January 30, 1979 [Z 245a IE]
German version: Angew. Chem. 91, 568 (1979)
Publication delayed at authors' request

[1] Preparation and Properties of, and Reactions with, Metal-Containing Heterocycles, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. – Part 1: *E. Lindner, G. von Au, H.-J. Eberle*, Z. Naturforsch. *B 33*, 1296 (1978).
[2] *M. I. Bruce*, Angew. Chem. *89*, 75 (1977); Angew. Chem. Int. Ed. Engl. *16*, 73 (1977).
[3] *E. Lindner, B. Schilling*, Chem. Ber. *110*, 3889 (1977).
[4] *(2a)* is obtained as triclinic crystals from cyclohexane/dichloromethane (space group $P\bar{1}$), $a = 902.3(2)$, $b = 1692.1(3)$, $c = 867.0(2)$ pm, $\alpha = 102.01(2)$, $\beta = 94.87(2)$, $\gamma = 90.68(2)$, $Z = 2$, $\rho_{calc} = 1.439$ $g \cdot cm^{-3}$. The structure was solved by Patterson and difference-Fourier syntheses; anisotropic refinement for 5914 independent reflections with program system SHEL-76 (except H)

to $R = 0.046$. We are grateful to Dr. *K. Peters* and Prof. *H. G. von Schnering*, Max-Planck-Institut für Festkörperforschung Stuttgart, for the diffractometer measurements.

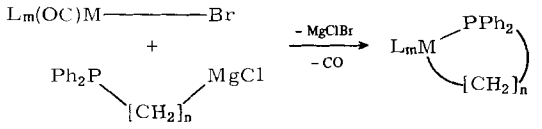
[5] We are grateful to Dipl.-Chem. *J. C. Wuhrmann* for recording the ^{13}C-NMR spectrum.

[6] *M. R. Churchill, R. Mason*, Adv. Organomet. Chem. 5, 93 (1967), and references cited therein.

Synthesis of Metallacycles with Reactive Metal-Carbon σ Bonds[1]

By *Ekkehard Lindner, Guido Funk*, and *Sigurd Hoehne*[*]

Metallacycloalkane derivatives play an important role in the activation of C–H bonds[2] and in transition-metal catalyzed reactions[3]. Most of these heterocycles have so far only been obtained with various Group 8 metals[4]. A new general procedure now also permits the synthesis of metallacycloalkanes with other metals, such as those from Group 7 whose weak metal-carbon σ bonds ensure that the products are highly reactive.



(1a), M = Mn, L = CO, m = 4, n = 3
(1b), M = Re, L = CO, m = 4, n = 3
(1c), M = Fe, $L_m = \eta^5$-C_5H_5 + CO, n = 3

β-Hydrogen elimination is avoided by performing the reaction in such a way that simultaneous α,ω attack of the difunctional alkylphosphane takes place on the metal (with elimination of CO and MgClBr). The metallacycles *(1)* are surprisingly stable owing to the chelate effect; they can be sublimed in a high vacuum, melt above 110 °C (except *(1c)*), and dissolve in all the common organic solvents. They were characterized by complete elemental analysis, IR, and mass spectra (Table 1). Further characterization of *(1a)* was by X-ray crystal structure analysis[5] (Fig. 1) and by its $^{13}C\{^1H\}$-NMR spectrum C_6D_6, rel. to TMS: δ = 18.1 (s; C-4), 31.0 (d, J = 15 Hz; C-3), 34.6 (d, J = 29 Hz; C-5).

Table 1. IR and MS data and colors of the new heterocycles *(1)* and *(2)*.

	(1a)	*(1b)*	*(1c)*	*(2a)*	*(2c)*
ν(CO) [cm^{-1}]	2058 m [a] 1987 m-s 1971 vs 1942 m-s	2078 m [a] 1990 m-s 1977 vs 1940 m-s	1925 vs [a]	2095 m-s [b] 2040 m-s 2003 vs 1991 m-s	1967 vs [c]
m/e (M^+)	394	526 [d]	376	458 [e]	440 [e]
Color	Colorless	Colorless	Red-brown	Light yellow	Light brown

[a] In *n*-hexane. [b] In CH_2Cl_2/CCl_4 (1:1). [c] In CH_2Cl_2. [d] Relative to ^{187}Re. [e] Field desorption.

The five-membered ring of *(1a)* has an envelope conformation with a dihedral angle of 48.7°. The Mn–C3 distance is considerably greater than the sum of the single bond radii. The *trans* CO groups are bent towards the heterocycle (C8–Mn2–C9 = 166.6°). The coordination polyhedra of the manganese and the phosphorus atoms are strongly distorted as a result of ring strain.

[*] Prof. Dr. E. Lindner, Dipl.-Chem. G. Funk, Dipl.-Chem. S. Hoehne
Institut für Anorganische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)

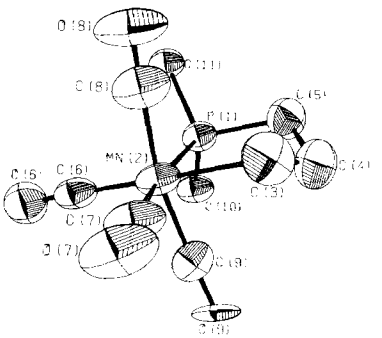
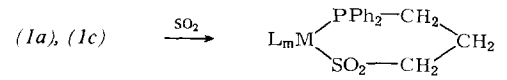


Fig. 1. ORTEP drawing of *(1a)* (vibrational ellipsoids correspond to 50% probability density).

Bond lengths [pm]		Angles [°]	
Mn2–C3	216.1(9)	P1–Mn2–C3	81.7(3)
C3–C4	155.9(17)	Mn2–C3–C4	111.7(6)
C4–C5	152.7(12)	C3–C4–C5	109.1(8)
C5–P1	182.1(9)	C4–C5–P1	107.4(6)
P1–Mn2	229.5(2)	C5–P1–Mn2	105.9(3)

The weak M–C σ bonds in *(1a)* and *(1c)* are highly reactive: quantitative insertion of SO_2 to form the ring-expanded heterocyclic sulfinato-*S* complexes *(2a)* and *(2c)* is observed at as low a temperature as −60 °C [dec. >175 °C, $\nu_{as}(SO_2) = 1183$ and 1160 s, $\nu_s(SO_2) = 1040$ s cm^{-1} (KBr)].



(2a), (2c)

The composition of compounds *(2)*, which are soluble only in polar solvents, follows from elemental analysis and IR and mass spectra (Table 1).

Procedure[6]

(1a) is obtained by reaction of $(CO)_5MnBr$ (3 mmol) in tetrahydrofuran (THF) (10 ml) with a solution of $Ph_2P(CH_2)_3MgCl$ (3 mmol) in THF (100 ml) at 65 °C. After evolution of CO has ceased, the solvent is stripped off and the residue extracted with *n*-hexane. The solvent is again removed and *(1a)* is sublimed at 80 °C in a high vacuum; yield *ca.* 30%.

Compound *(1a)* (0.3 mmol) is treated at −60 °C with liquid SO_2 (40 ml) for 1 h. After evaporation of the SO_2, analytically pure compound *(2a)* is obtained quantitatively.

Received: March 2, 1979 [Z 245 b IE]
German version: Angew. Chem. 91, 569 (1979)

CAS Registry numbers:
(1a), 70623-47-1; *(1b)*, 70631-98-0; *(1c)*, 70623-48-2; *(2a)*, 70623-49-3; *(2c)*, 70623-50-6; $(CO)_5MnBr$, 14516-54-2; $(CO)_5ReBr$, 14220-21-4; $(\eta$-$C_5H_5)(CO)_2FeBr$, 12078-20-5; $Ph_2P(CH_2)_3MgCl$, 57137-55-0

[1] Preparation and Properties of, and Reactions with, Metal-Containing Heterocycles, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.– Part 2: *E. Lindner, A. Rau, S. Hoehne*, Angew. Chem. 91, 568 (1979); Angew. Chem. Int. Ed. Engl. 18, 534 (1979).

[2] *D. E. Webster*, Adv. Organomet. Chem. 15, 147 (1977).

[3] *P. Diversi, G. Ingrosso, A. Lucherini*, J. Chem. Soc. Chem. Commun. 1977, 52.

[4] *P. Diversi, G. Ingrosso, A. Lucherini, P. Martinelli, M. Benetti, S. Pucci*, J. Organomet. Chem. 165, 253 (1979).

[5] *(1a)* forms monoclinic crystals from *n*-hexane (space group C2/c) $a = 1533(3)$, $b = 1518(2)$, $c = 1586(1)$ pm, $\beta = 97.4(1)°$, $Z = 8$, $\rho_{calc.} = 1.432$ g·cm^{-3}. The structure was solved by direct methods and difference-Fourier syntheses; anisotropic refinement to $R = 0.066$ for 2689 independent reflections with program system SHEL-76.

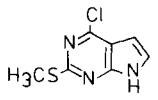
[6] The six-membered homolog ($n = 4$) of *(1a)* has meanwhile also been prepared in analogous manner.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0535 $ 02.50/0

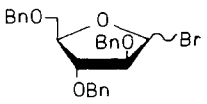
Preferred β-Glycoside Formation by Phase Transfer Catalysis in the Synthesis of D-Arabinofuranosyl-7-deazapurine Nucleosides

By *Frank Seela* and *Dieter Winkeler*[*]

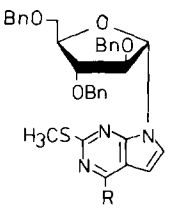
We have found that 1-bromo-2,3,5-tri-*O*-benzyl-D-arabinofuranose *(2)* couples with 4-chloro-2-methylthio-7*H*-pyrrolo[2,3-*d*]pyrimidine *(1)*[1] (a key substance for the synthesis of 7-deazapurine nucleosides[2-4]) by phase transfer catalysis[5] to give the N^7-glycosides [*(3a)* + *(4a)*] in yields of over 85%. The method has the advantage that the anomeric mixture contains more than 80% of the β-anomer *(4a)*. Moreover, it eliminates the necessity of working with anhydrous reagents, and can also be used for the synthesis of other nucleosides.



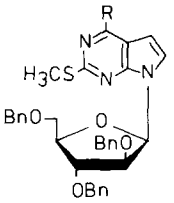
(1)



(2)



(3a), R = Cl
(3b), R = OCH_3



(4a), R = Cl
(4b), R = OCH_3

Table 1. Data for the α-anomer *(3a)* and the β-anomer *(4a)*.

(3a), TLC (silica gel, $CHCl_3/CH_3OH$, 200:1): $R_f = 0.25$; ^{1}H-NMR (D_6-dimethyl sulfoxide): $\delta = 2.56$ (s, CH_3S), 3.67 (d, CH_2-5', $J = 5.0$ Hz), 4.28 (t, H-4', $J = 4.0$ Hz); 4.5—4.7 (m, H-3', 3 Benzyl-CH_2), 4.83 (t, H-2', $J = 4.0$ Hz), 6.40 (d, H-1', $J = 4.0$ Hz), 6.63 (d, H-5, $J = 4.0$ Hz), 7.1—7.3 (m, 15 arom. H), 7.75 ppm (d, H-6, $J = 4.0$ Hz).

(4a), TLC: $R_f = 0.20$; UV (CH_3OH): $\lambda_{max} = 253$, 276, 310 nm ($\varepsilon = 22400$, 6500, 6500); ^{1}H-NMR: $\delta = 2.56$ (s, SCH_3), 3.75 (d, CH_2-5', $J = 5$ Hz), 4.0—4.5 (m, H-2', H-3', H-4'), 4.55—4.75 (3 Benzyl-CH_2), 6.53 (d, H-5, $J = 4.0$ Hz), 6.73 (d, H-1', $J = 6.0$ Hz), 6.8—7.5 (m, 15 arom. H), 7.65 ppm (d, H-6, $J = 4.0$ Hz)

Starting from aglycon *(1)* and the halosugar *(2)*, both in the organic phase, and 50% sodium hydroxide as inorganic phase, *N*-glycosidation in the presence of benzyltriethylammonium chloride[5] is quantitative after 2 hours' vigorous mixing. The reaction mixture is worked-up chromatographically on silica gel with chloroform/methanol (200:1). For determination of the position of glycosidation and assignment of the anomers, the substance contained in the slowly migrating zone B (main product) was converted with methanolic sodium methoxide into the 4-methoxy compound. In the thin layer chromatogram (silica, chloroform/methanol, 200:1) this zone migrates like authentic *(4b)*[6] with $R_F = 0.17$. Since the ^{1}H-NMR spectrum of the 4-methoxy compound is also consistent with that of *(4b)*, it follows that the main product of the phase transfer catalysis is the N^7-coupled β-anomer *(4a)*. On the basis of the NMR spectrum of *(3b)*[6] the component of the rapidly migrating zone A (byproduct) can be assigned as the α-anomer *(3a)* (see Table 1). The anomeric ratio (β:α) can be influenced by the phase-transfer catalyst. For tetrabutylammonium hydrogen sulfate it is 6:4, for benzyltriethylammonium chloride 8:2.

[*] Prof. Dr. F. Seela, Dipl.-Chem. D. Winkeler
Universität Paderborn—Gesamthochschule
Fachbereich 13 (Organische Chemie)
Warburger Strasse 100, D-4790 Paderborn (Germany)

Procedure

Dry hydrogen bromide is passed into a solution of 2,3,5-tri-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-D-arabinofuranose[7] (2.85 g, 5 mmol) in dichloromethane (15 ml) until no further *p*-nitrobenzoic acid precipitates. The acid is filtered off and washed with a small volume of cold dichloromethane. Evaporation of the combined filtrates affords *(2)* as a yellow viscous oil.—*(1)* (1.0 g, 5.0 mmol) is suspended in benzene (10 ml) and then just brought into solution by addition of a small volume of dimethoxyethane. The mixture is treated with benzyltriethylammonium chloride (0.3 g, 1.1 mmol) and the same volume of 50% aqueous sodium hydroxide and stirred for 5 min with a vibromixer.—A solution of the halosugar *(2)* in benzene (3 ml) is added dropwise (slowly) into the stirred (vibromixer) emulsion, and mixing continued for 2 h. The organic phase is separated off, extracted with water, dried with sodium sulfate, filtered, and the solvent removed by distillation *in vacuo*. The oily residue is dissolved in a little chloroform/methanol (200:1) and chromatographed in the same solvent on a silica gel column (70 × 5 cm, Kieselgel 60, Merck, 0.04—0.063 mm). The two main zones are separated; evaporation of the more rapidly migrating zone A affords 0.44 g (15%) *(3a)* and the more slowly migrating zone B 2.1 g (70%) *(4a)* as colorless viscous substances.

Received: March 26, 1979 [Z 241 IE]
German version: Angew. Chem. *91*, 570 (1979)

CAS Registry numbers:
(1), 57564-94-0; *(2)*, 70613-79-5; *(3a)*, 70550-63-9; *(4a)*, 70550-64-0

[1] *J. Davoll*, J. Chem. Soc. *1960*, 131.
[2] *R. L. Tolman, G. L. Tolman, R. K. Robins, L. B. Townsend*, J. Heterocycl. Chem. *7*, 799 (1970).
[3] *T. Kondo, T. Ohgi, T. Goto*, Agric. Biol. Chem. *41*, 1501 (1977).
[4] *R. J. Suhadolnik*: Nucleoside Antibiotics. Wiley-Interscience, New York 1971.
[5] *E. V. Dehmlow*, Angew. Chem. *86*, 187 (1974); *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974); *16*, 493 (1977).
[6] *U. Lüpke, F. Seela*, Chem. Ber., in press.
[7] *R. Barker, H. G. Fletcher, Jr.*, J. Org. Chem. *26*, 4605 (1961).

Fully Active Insulin by Selective Formation of the Disulfide Bridges between a Synthetic A-Chain and Natural B-Chain[**]

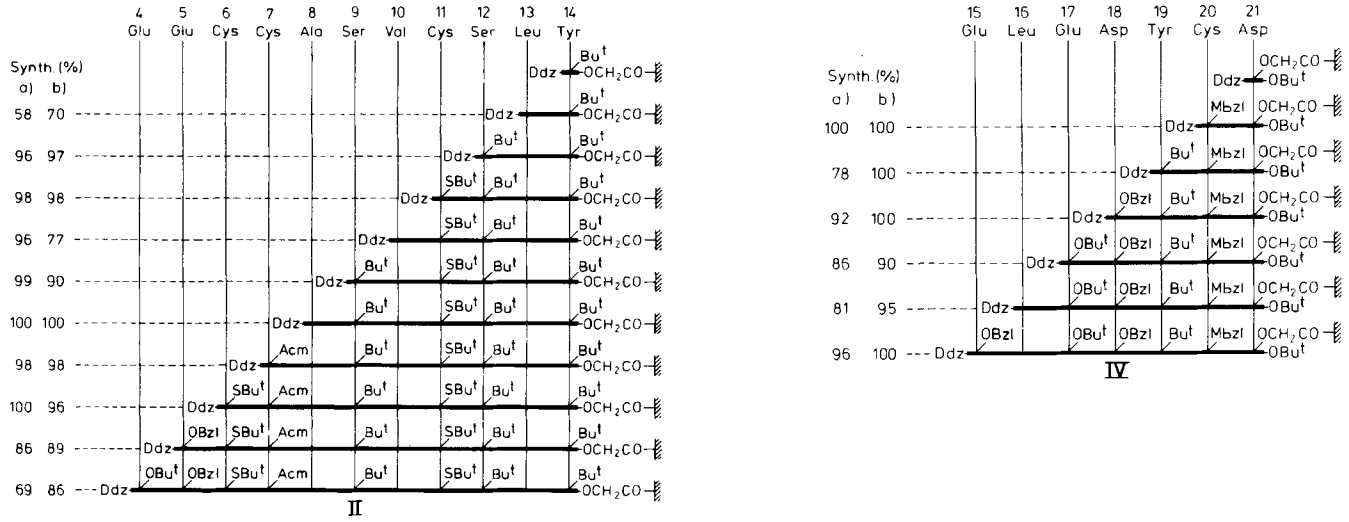
By *Christian Birr* and *Rüdiger Pipkorn*[*]

In the synthesis of insulin in *E. coli* by effective "genetic engineering"[1], A-chain and B-chain are synthesized in separate cultures and harvested as free polypeptides. Similarly as in earlier total syntheses the random disulfide oxidation to the insulin molecule is accompanied by high losses[2]. Recombination experiments with natural A- and B-chains (1:1) also gave insulin yields of only *ca.* 10%[3]. To improve the yields it is essential therefore that the three disulfide bridges be constructed selectively and not randomly.

[*] Priv.-Doz. Dr. Ch. Birr, Phil. cand. R. Pipkorn
Max-Planck-Institut für Medizinische Forschung
Abteilung Naturstoff-Chemie
Jahnstr. 29, D-6900 Heidelberg 1 (Germany)

[**] Delivered in part as a lecture at the 15th European Peptide Symposium, Gdansk 1978.—We thank Prof. Dr. *H. Zahn* and Dr. *H.-G. Gattner*, Aachen, for instructions on the recombination technique and for insulin B-chain; thanks are also due to Dr. *R. Renner*, München, and Dr. *H.-G. Gattner*, Aachen, for the biological assays.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0536 $ 02.50/0

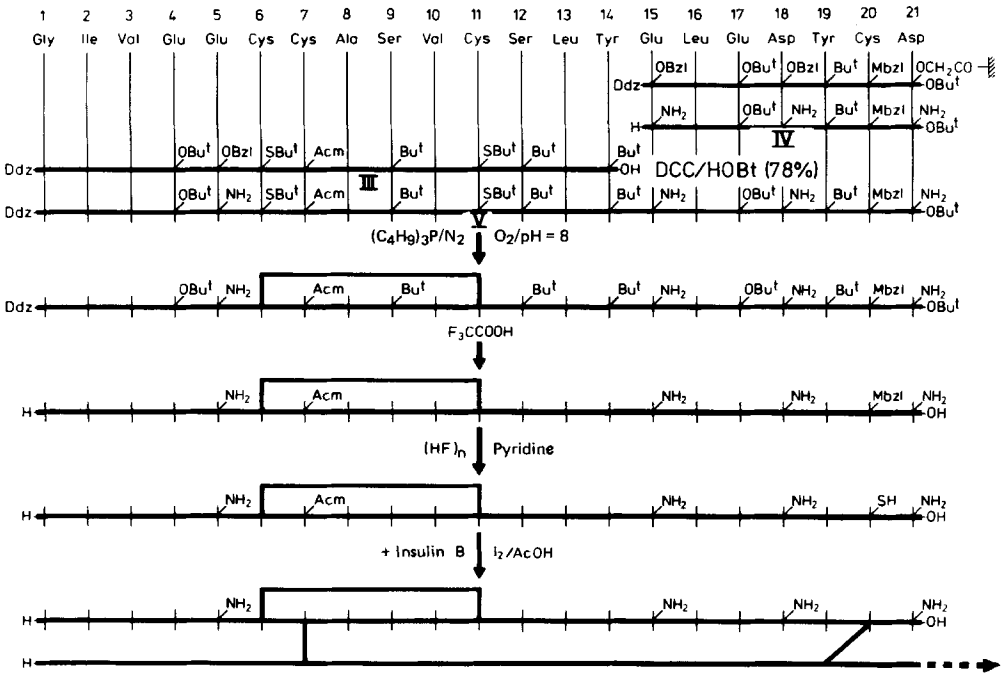


Scheme 1. Synthesis of the carrier-bound fully protected [5] fragment II (4 – 14) (left) and IV (15 – 21) (right) of the bovine insulin A-chain with the stepwise yields in two runs (a and b) of the synthesis. The overall yields are averaged for both syntheses and are determined with respect to initial loading of the carrier; they are 90 and 93% respectively.

We describe here the synthesis of an insulin A-chain, containing selectively cleavable sulfur protecting groups, on a polymer carrier and the reaction of this A-chain under stepwise oxidative formation of the disulfide bridges with a natural B-chain to give fully active crystalline bovine insulin. The concept applied here is a further development of the principles employed in the synthesis of MCD peptide[4].

We synthesized the fragment I (1—3) in 84% yield from Ddz-amino acids[5] in solution[6]. The fragments II (4—14) (Scheme 1, left) and IV (15—21) were each synthesized twice on 0.5% cross-linked polystyrene gel to check optimization of the syntheses. All the synthetic steps were followed photometrically[7] (cf. [4]). Instead of Gln^5 and Gln^{15} and Asn^{18}, we used Glu(OBzl) and Asp(OBzl) in order to avoid nitrile formation at the amide side function by the condensation reagent dicyclohexylcarbodiimide (DCC). In fragment IV, Asp^{21} is linked to the carrier with its β-carboxy function *via* an electrophilic 2-oxoethyl ester bond. In this way all the later amide side functions could be incorporated simultaneously at the end of the synthesis by ammonolysis of the benzyl ester and 2-oxoethyl ester bonds on release of IV and V from the carrier (Scheme 2).

On condensation of a 15-fold excess of I with the carrier-bound fragment II in the presence of DCC/1-hydroxybenzotriazole (HOBt), the fragment III was formed on the carrier in 86% yield (referred to II-gel polymer). Cleavage of III from the carrier (0.5 N triethylamine in methanol/dioxane 1:1 (v/v) + 0.5 vol-% 1 N NaOH) and subsequent chromatographic purification of the released and fully protected peptide acid afforded 1 gram of pure III (59% yield referred to III-gel polymer). Proof of the stability of the benzyl ester in position A^5 under the cleavage conditions was provided by the mass spectrum. The fragment IV was cleaved from the carrier by treatment with dioxane saturated with ammonia



Scheme 2. Synthesis of the fully protected bovine insulin A-chain by condensation in solution of the purified fragments III and VI removed from the carrier, and the liberation of the A-chain and its selective disulfide bridging with natural B-chain. Fragment III was formed in 86% yield on the carrier by reaction of I (1 – 3) with carrier-bound II.

and then with liquid ammonia/methanol 4:1 (v/v) under pressure at 20 °C. After chromatographic purification (DEAE A25 Sephadex/methanol-0.5 N acetic acid 4:1 (v/v) and Sephadex LH 20/methanol) we obtained 1.45 g (86% based on the carrier-bound precursor) of pure IV. The formation of the C-terminal β-amide could be confirmed by model experiments.

Condensation of 0.5 mmol of III with 1 mmol IV for the synthesis of the fully protected sequence V (1—21) using DCC/HOBt (4 days) in dimethylformamide gave after chromatographic separation 1.3 g of V (78%, based on III). Simultaneous condensation of III in 2.4-fold excess with IV on the carrier using carbonyldiimidazole afforded V in 12% yield; 50% of the excess of III in this case could be recovered. In V the benzyl ester at position A^5 can be converted into the amide with NH_3/methanol under pressure. For selective formation of the intrachain disulfide ring A^6—A^{11} by air oxidation (Scheme 2) the *tert*-butyl disulfides in position A^6 and A^{11} were reductively cleaved with tributylphosphane (84% yield of ring formation, based on fully protected V). All *tert*-butyl groups were subsequently cleaved with trifluoroacetic acid. The *p*-methoxybenzyl group can be removed selectively with HF in pyridine in the presence of anisole (*ca.* 80%, by analogy with model studies). The remaining A-chain containing a single free SH-function was immediately dissolved in 30% acetic acid, mixed with the acetic acid solution of an equimolar amount of reduced natural B-chain from bovine insulin (two free SH-functions), and oxidized with 0.1 N iodine solution. The desired interchain disulfide bridge A^{20}—B^{19} was formed; subsequently, in the same reaction vessel the last Acm protective group was removed iodolytically and then also the second interchain disulfide bridge was formed oxidatively. The reaction product was immediately chromatographed in 10% acetic acid on Sephadex G 50. The fourth and fifth fractions of this first purification contained pure bovine insulin, which was electrophoretically and thin-layer chromatographically identical with authentic samples; yield 25%. This lyophilized crude product already showed 52% activity in the biological lipogenesis assay on fat cells and 65% activity in the competitive receptor binding assay. The Zn-complex showed the characteristic crystal form of insulin. After repeated gel chromatography on Biogel P6 in 1% acetic acid and ion-exchange chromatography on carboxymethylcellulose our semisynthetic bovine insulin was completely biologically active in both of the above mentioned assay systems.

Selectively cleavable sulfur protecting groups only on the insulin A-chain thus improve the yields of the combination of A- and B-chains (1:1) by more than 100% compared to the random combination. The strategy outlined here will be totally effective when B^7 is protected with Acm, and B^{19} protected with Mbzl allowing the SH-groups to be selectively liberated also in the B-chain.

Received: March 19, 1979 [Z 240 IE]
German version: Angew. Chem. *91*, 571 (1979)

[1] *D. V. Goeddel, D. G. Kleid, F. Bolivar, H. L. Heynecker, D. G. Yansura, R. Crea, T. Hirose, A. Krazewski, K. Itakura, A. D. Riggs*, Proc. Natl. Acad. Sci. USA *76*, 106 (1979).

[2] *R. E. Humbel, H. R. Bosshard, H. Zahn* in *D. F. Steiner, N. Freinkel:* Handbook of Physiology. Vol. 1. Williams & Wilkins, Baltimore 1972, p. 111 ff.

[3] *H.-G. Gattner*, Aachen, private communication 1979.

[4] *Ch. Birr, M. Wengert-Müller*, Angew. Chem. *91*, 156 (1979); Angew. Chem. Int. Ed. Engl. *18*, 147 (1979).

[5] Protecting groups: Acm: acetamidomethyl; Bu^t: *tert*-butyl; Ddz: 3,5-dimethoxy-α,α-dimethylbenzyloxycarbonyl; Mbzl: 4-methoxybenzyl; OBu^t: *tert*-butyloxy; OBzl: benzyloxy; SBu^t: *tert*-butylthio.

[6] *Ch. Birr, M. Nassal, R. Pipkorn*, Int. J. Pept. Protein Res. *13*, 287 (1979).

[7] *Ch. Birr* in *Y. Wolman:* Peptides 1974. Halsted Press, New York 1975, p. 117 ff.

Boat Conformation of *cyclo*-[L-Pro_2-D-Pro][**]

By *Jan Willem Bats, Axel Friedrich, Hartmut Fuess, Horst Kessler, Werner Mästle,* and *Manfred Rothe*[*]

Small cyclic peptides are particularly well suited for conformational studies since their restricted molecular mobility permits only few conformations. Most cyclotripeptides exist in solution in a crown conformation having C_3 skeletal symmetry[1] and in an unsymmetrical boat conformation[2]. In the crystalline state only the crown conformation has been detected so far[3]. NMR studies and stereochemical considerations showed that crown and boat forms coexist in solution whenever the cyclotripeptide contains at least one achiral amino acid (sarcosine, *N*-benzylglycine)[2]. However, if it consists exclusively of chiral amino acids then the conformation will be determined by their chirality: three amino acids of identical chirality impose the crown form; for differing chiralities the boat form has been predicted. Indeed we have proven that *cyclo*-[L-Pro_2-D-Pro][4] exists in the boat conformation in solution and in the crystal.

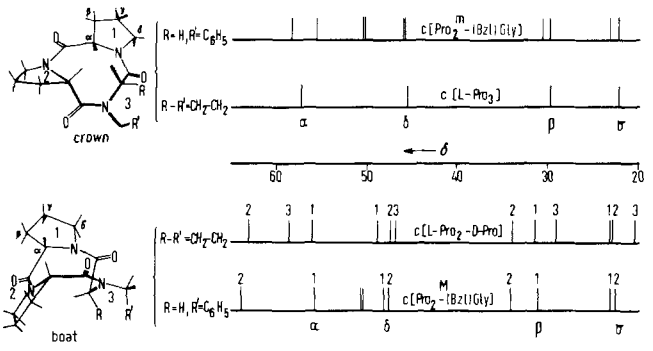


Fig. 1. Correlation of the ^{13}C-NMR chemical shifts of the aliphatic proline carbon atoms in cyclic tripeptides.

The ^1H- and ^{13}C-NMR spectra of the title compound show differences in the environment of the three proline rings. The chemical shifts of the ^{13}C-NMR signals in the aliphatic region (Fig. 1) closely resemble those of the conformation M of *cyclo*-[L-Pro_2-(Bzl)Gly] predominating in chloroform which has been shown to have the boat form[2a,5]. They differ characteristically from the spectra of *cyclo*-[L-Pro_3][6] which adopts the crown conformation and the crown form m of *cyclo*-[L-Pro_2-(Bzl)Gly][2a]. The signals of C_α and C_β of the proline ring 2 (Fig. 1) are shifted downfield as a consequence of the unusual value of the angle ψ at Pro^2 (see Table 1). In the 270-MHz ^1H-NMR spectrum recorded in $CDCl_3$, the α-protons appear as two triplets at $\delta = 4.47$ (ring 1) and 4.72 (ring 2), and as a doublet at $\delta = 4.70$ (ring 3)[7]. The coupling constants with the β-protons are in full accord with the values expected from the spectrum of *cyclo*-[Pro_2-(Bzl)Gly] and from consideration of models: Pro^1, $J_{12} \approx J_{13} \approx 7.2$ Hz; Pro^2, $J_{12} \approx J_{13} \approx 7.4$ Hz; Pro^3, $J_{12} \approx 1.4$ Hz, $J_{13} \approx 6.4$ Hz.

[*] Prof. Dr. H. Fuess, Dr. J. W. Bats
Institut für Kristallographie der Universität
Senckenberganlage 30, D-6000 Frankfurt am Main 1 (Germany)
Prof. Dr. H. Kessler [+], Dipl.-Chem. A. Friedrich
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. M. Rothe, Dipl.-Chem. W. Mästle
Lehrstuhl Organische Chemie II der Universität
Oberer Eselsberg, D-7900 Ulm (Germany)
[+] To whom correspondence should be addressed.

[**] Peptide Conformations, Part 7. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Calculations were performed at the University Computing Center at Frankfurt.—Part 6: *H. Kessler, P. Kondor*, Chem. Ber., in press.

The title compound crystallizes from ether in the orthorhombic space group $P2_12_12_1$ with two independent molecules in the asymmetric unit. X-ray structure analysis also revealed the boat conformation for both molecules in the crystalline state[3c]. One of the two molecules is shown in Figure 2. The corresponding second molecule shows only minor differences. The conformational angles[8] are compared in Table 1 with those of *cyclo*-[L-Pro-(Bzl)Gly_2] which adopts the crown conformation in crystals obtained from methanol solution. The corresponding values in previously studied "crowns" are similar[3a, b].

Table 1. Conformational angles [°] in cyclic tripeptides [a].

	cyclo-[L-Pro-(Bzl)Gly_2] [3c]			*cyclo*-[L-Pro_2-D-Pro] Molecule A			Molecule B		
ϕ	−95	−103	−104	−45	−52	104	−47	−50	108
ψ	95	96	88	107	−21	−56	109	−20	−48
ω	0	9	6	−12	6	3	−17	7	−8
θ	93	80	82	131	137	−77	120	133	−89
$\theta-\phi$	188	183	186	176	189	−181	167	183	−197

[a] Definition of angles according to [8]: $\phi = C' \; C^{\alpha} \; N \; C$; $\psi = N \; C_{\alpha} \; C' \; N'$; $\omega = C_{\alpha} \; C' \; N \; C^{\alpha}$; $\theta = C_{\alpha} \; N \; C_{\alpha} \; C'$.

Surprisingly, the crystal structure deviates from the "ideal" boat conformation (Fig. 1) deduced from molecular models: steric hindrance between the C_{α} protons of Pro^1 and Pro^2 and between the C_{α} proton of Pro^3 and the peptide bond Pro^1–Pro^2 is alleviated by a twisting of the boat, although this leads to a certain degree of ring strain in a Dreiding model. The conformational angles for the "ideal" boat and for the twisted form (from models) are compared with the X-ray data in Table 2. The conformation in the crystal is seen to lie somewhere between the two idealized models.

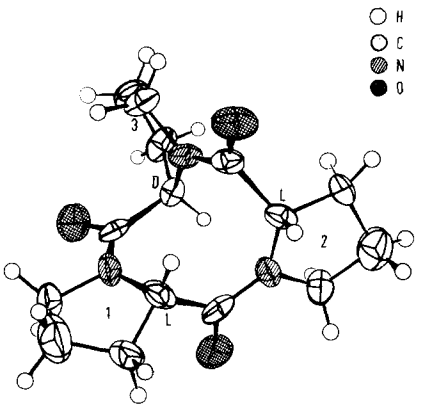


Fig. 2. Crystal structure of *cyclo*-[L-Pro^1-L-Pro^2-D-Pro^3].

Table 2. Comparison of the conformational angles ϕ and ψ [°] in the crystal (X-ray structure analysis) and in models.

	Pro	Boat [a]	Crystal [b]	Twisted boat [a]
ϕ	1	−33	−45	−70
	2	−85	−52	−20
	3	+100	+104	+105
ψ	1	+100	+107	+110
	2	+20	−21	−50
	3	−95	−56	−55

[a] Error ±5°. [b] Error ±2°.

Further remarkable features of the crystal structure are (i) the relatively slight deviation of the peptide bonds from coplanarity ($\omega = 0°$, $\theta - \phi = 180\,°C$, cf. Table 1) and (ii) the difference between the six proline rings in the two molecules of the crystal: only one of them has a twisted conformation while the other five have envelope conformations[3b, 3c]. These structures are probably separated by only slight energy barriers. This follows (a) from the difference in the proline ring conformations, which would appear to have its origin in crystal packing effects, and (b) from the large values of the thermal parameters of the β and γ carbons in the proline rings 2 and 1 (Fig. 2). We found that the volume of the ellipsoids of the title compound correlates well with the individual ^{13}C-NMR relaxation parameter (NT^1)[9] indicating a similar mobility in the solid state and in solution. A detailed report will be given elsewhere.

Received: March 19, 1979;
Supplemented: March 26, 1979 [Z 236 IE]
German version: Angew. Chem. *91*, 573 (1979)

[1] *C. M. Deber, D. A. Torchia, E. R. Blout*, J. Am. Chem. Soc. *93*, 4893 (1971).

[2] a) *H. Kessler, P. Kondor, G. Krack, P. Krämer*, J. Am. Chem. Soc. *100*, 2548 (1978); b) *H. Kessler, G. Krack, P. Krämer* in *J. Z. Siemion, G. Kupryszewski:* Peptides 1978. Proc. 15th Europ. Peptide Symposium Gdansk, Wrocław.

[3] X-ray structure determinations: *cyclo*-[L-Pro_4] [3a, b], *cyclo*-[L-Pro_2-L-Hyp] [3b], and *cyclo*-[L-Pro-(Bzl)Gly_2] [3c]; a) *G. Kartha, G. Ambady*, Acta Crystallogr. *B31*, 2035 (1975); b) *M. E. Druyan, C. L. Coulter, R. Walter, G. Kartha, G. K. Ambady*, J. Am. Chem. Soc. *98*, 5496 (1976); c) *J. W. Bats, H. Fuess*, to be published.

[4] *W. Mästle, M. Rothe* in *J. Z. Siemion, G. Kupryszewski:* Peptides 1978. Proc. 15th Europ. Peptide Symposium Gdansk, Wrocław.

[5] In *cyclo*-[L-Pro_2-(Bzl)Gly], steric constraints permit the benzylglycine moiety to take the place of proline ring 3 only.

[6] *R. Deslauriers, M. Rothe, I. C. P. Smith* in *J. Meienhofer, R. Walter:* Peptides. Proc. 4th Amer. Peptide Symposium New York, Ann Arbor Science Publ., Ann Arbor 1975.

[7] The complex ^1H-NMR spin system of three superimposed 7-spin systems is resolved sufficiently by addition of benzene for the individual spin systems to be determined by decoupling experiments. Selective stepwise ^1H-decoupling also leads to correlation of the ^1H-spin systems with the corresponding ^{13}C-NMR signals. Assignment to the three proline rings is based on the absence of Pro^3 in M (Fig. 1), on the characteristic C_{α} and C_{β} shifts for Pro^2, and on the ^1H-NMR coupling constants.

[8] IUPAC-IUB Commission on Biochemical Nomenclature, J. Mol. Biol. *52*, 1 (1970).

[9] a) *R. Deslauriers, R. Walter, I. C. P. Smith*, J. Biol. Chem. *249*, 7006 (1974); b) *A. Friedrich, H. Kessler*, unpublished results.

Use of Biogenetic Key Compounds for the Biomimetic Synthesis of Natural Products: (*S*)-Elenolide from Secologanin[**]

By *Lutz-F. Tietze* and *Horst C. Uzar*[*]

Biogenetic key compounds are excellent starting substances for the biomimetic synthesis of natural products and their analogs, since they can lead in a few steps to formation of enantiomerically pure products. Particularly interesting in this respect is the use of the monoterpene glycoside secologanin *(1)*, from which more than 1000, in part highly biologically active, alkaloids and other monoterpenes are formed *in vivo*[1]. In the present communication we describe a three-step synthesis of (*S*)-elenolide *(2)* from secologanin *(1)*.

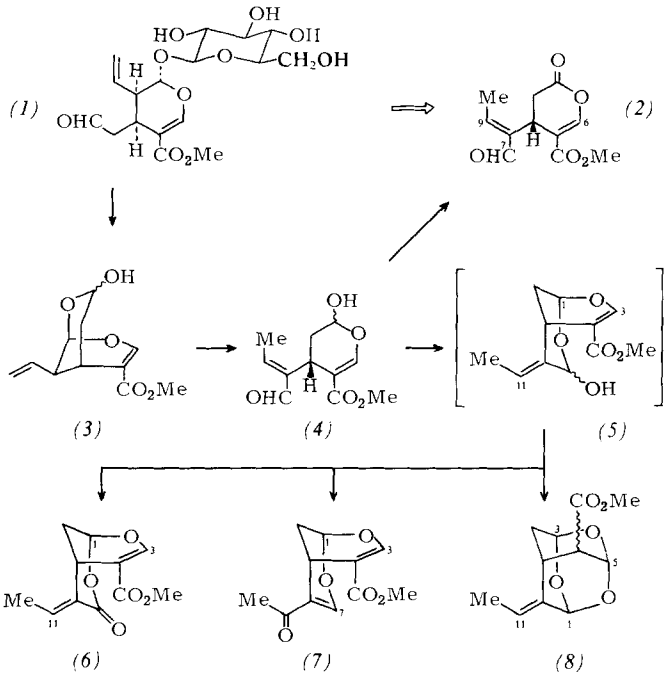
Elenolide *(2)* was isolated together with the secologanin derivative oleuropein from *Olea europa* L.[2]; hence, it can be assumed that *(2)* is also formed from *(1)* in these plants[3]. We therefore examined the products of the enzymic cleavage of the glycoside bond in *(1)*. Acid catalyzed rearrangement (ether/HCl, 72 h) of the initially formed bicyclic compound *(3)* furnished the semiacetal *(4)* (53% yield) with *E*-configu-

[*] Prof. Dr. L.-F. Tietze, Dipl.-Chem. H. C. Uzar
Organisch-chemisches Institut der Universität
Tammannstr. 2, D-3400 Göttingen (Germany)

[**] Iridoids, Part 11. This work was supported by the Ministerium für Wissenschaft und Forschung des Landes Nordrhein-Westfalen and the Fonds der Chemischen Industrie.—Part 10: *L.-F. Tietze, P. Marx*, Chem. Ber. *111*, 2441 (1978).

ration of the exocyclic double bond[4]. Oxidation of *(4)* with pyridinium chlorochromate in the presence of sodium acetate[5] afforded elenolide *(2)*[6] in 85% yield [CH_2Cl_2, 20 °C, 90 min; $R_F = 0.31$ (silica gel/ether), m.p. 156 °C (155–156 °C[2])] and, *via* the semiacetal *(5)*, 5% of the lactone *(6)*[6] ($R_F = 0.38$).

From the NMR signal of the aldehyde proton of *(2)* at $\delta = 9.20$ we assume that the exocyclic double bond is in the *E*-configuration (*Z*-configuration, see [2, 7]). Synthesis of *(2)* from *(1)* with known absolute configuration shows the chirality center in *(2)* to be in the *S*-configuration.



Oxidation of *(4)* in the absence of sodium acetate requires 9 h and, in addition to *(2)* (28% yield) and *(6)* (16%), ketone *(7)*[6] (11%, $R_F = 0.26$) and the trioxaadamantane *(8)*[6, 8] (1.2%, $R_F = 0.54$) are also formed. The formation of *(7)* can be explained by oxidation of an intermediary allyl cation formed from *(5)* by acid catalysts, and formation of *(8)* by addition of the hydroxy group to the α,β-unsaturated ester system in *(5)*.

Received: March 26, 1979 [Z 243a IE]
German version: Angew. Chem. *91*, 574 (1979)

CAS Registry numbers:
(1), 19351-63-4; *(2)*, 24582-91-0; *(3)*, 70592-73-3; *(4)*, 70576-16-8; *(5)*, 70576-17-9; *(6)*, 70576-18-0; *(7)*, 70576-19-1; *(8)*, 70576-20-4

[1] *G. A. Cordell*, Lloydia *37*, 219 (1974); *H. Inouye, S. Ueda, Y. Takeda*, Heterocycles *4*, 527 (1976); *L.-F. Tietze*, Tetrahedron Lett. *1976*, 2535.

[2] *L. Panizzi, M. L. Scarpati, G. Oriente*, Gazz. Chim. Ital. *90*, 1449 (1960); *H. C. Beyerman, L. A. van Dijck, J. Levisalles, A. Melera, W. L. C. Veer*, Bull. Soc. Chim. Fr. *1961*, 1812.

[3] The possibility may not be ruled out that elenolide is an artefact of oleuropein.

[4] *L.-F. Tietze, G. Kinast*, Chem. Ber. *109*, 3640 (1976).

[5] *E. J. Corey, J. W. Suggs*, Tetrahedron Lett. *1975*, 2647.

[6] ^{1}H-NMR ($CDCl_3$): *(2)*: $\delta = 9.20$ (d, $J = 1$ Hz, 7-H), 7.58 (d, $J = 0.5$ Hz, 6-H), 6.68 (q, $J = 7$ Hz, 9-H); *(6)*: $\delta = 7.44$ (s, 3-H), 7.01 (q, $J = 7$ Hz, 11-H), 5.92 (dd, $J = 2$ Hz, 1-H); *(7)*: $\delta = 7.51$ (br. s, 3-H, 7-H), 5.96 (dd, $J = 2$ Hz, 1-H); *(8)*: $\delta = 5.58$ (m, 1-H), 5.46 (q, $J = 6.5$ Hz, 11-H), 5.18 (m, 3-H, 5-H).

[7] *K. C. Chan, R. A. Jewell, W. H. Nutting, H. Rapoport*, J. Org. Chem. *33*, 3382 (1968).

[8] The configuration of the methoxycarbonyl group cannot be determined unequivocally by spectroscopic methods. Chemical detection was not possible, owing to the small amounts of substance available.

Synthesis of 1,4-Dihydronicotinic Acid Derivatives by Photochemical Cycloaddition[**]

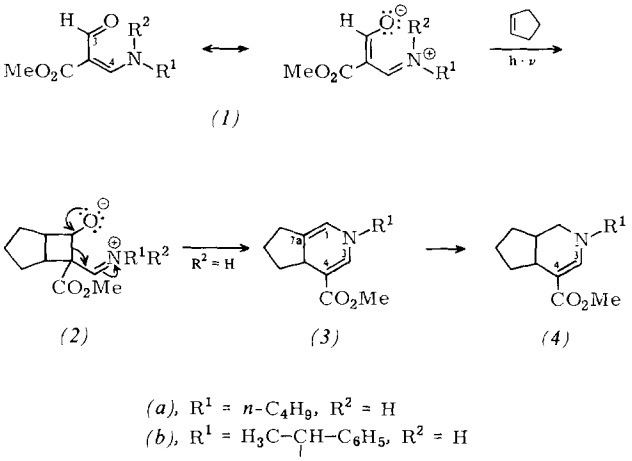
By *Lutz-F. Tietze* and *Klaus Brüggemann*[*]

1,4-Dihydronicotinic acid derivatives are of great therapeutical value in the treatment of coronary circulatory disorders[1]. They are also of interest as components of the oxidoreductases. We describe here a facile synthesis of this class of substances by photochemical cycloaddition of vinylogous formamides to olefins.

Irradiation of the *N*-monosubstituted compounds *(1)*[2] in cyclopentene at −40 °C with a high-pressure mercury vapor lamp affords the 1,4-dihydronicotinic acid derivatives *(3)*[3] in almost quantitative yields. A possible intermediate formed during the irradiation can be formulated as a cyclobutane derivative *(2)*, which can undergo hetero-retroaldol cleavage and recyclization to *(3)*. Hydrogenation of *(3)* with Pd/C in methanol affords *(4)*, and with Pt/C in glacial acetic acid the perhydrogenated products.

In contrast to *(1a)* and *(1b)* the *N,N*-diethyl- and *N,N*-dibenzyl-analogs fail to give any cycloaddition products. This is presumably due to the fact that the *cis*-s-*cis*-configuration[4] in these cases cannot be stabilized by hydrogen bonding[5].

The vinylogous formamides *(1)* can readily be obtained in 60–90% yield by reaction of methyl diformylacetate[6] with the corresponding amines in the presence of sodium sulfate (toluene, 20 °C, 2 h).



(a), $R^1 = n\text{-}C_4H_9$, $R^2 = H$
(b), $R^1 = H_3C\text{–}\underset{|}{C}H\text{–}C_6H_5$, $R^2 = H$

Procedure

A solution of *(1a)* (3.00 g, 16.2 mmol) in 300 ml cyclopentene/ether (1:1) was cooled to −40 °C, flushed with nitrogen to remove oxygen and irradiated in a Pyrex apparatus for 7 h with a high-pressure mercury vapor lamp (TQ 718, Hanau, cooling jacket −40 °C). The progress of the reaction could be followed chromatographically (silica gel/ether) and UV-spectroscopically. After removal of solvent by evaporation in a high vacuum the product *(3a)* was purified by preparative thin-layer chromatography (yield 82%). *(3a)* rapidly decomposes in the pure state and can be stored only for a limited period in solution at −30 °C.

[*] Prof. Dr. L.-F. Tietze, Dipl.-Chem. K. Brüggemann
Organisch-chemisches Institut der Universität
Tammannstr. 2, D-3400 Göttingen (Germany)

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

Received: March 26, 1979 [Z 243b IE]
German version: Angew. Chem. 91, 575 (1979)

CAS Registry numbers:
(1a), 70576-11-3; *(1b)*, 70576-12-4; *(3a)*, 70576-13-5; *R*,R*-(3b)*, 70576-14-6; *R*,S*-(3b)*, 70576-15-7; cyclopentene, 142-29-0; methyl diformylacetate, 50427-65-1; butylamine, 109-73-9; 1-phenylethylamine, 98-84-0

[1] *F. Bossert, W. Vater*, Naturwissenschaften *58*, 578 (1971).
[2] ^{1}H-NMR ($CDCl_3$): *(1a)*: $\delta = 9.76$ (d, $J = 4$ Hz, 3-H), 7.97 (dd, $J_{3,NH} = 14$ Hz, $J_{3,4} = 4$ Hz, 4-H); *(1b)*: $\delta = 9.80$ (d, $J = 4$ Hz, 3-H), 7.93 (dd, $J_{3,NH} = 14$ Hz, $J_{3,4} = 4$ Hz, 4-H); UV (MeOH): *(1a)*: $\lambda_{max}(\lg\varepsilon) = 299$ nm (4.19); *(1b)*: $\lambda_{max}(\lg\varepsilon) = 300$ nm (4.27).
[3] ^{1}H-NMR ($CDCl_3$): *(3a)*, *(3b)*: $\delta = 7.45$ (s, 3-H), 5.50 (br. s, 1-H); UV (MeOH): *(3a)*, *(3b)*: $\lambda_{max}(\lg\varepsilon) = 345$ nm (≈ 3.4); *(3b)* present as a mixture of the two diastereomers.
[4] *D. L. Ostercamp*, J. Org. Chem. *35*, 1632 (1970).
[5] *A. J. Merer, R. S. Mulliken*, Chem. Rev. *69*, 639 (1969); *P. E. Eaton*, Acc. Chem. Res. *1*, 50 (1968), and references cited therein.
[6] *G. Büchi, J. A. Carlson, J. E. Powell, L.-F. Tietze*, J. Am. Chem. Soc. *95*, 540 (1973).

Fragmentation of γ-Hydroxyammonium Compounds to Unsaturated Aldehydes by Flash Thermolysis[**]

By *Lutz-F. Tietze, Günther Kinast*, and *Horst C. Uzar*[*]

The base-induced fragmentation of the monotosylates of 1,3-diols[1] is a simple and well-known method for the synthesis of unsaturated ketones. Only in exceptional cases can unsaturated aldehydes, *e.g. (3a)*, be synthesized *via* this route, *e.g.* from *(1)*, since addition occurs as a rapid secondary reaction[2]. We have now demonstrated that flash thermolysis[3] of the analogous γ-hydroxyammonium hydroxides *(2)*, *(4)* and *(6)* at 350—450 °C, on the other hand, leads to the aldehydes *(3)*, *(5)*, and *(7)* in good yields[4]. Unsaturated ketones can also be prepared by this method[5].

A 1 M aqueous solution of the γ-hydroxyammonium hydroxides or hydrogen carbonates is used for the reaction. The ammonium acetates or halides give only small amounts of fragmentation product, while the ammonium hydrogen sulfides are almost quantitatively demethylated at the nitrogen.

The difficult problem of optimization of the contact times in the flash thermolysis is not encountered since the reactants are non-volatile salts. Likewise, other than in *(1)*, the relative configuration of the substituents on the ring system has no influence on the proportion of fragmentation in the overall decomposition[2,6]. The results are listed in Table 1.

The requisite γ-hydroxyammonium compounds can be prepared from cyclic ketones by aminomethylation[7], reduction ($NaBH_4/MeOH/NH_3$), reaction with MeI and ion-exchange. The synthetic sequence with subsequent fragmentation permits conversion of cyclic ketones into open-chain, terminally unsaturated aldehydes containing one more carbon atom. Thus, this method could also be used for the synthesis of the aglycon *O*-methyl ether *(10)*[2] of secologanin[8], a key compound for the biogenesis of more than 1000 alkaloids and other monoterpenes. The ammonium hydrogen carbonate *(9)* was prepared from the ketone *(8)*[9]. Subsequent thermal fragmentation in a flow system at 350 °C/15 torr led to *(10)*, which was isolated by column chromatography in a total yield of 10% (based on *(8)*; not optimized). Structural isomers of *(10)*, which could be formed by aminomethylation at C-5, could not be detected.

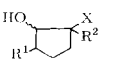
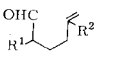
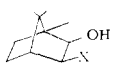
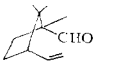
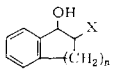
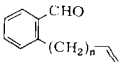
(8) → *(9)* → *(10)*

Procedure

A 1 M aqueous solution of γ-hydroxyammonium hydroxide (50 mmol) is introduced dropwise at a rate of *ca.* 1 ml/min onto heated silica beads (350—450 °C) in a thermolysis system fitted with a quartz condenser (length: 25 cm, diameter: 1.6 cm, external heating up to condenser) and through which a stream of N_2 is flowing at the rate of 20 ml/min. The system is subsequently flushed twice with 5 ml H_2O and twice with 5 ml dichloromethane. The thermolyzate is extracted three times with 50 ml dichloromethane, washed with 3 × 5 ml 2 N HCl and twice with 5 ml 5% $NaHCO_3$ solution, and the residue left on removal of solvent is distilled.

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

Table 1. Unsaturated aldehydes by fragmentation of γ-hydroxyammonium hydroxides. X = CH_2 $\overset{\oplus}{N}Me_3OH^{\ominus}$.

	Reactants [a]		M.p. of the iodide [°C]		Products [a]	Reaction temp. [°C]	Yield [b] [%]
(2a)		$R^1 = R^2 = H$	183	*(3a)*		450	73/43
(2b)		$R^1 = H$, $R^2 = Me$	166	*(3b)*		350	78/62
(2c)		$R^1 = R^2 = Me$	—	*(3c)*		350	82/70
(4)			298—299	*(5)*		450	89/80
(6a)		$n = 1$	219—220	*(7a)* [d]		450	82/60 [c]
(6b)		$n = 2$	189—191	*(7b)*		350	62/55
(6c)		$n = 3$	234—235	*(7c)*		350	81/70

[a] Constitution and configuration of the reactants (as ammonium iodides instead of hydroxides) and products are confirmed by spectroscopic data and combustion analysis. [b] Gas-chromatographically determined yields (2.5% silicone rubber SE 52 on Chromosorb G-NW-DMCS, 2 m, internal standard)/yields isolated after distillation. [c] The 2-methyl-1-indanone that is also formed was separated by column chromatography on silica gel (benzene). [d] Double-bond isomers are also formed.

[*] Prof. Dr. L. F. Tietze, Dr. G. Kinast, Dipl.-Chem. H. C. Uzar
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

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

Received: March 26, 1979 [Z 243c IE]
German version: Angew. Chem. 91, 576 (1979)

CAS Registry numbers:
(1), 2602-28-0; (2a) (anion = OH), 70592-71-1; (2a) (anion = I⁻), 70576-21-5; (2b) (anion = OH), 70592-70-0; (2b) (anion = I⁻), 70592-69-7; (2c) (anion = OH), 70592-68-6; (2c) (anion = I⁻), 70576-22-6; (3a), 764-59-0; (3b), 64825-78-1; (3c), 70576-23-7; (4) (anion = OH), 70592-67-5; (4) (anion = I⁻), 70576-24-8; (5), 70576-25-9; (6a) (anion = OH), 70592-66-4; (6a) (anion = I⁻), 70576-26-0; (6b) (anion = OH), 70592-65-3; (6b) (anion = I⁻), 70576-27-1; (6c) (anion = OH), 70592-64-2; (6c) (anion = I⁻), 70576-28-2; (7a) (isomer 1), 62708-42-3; (7a) (E) isomer 2, 62708-40-1; (7a) (Z) isomer 2, 62708-41-2; (7b), 70576-29-3; (7c), 70576-30-6; (8), 29748-07-0; (9), 70576-32-8; (10), 70629-74-2

[1] C. A. Grob, P. W. Schiess, Angew. Chem. 79, 1 (1967); Angew. Chem. Int. Ed. Engl. 6, 1 (1967); C. A. Grob, ibid. 81, 543 (1969) and 8, 535 (1969), and references cited therein.
[2] G. Kinast, L.-F. Tietze, Chem. Ber. 109, 3626 (1976), and references cited therein.
[3] Traynelis and Krieger had already investigated the thermal fragmentation of two γ-hydroxyammonium compounds in a reaction flask. The yields of aldehyde were 2.5%, or not quoted: V. J. Traynelis, J. G. Dadura, J. Org. Chem. 26, 1813 (1961); K. Mannien, H. Krieger, Tetrahedron Lett. 1967, 2071.
[4] G. Seybold, Angew. Chem. 89, 377 (1977); Angew. Chem. Int. Ed. Engl. 16, 365 (1977).
[5] L.-F. Tietze, G. Kinast, unpublished.
[6] R. Gleiter, W.-D. Stohrer, R. Hoffmann, Helv. Chim. Acta 55, 893 (1972).
[7] G. Kinast, L.-F. Tietze, Angew. Chem. 88, 261 (1976); Angew. Chem. Int. Ed. Engl. 15, 239 (1976).
[8] A. R. Battersby, A. R. Burnett, P. G. Parsons, J. Chem. Soc. C 1969, 1187.
[9] G. Büchi, J. A. Carlson, J. E. Powell, Jr., L.-F. Tietze, J. Am. Chem. Soc. 95, 540 (1973).

Co^{II} with Coordination Number 3: $Na_4[CoO_3]$—The First Oxocobaltate(II) with an Island Structure[1]

By *Wilfried Burow* and *Rudolf Hoppe*[*]

"Cation-rich" oxides of the alkali metals[2] exhibit surprising structural characteristics. Thus $K_2[NiO_2]$[3] contains CO_2-analogous dumbells O Ni O having an extremely short interatomic distance d(Ni O) = 1.68 Å with a three-dimensional arrangement corresponding to the XeF_2 type[4]. The first CO_3^{2-}-analogous "anion" in such oxides was found in the case of $Na_4[FeO_3]$[5], the only oxoferrate(II) known so far. The search for the corresponding cobaltate led first to $Na_{10}[Co_4O_9]$[6] with an anion analogous to tetracarbonate.

We have now been able to synthesize $Na_4[CoO_3]$, which is an oxocobaltate having an island structure [mixture of Na_2O + CoO, Na:Co = 4.4:1, sealed Co tube, 550 °C, 20 d, under dry argon in Supremax ampoule]. The preparation of untwinned single crystals proved extremely difficult.

$Na_4[CoO_3]$ appears bright red; the single crystals are coarse and transparent. Hydrolysis occurs immediately on contact with atmospheric moisture; this is accompanied by oxidation of Co^{II} to Co^{III} with dark coloration.

According to Weissenberg photographs, $Na_4[CoO_3]$ forms triclinic crystals with $a = 8.14_4$, $b = 6.22_0$, $c = 5.75_8$ Å, $\alpha = 117.5_4$, $\beta = 89.9_9$, $\gamma = 111.2_4$° in the space group P1; $Z = 2$ (four-circle diffractometer data). The structure was determined from 2358 symmetry-independent reflections (Mo-Kα, graphite monochromator, $6° \leq \theta \leq 36°$)[7] by three-dimensional Patterson synthesis; refinement with anisotropic temperature parameters for all particles gave $R = 5.97\%$ for 1808 reflections (cf. Fig. 1).

Primary structure: Each Co atom is in a planar environment of three O atoms d(Co^1 O) = 1.81, 1.86, 1.92 Å; d(Co^2 O) = 1.80, 1.88, 1.90 Å; sum of the O Co O angles = 359.8° for the two Co. One quarter of the eight Na particles have coordination number (C.N.) 3, and the others C.N. 4 with regard to oxygen. This follows from the composition, assuming that all O have C.N. 6 with respect to the cations and each Co a C.N. of at least 3 with regard to O (cf. the motives of the mutual adjunction in Table 1). The distances d(Na O) vary between 2.21 and 2.54 Å; d(Na^2 O^5) = 2.79 and d(Na^3 O^6) = 2.80 Å were also considered.

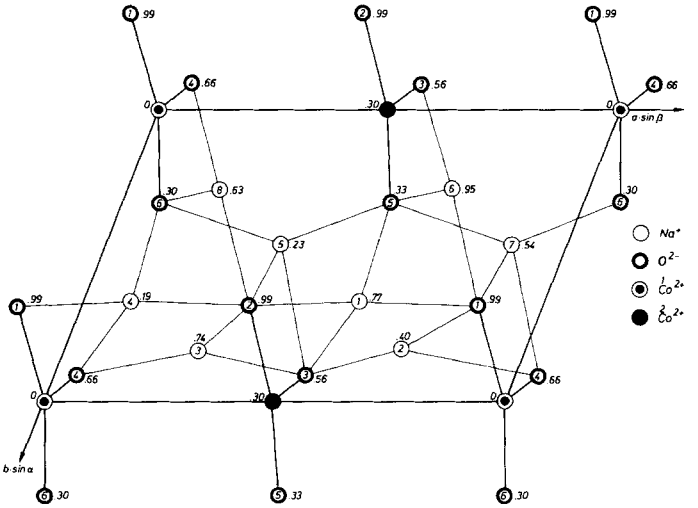


Fig. 1. Crystal structure of $Na_4[CoO_3]$ projected along [001]. Heights z as fractions of c.

Table 1. Motives of mutual adjunction in $Na_4[CoO_3]$.

	O^1	O^4	O^6	O^2	O^3	O^5	C.N.
Co^1	1/1	1/1	1/1				3
Co^2				1/1	1/1	1/1	3
Na^4	1/1	1/1	1/1	1/1			4
Na^7	1/1	1/1	1/1			1/1	4
Na^2	1/1	1/1			1/1	1/1 (2.79)	3 (+1)
Na^3		1/1	1/1 (2.80)	1/1	1/1		3 (+1)
Na^1	1/1			1/1	1/1	1/1	4
Na^5			1/1	1/1	1/1	1/1	4
Na^6	1/1				1/1	1/1	3
Na^8		1/1	1/1	1/1			3
C.N.	6	6	5 (+1)	6	6	5 (+1)	

"Long" Na O distances [Å] given in parentheses.

Secondary structure: Neither the coordination polyhedra around Co nor those around Na form discrete groups such as $[Co_2O_6]$.

Tertiary structure: The coordination polyhedra of O around Na undergo complicated three-dimensional linkage, with Co occupying vacancies in the three-dimensional Na_8O_6 network.

The Madelung part of the lattice energy (MAPLE[8] = 5006.6 kcal/mol) is in accord with the sum of the MAPLE values of the binary oxides (4957.2 kcal/mol, ΔMAPLE = 0.99%).

[*] Prof. Dr. R. Hoppe, Dipl.-Chem. W. Burow
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Lahn-Giessen 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0542 $ 02.50/0

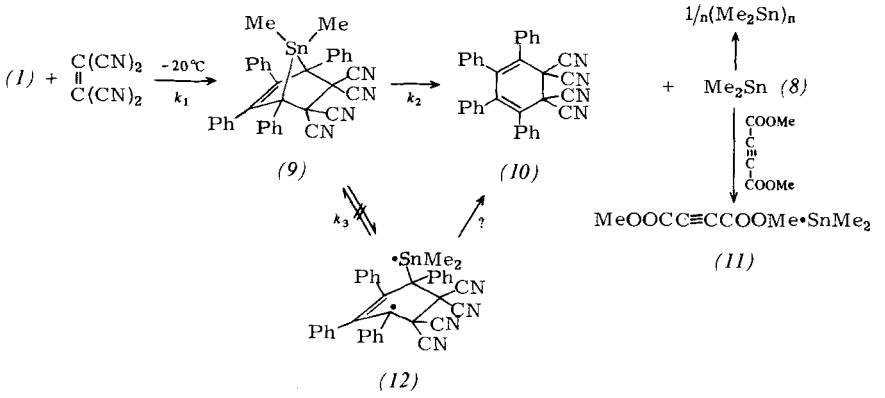
Received: April 2, 1979 [Z 244 IE]
German version: Angew. Chem. 91, 577 (1979)

CAS Registry numbers:
$Na_3[CoO_3]$, 70576-07-7

[1] Part of Dissertation by *W. Burow*, Universität Giessen.
[2] *R. Hoppe*, The Alkali Metals, Spec. Publ. Chem. Soc. No. 22, 452 (1967).
[3] *H. Rieck, R. Hoppe*, Z. Anorg. Allg. Chem. *400*, 311 (1973).
[4] *R. Hoppe, H. Mattauch, K. M. Rödder, W. Dähne*, Z. Anorg. Allg. Chem. *324*, 214 (1963); *H. Siegel, E. Gebert*, J. Am. Chem. Soc. *85*, 240 (1963).
[5] *R. Hoppe, H. Rieck*, Z. Anorg. Allg. Chem. *437*, 95 (1977); Naturwissenschaften *61*, 126 (1974).
[6] *W. Burow, R. Hoppe*, Angew. Chem. *91*, 71 (1979); Angew. Chem. Int. Ed. Engl. *18*, 61 (1979).
[7] Measured by Dr. *M. Jansen* in our institute with a Philips PW 1100 four-circle automatic diffractometer.
[8] *R. Hoppe*, Angew. Chem. *78*, 52 (1966); *82*, 7 (1970); Angew. Chem. Int. Ed. Engl. *5*, 95 (1966); *9*, 25 (1970); Adv. Fluorine Chem. *6*, 387 (1970).

Reaction of *(1)* with tetracyanoethylene at $-30\,^{\circ}C$ proved more successful: The [4+2]-cycloadduct 5,5,6,6-tetracyano-7,7-dimethyl-1,2,3,4-tetraphenyl-7-stannanorbornene *(9)* could be isolated as colorless crystals and was unequivocally identified by elemental analysis and ^1H-NMR spectroscopy [CH_2Cl_2; $\delta = 1.2$ (3H, s), $J(SnCH_3) = 52$ Hz; 1.43 (3H, s), $J(SnCH_3) = 48$ Hz; 6.8–7.5 (20H, m)].

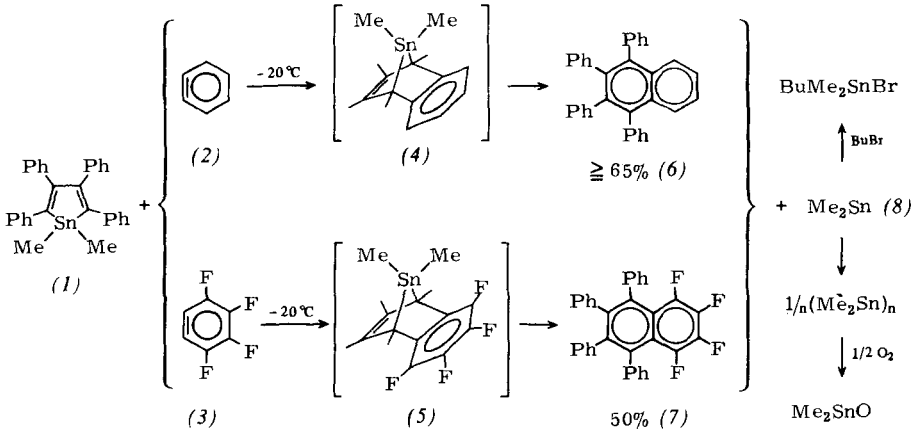
The new compound *(9)* is stable at $-30\,^{\circ}C$ for at least several weeks but decomposes above $-20\,^{\circ}C$ in a first order reaction [$t_{1/2} = 17$ min, $k_2 = 6.8 \times 10^{-4}\ s^{-1}$ at $-10\,^{\circ}C$] to *(8)* and 5,5,6,6-tetracyano-1,2,3,4-tetraphenyl-1,3-cyclohexadiene *(10)*, hitherto unknown. In the presence of the strong stannylene scavenger dimethyl acetylenedicarboxylate *(8)* gives a polymer or is trapped as the adduct *(11)* of still unknown structure. As can be seen, k_2 is much smaller than k_1



The First Stable Derivative of 7-Stannanorbornane and Its Thermolysis[1]

By *Christian Grugel, Wilhelm P. Neumann*, and *Michael Schriewer*[*]

Unsaturated 7-heteronorbornanes are important as precursors of carbene analogues[2]. In connection with our investigations on "stannylenes" (stannanediyls) R_2Sn[3], we became interested in the unsaturated 7-stannanorbornanes which were apparently hitherto unknown[4]. Attempted Diels-Alder type reaction of the stannol *(1)* with the highly reactive dienophile dehydrobenzene *(2)* or 1,2,3,4-tetrafluorodehydrobenzene *(3)* failed to give the expected 7-stannanorbornadienes *(4)* or *(5)*. Instead, we isolated only *(6)* and *(7)*, and products apparently resulting from the transient stannylene Me_2Sn *(8)*:



at $-10\,^{\circ}C$, and is neither increased nor diminished by the scavenger.

^{119}Sn-CIDNP effects, which could occur as a two-step mechanism by recombination (k_3) of the diradical *(12)*, have not been observed during thermolysis of *(9)*[5]. Thus, we assume the *formation of a free stannylene (8) by a concerted mechanism.*

Procedure

(1) (1.00 g, 2 mmol) and tetracyanoethylene (0.26 g, 2 mmol) are dissolved in 5 ml CH_2Cl_2 at $-30\,^{\circ}C$. The reaction mixture is stirred for 1 h before adding 10 ml of previously cooled pentane. Within 2 h a colorless finely crystalline precipitate of *(9)* is formed. This is filtered off at $-30\,^{\circ}C$, washed with pentane, and dried at 10^{-3} torr; yield *ca.* 1 g (80%).

When a solution of *(9)* (0.63 g) in CH_2Cl_2 (5 ml) prepared at $-30\,^{\circ}C$ is allowed to warm to room temperature, subsequent passage of air leads to precipitation of Me_2SnO (106

[*] Prof. Dr. W. P. Neumann, Dr. Ch. Grugel, Dipl.-Chem. M. Schriewer
Lehrstuhl für Organische Chemie I der Universität Dortmund
Otto-Hahn-Strasse, D-4600 Dortmund 50 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0543 $ 02.50/0

mg, 64%). After filtration and addition of ethanol to the filtrate (v/v = 1:1), cooling of the mixture affords *ca.* 300 mg (60%) of colorless feathery crystals of *(10)* which slowly turn yellow on exposure to air, decomp. pt. 217 °C ^{1}H-NMR: $\delta = 7.3$ (m), 7.7 (m). The kinetics of the thermolysis of *(9)* can be determined by ^{1}H-NMR spectroscopy from the diminution of the two $SnCH_3$ singlets.

Received: March 26, 1979 [Z 247 IE]
German version: Angew. Chem. *91*, 577 (1979)

CAS Registry numbers:
(1), 20195-60-2; *(2)*, 462-80-6; *(3)*, 5488-71-1; *(6)*, 751-38-2; *(7)*, 25107-39-5; *(8)*, 23120-99-2; *(9)*, 70728-20-0; *(10)*, 70728-21-1; *(11)*, 70775-74-5; $(CN)_2C$ $C(CN)_2$, 620-54-2; MeOOC—C≡C—COOMe, 762-42-5

[1] *M. Schriewer*, Diploma Thesis, Univ. Dortmund 1978.
[2] See, *e.g.*, *P. P. Gaspar*, "Silylenes", in *M. Jones, R. A. Moss*: Reactive Intermediates. Wiley, New York 1978.
[3] *Ch. Grugel, W. P. Neumann, J. Sauer, P. Seifert*, Tetrahedron Lett. *1978*, 2847; review: *W. P. Neumann*, "The Stannylenes R_2Sn", in *M. Gielen, P. G. Harrison*: The Organometallic and Coordination Chemistry of Germanium, Tin and Lead. Freund Publ., Tel Aviv 1978.
[4] *K. Kuno, K. Kobayashi, M. Kawanisi, S. Kozima, T. Hitomi*, J. Organometal. Chem. *137*, 349 (1977). A patented procedure [US Pat. 3240795 (1966)] could not be reproduced either under the stipulated conditions or otherwise: *R. Moser*, unpublished results.
[5] *M. Lehnig*, personal communication. Concerning ^{119}Sn-CIDNP, see *M. Lehnig*, Chem. Phys. *8*, 419 (1975).

1,3-Di-*tert*-butylcyclooctatetraene[**]

By *Gregory Wells, Yuji Hanzawa*, and *Leo A. Paquette*[*]

Despite a recent renewed surge of interest in cyclooctatetraene chemistry, directed synthetic approaches to certain derivatives of this ring system are still lacking. The problem is most acute when the 1,3-disubstitution plan is desired, 1,3-dimethylcyclooctatetraene, available by pyrolysis of 2,8-dimethylsemibullvalene, constituting the only known example. Presently, we describe an expeditious new entry to such molecules as exemplified by the preparation of 1,3-di-*tert*-butylcyclooctatetraene *(4)*.

Oxidation of commercially available 3,5-di-*tert*-butylcatechol *(1)* according to literature directions[1] gave the *o*-quinone *(2)* (maroon needles, m.p. 114–115 °C). On treatment with cyclobutadiene as liberated from its $Fe(CO)_3$ complex[2], *(2)* was transformed in 51% yield to the Diels-Alder adduct *(3)* which was isolated as a bright yellow crystalline solid (see Table 1).

Advantage was now taken of the reported ease of photochemical bisdecarbonylation of unsaturated bicyclic α-diketones to dienes and carbon monoxide[3]. Thus, irradiation of chloroform solutions of *(3)* with a 450-W Hanovia lamp at 0 °C for 90 min afforded the title cyclooctatetraene *(4)* in 77% yield. Compound *(4)* enters into cycloaddition with 4-phenyl-1,2,4-triazolinedione in refluxing ethyl acetate solution and delivers exclusively the cycloadduct *(5)* (Table 1) where the bulky *tert*-butyl substituents are expectedly[4] positioned on the cyclobutene ring. Submission of *(5)* to sequential alkaline hydrolysis and manganese dioxide oxidation[5] regenerated *(4)*, a colorless liquid.

[*] Dipl.-Chem. G. Wells, Dr. Y. Hanzawa, Prof. Dr. L. A. Paquette
Evans Chemical Laboratories, The Ohio State University
Columbus, Ohio 43210 (USA)

[**] We acknowledge the financial support of the National Science Foundation to *L. A. P.* and an Ohio State University postdoctoral fellowship award to *Y. H.*

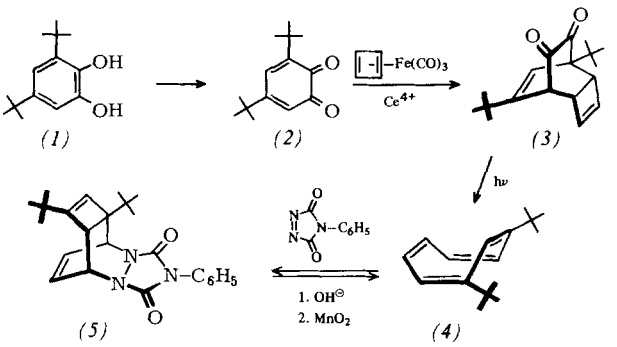


Table 1. Physical data of the new compounds *(3)*—*(5)*.

(3), m.p. 120–122 °C; ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 6.0$—5.75 (m, 3H), 3.6–3.38 (m, 1H), 3.34–3.12 (m, 2H), 1.14 (s, 9H), 0.98 (s, 9H); MS: $m/e = 272.1776$ (calc.), 272.1783 (exp.)

(4), ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 6.08$–5.37 (m, 6H), 1.08 (s, 9H), 1.05 (s, 9H); ^{13}C-NMR ($CDCl_3$, TMS): $\delta = 153.66$, 150.86, 132.61, 132.32, 130.43, 130.00, 123.41, 120.90, 36.55, 36.27, 29.87, 29.77

(5), m.p. 149–150 °C; ^{1}H-NMR ($CDCl_3$, TMS): $\delta = 7.38$ (m, 5H), 6.3 (ddd, $J = 7$, 6.5, 2 Hz, 1H), 5.94 (ddd, $J = 6.5$, 6.5, 1.5 Hz, 1H), 5.60 (d, $J = 2$ Hz, 1H), 5.2–4.82 (m, 2H), 3.12 (dd, $J = 4.5$, 2 Hz, 1H), 1.13 (s, 9H), 1.02 (s, 9H)

Consideration of the ground state "tub" geometry of *(4)* reveals the molecule to belong to the C_1 point group. This asymmetry requires the two *tert*-butyl groups to be chemically different, barring rapid π-bond shifting under the conditions of spectral measurement. In agreement with the *apparently* static nature of *(4)* at ambient temperature, its ^{1}H-NMR spectrum (Table 1) consists of a series of multiplets due to the six olefinic protons and a pair of singlets at $\delta = 1.08$ and 1.05 (9H each). Additionally, the ^{13}C-NMR spectrum (Table 1) displays 12 peaks. The chiral nature of *(4)* is currently being investigated[6].

The scope of the illustrated cyclooctatetraene synthesis is, of course, dictated by the availability of monocyclic *o*-benzoquinones. This class of compounds has proven to be conveniently accessible[7].

Received: January 30, 1979 [Z 237a IE]
German version: Angew. Chem. *91*, 578 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(1), 1020-31-1; *(2)*, 3383-21-9; *(3)*, 70528-24-4; *(4)*, 70528-25-5; *(5)*, 70528-26-6; tricarbonyl(η^4-1,3-cyclobutadiene)iron, 12078-17-0; 4-phenyl-1,2,4-triazolinedione, 4233-33-4

[1] *W. Flaig, T. Ploetz, H. Biergans*, Justus Liebigs Ann. Chem. *597*, 196 (1955); *R. C. DeSelms, W. R. Schleigh*, Synthesis *1973*, 614.
[2] *L. A. Paquette, L. M. Leichter*, J. Am. Chem. Soc. *93*, 5128 (1971); *L. Brener, J. S. McKennis, R. Pettit*, Org. Synth. *55*, 43 (1976).
[3] *D. Bryce-Smith, A. Gilbert*, Chem. Commun. *1968*, 1702; *J. Strating, B. Zwanenburg, A. Wagenaar, A. C. Udding*, Tetrahedron Lett. *1969*, 125; *M. B. Rubin, M. Weiner, H.-D. Scharf*, J. Am. Chem. Soc. *98*, 5699 (1976), and references cited therein; *R. N. Warrener, E. E. Nunn, M. N. Paddon-Row*, Tetrahedron Lett. *1976*, 2355; *R. N. Warrener, P. A. Harrison, R. A. Russell, M. N. Paddon-Row, ibid. 1977*, 2031; *R. N. Warrener, R. A. Russell, T. S. Lee, ibid. 1977*, 49.
[4] *L. A. Paquette, D. R. James, G. H. Birnberg*, J. Am. Chem. Soc. *96*, 7454 (1974).
[5] *D. R. James, G. H. Birnberg, L. A. Paquette*, J. Am. Chem. Soc. *96*, 7465 (1974).
[6] *L. A. Paquette, J. M. Gardlik, J. M. Photis*, J. Am. Chem. Soc. *98*, 7096 (1976); *J. M. Gardlik, L. K. Johnson, L. A. Paquette, B. A. Solheim, J. P. Springer, J. Clardy, ibid. 101*, 1615 (1979); *J. M. Gardlik, L. A. Paquette, R. Gleiter, ibid. 101*, 1617 (1979).
[7] *J. Cason*, Org. Reactions *4*, 305 (1948); *H. W. Wanzlich*, Angew. Chem. *76*, 313 (1964); Angew. Chem. Int. Ed. Engl. *3*, 401 (1964); *W. M. Horspool*, Qu. Rev. Chem. Soc. *23*, 204 (1969); *S. Patai*: The Chemistry of the Quinonoid Compounds. Wiley-Interscience, New York 1974.

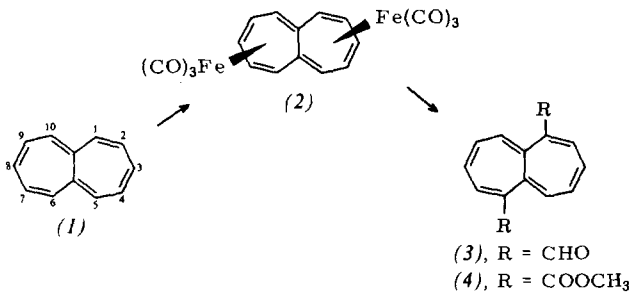
 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0544 $ 02.50/0

Heptalenebis(tricarbonyliron)

By *Emanuel Vogel, Dimitrios Kerimis, Neil T. Allison, Robert Zellerhoff,* and *Jürgen Wassen*[*]

Dedicated to Professor Tetsuo Nozoe on the occasion of his 77th birthday

In accord with expectation, the 12π-electron system heptalene *(1)* previously characterized by spectroscopic[1a] and structural[1b] investigations as being an olefin, readily reacts with electrophilic agents, but the heptalenium salts formed thereby in some cases have hitherto defied all attempts at transforming them into substituted heptalenes. However, after independently synthesized disubstituted heptalenes had been shown to be stable compounds[2], renewed attempts at the derivatization of *(1)* seemed warranted. We have now found that *(1)* can be substituted in the 1,6 position by way of heptalenebis(tricarbonyliron) *(2)*.



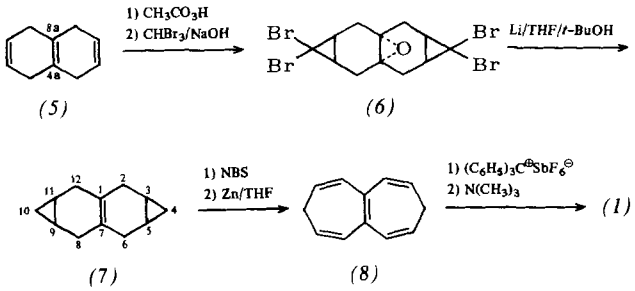
Heptalenebis(tricarbonyliron) *(2)*, which in contrast to the free ligand is completely air-stable, is formed as the major product when *(1)* is heated with benzylideneacetone(tricarbonyliron) (molar ratio 1:2.5) in toluene for 15 h at 50 °C. After chromatographic separation on silica gel (ether/pentane), *(2)* crystallizes from tetrachloromethane as deep-red rhombs; yield 35—40%.

The structure of the new heptalene-transition metal complex *(2)* (excluding the stereochemistry) follows from the ^{1}H-NMR spectrum (Table 1). This shows an ABCDE spin system which, considering both decoupling experiments and the fact that the protons of diene-Fe(CO)$_3$ moieties absorb at higher field strength than the protons of uncomplexed double bonds, is compatible only with the structure *(2)*. The number and positions of the ^{13}C-NMR signals also lend support to structure *(2)*. The stereochemistry of the complex *(2)* has recently been elucidated by an X-ray structure analysis by *H. J. Lindner et al.*[3]: surprisingly, it is found that both Fe(CO)$_3$ groups are located on the same side of the heptalene ligand.

From experience gained with other olefin-tricarbonyliron complexes[4] it appeared that formylation by the Vilsmeier method would be the most favorable approach for electrophilic substitution of *(2)*. Indeed, it was found that reaction of *(2)* with phosphorus oxide chloride (molar ratio 1:20) in dimethylformamide (initially at 0 °C and then 12 h at 50 °C) afforded a formylation product, which was isolated as red-brown crystals after chromatography on silica gel (ether/pentane) and recrystallization from ether/pentane; yield 20%. Interestingly, this product proved to be the uncomplexed 1,6-heptalenedicarbaldehyde *(3)*. Like the known heptalenes bearing two electronegative substituents, *(3)* is also air-stable.

It could be concluded from the changes observed in the ^{1}H-NMR spectrum of *(3)* below −40 °C that a rapid π-bond shift takes place in the molecule and that the two nonequivalent double bond isomers existing in equilibrium with each other are present in a ratio of 1:1. From the coalescence ($T_c = -70$ °C; $\delta\nu = 38$ Hz) of the aldehyde proton signals it follows that the activation enthalpy $\Delta G^{\neq}$ of the π-bond shift is 9.9 kcal/mol.

1,6-Heptalenedicarbaldehyde *(3)* is a suitable starting compound for the synthesis of dimethyl 1,6-heptalenedicarboxylate *(4)* and other 1,6-disubstituted heptalenes. The diester *(4)*, readily accessible by *Corey*'s method[5] [red prisms (from hexane); yield 41%], is likewise a dynamic system containing almost equal proportions of the two double-bond isomers, as was deduced from the temperature dependence of the ^{1}H-NMR spectrum (Table 1) (changes in the methyl proton signals: $T_c = -17$ °C; $\delta\nu = 2.8$ Hz). It seems remarkable that the replacement of the aldehyde groups in *(3)* by the carbomethoxy groups increases the free enthalpy of activation of the π-bond shift from 9.9 to 14 kcal/mol. This is undoubtedly due to steric effects.



The complex *(2)* promises to open up new perspectives in heptalene chemistry provided that better routes to the hydrocarbon become available. A practical novel synthesis of heptalene, based on the observation that the tetrasubstituted double bond of isotetralin *(5)* can be protected by a reversible epoxidation, has now been developed.

11-Oxatricyclo[4.4.1.0]undeca-3,8-diene, which can be obtained selectively from isotetralin *(5)*, reacts with bromoform (fivefold excess) and 50% sodium hydroxide in the presence of benzyltriethylammonium chloride (TEBA) to give the bisadduct *(6)*[6] having cyclopropane rings *trans* to the oxirane ring [m.p. 100 °C (decomp.); yield 60—70%]. Treatment of *(6)* with lithium and *tert*-butanol in tetrahydrofuran (24 hours' heating under reflux after the initially vigorous reaction has subsided) leads both to the reductive elimination of the four bromine atoms as well as to deoxygenation of the epoxide ring, *i.e.* the hydrocarbon *(7)* is formed in one step (yield 50—55%; see Table 1). Since the bromine atoms are removed more rapidly than the epoxide oxygen, it is possible to isolate the epoxide of *(7)*, *trans,trans*-13-oxapentacyclo[5.5.1.0^{1,7}.0^{3,5}.0^{9,11}]tridecane (m.p. 71—72 °C; yield 60—65%) if the duration of reaction is kept short. In order to transform *(7)* into *(8)*, *(7)* was heated with *N*-bromosuccinimide (NBS) (molar ratio 1:6) in the presence of azobisisobutyronitrile in tetrachloromethane (60 min), and the resulting semicrystalline mixture, consisting mainly of the expected tetrabromo-substitution product (stereoisomers), was then dehalogenated in the crude state with zinc in tetrahydrofuran (30 min reflux). Subsequent distillation in a high

[*] Prof. Dr. E. Vogel, Dipl.-Chem. D. Kerimis, Dr. N. T. Allison [**], Dr. R. Zellerhoff, Dr. J. Wassen
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

[**] Alexander-von-Humboldt Fellow.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0707-0545 $ 02.50/0*

vacuum afforded the previously unknown 3,8-dihydroheptalene (b.p. 44—45 °C/*ca.* 10 $^{-4}$ torr) having a purity of 95% (yield 35—40%). At this stage *(8)* is sufficiently pure for use in further reactions, but if necessary it can be purified by crystallization from pentane at low temperature, albeit at the expense of loss in yield[7]. Conversion of *(8)* into *(1)* could be accomplished, as already described for the isomeric dihydroheptalenes[1a], by dehydrogenation–hydride abstraction with triphenylmethyl hexafluoroantimonate in dichloromethane and deprotonation with trimethylamine (yield 88—93% and 55—60%, respectively). The hitherto unknown intermediary heptalenium salt was isolated, m.p. 155 °C (decomp). Another practical heptalene synthesis, also starting from isotetralin, has been developed independently by *Paquette* and co-workers[8].

Table 1. Physical data of compounds *(2)*, *(3)*, *(4)*, *(7)*, and *(8)*.

(2). m.p. 185 °C (decomp.); UV (cyclohexane): $\lambda_{max} = 286$ nm ($\varepsilon = 17200$), 329 (21100), 443 (8800); IR (CCl_4): 2058, 2040, 1988, 1975 cm^{-1} (C O); ^{1}H-NMR (C_6D_6): $\delta = 2.44$ (t, H-4, 9), 2.98 (d, H-1, 6), 4.60 (m, H-2, 7), 4.79 (m, H-3, 8), 5.46 (d, H-5, 10) [a]

(3). m.p. 105 °C; UV (ethanol): $\lambda_{max} = 290$ nm ($\varepsilon = 15800$), 362 (5100), 485 (860); IR (CsI): 1670 cm^{-1} (C O); ^{1}H-NMR [$CDCl_3$; room temperature (region of rapid exchange)]: $\delta = 6.11$ (d, H-5, 10), 6.65 (m, H-3, 4, 8, 9), 7.08 (d, H-2, 7), 9.80 (s, 2 CHO)

(4). m.p. 90–91 °C; UV (ethanol): $\lambda_{max} = 271$ nm ($\varepsilon = 1700$), 334 (4300), 420 (790, sh); IR (CsI): 1720 cm^{-1} (C O); ^{1}H-NMR [[D_2]-tetrachloroethane; +110 °C (region of rapid exchange)]: $\delta = 3.70$ (s, 2 CH_2), 6.13 (m, H-5, 10), 6.50 (m, H-3, 4, 8, 9), 7.15 (d, H-2, 7)

(7). b.p. 52–53 °C/0.4 torr: ^{1}H-NMR ($CDCl_3$): $\delta = 0.22$ (m; H-4, 4, 10, 10), 0.95 (m, H-3, 5, 9, 11); 2.1 (m, H-2, 2, 6, 6, 8, 8, 12, 12)

(8). m.p. 33–34 °C; UV (cyclohexane): $\lambda_{max} = 230$ nm ($\varepsilon = 40900$, sh), 234 (43100), 299 (7700); ^{1}H-NMR (CCl_4): $\delta = 2.16$ (t, $J = 6.8$ Hz, H-3, 3, 8, 8), 5.50 (dt, $J_{12} = 10.2$ Hz, $J_{23} = 6.8$ Hz, H-2, 4, 7, 9), 6.25 (d, $J = 10.2$ Hz, H-1, 5, 6, 10)

[a] A closer study of the ^{1}H- and ^{13}C-NMR spectra of this complex has shown that the double bonds which are localized at room temperature, as in structure *(2)*, migrate at higher temperature with simultaneous 1,2-shift of the $Fe(CO)_3$ groups, the reactant and product being in the relationship of enantiomers; cf. the dynamic behavior of cyclooctatetraene(tricarbonyliron): *F. A. Cotton, D. L. Hunter*, J. Am. Chem. Soc. *98*, 1413 (1976).

Received: February 22, 1979 [Z 237b IE]
Publication delayed at authors' request
German version: Angew. Chem. *91*, 579 (1979)

CAS Registry numbers:
(1), 257-24-9; *(2)*, 70629-73-1; *(3)*, 70576-00-0; *(4)*, 70576-01-1; *(7)*, 70576-02-2; *(8)*, 70576-03-3; benzylideneacetone(tricarbonyliron), 61216-69-1; *(5)*, 493-04-9; *(6)*, 70576-04-4; *trans,trans*-13-oxapentacyclo[5.5.1.$0^{4,7}$.$0^{3,5}$.$0^{9,11}$]tridecane, 70592-72-2

[1] a) *H. J. Dauben, Jr., D. J. Bertelli*, J. Am. Chem. Soc. *83*, 4659 (1961); *E. Vogel, H. Königshofen, J. Wassen, K. Müllen, J. F. M. Oth*, Angew. Chem. *86*, 777 (1974); Angew. Chem. Int. Ed. Engl. *13*, 732 (1974); b) *H. J. Lindner, B. Kitschke, ibid. 88*, 123 (1976) and *15*, 106 (1976); *J. Stegemann, H. J. Lindner*, Tetrahedron Lett. *1977*, 2515.

[2] *E. Vogel, J. Ippen*, Angew. Chem. *86*, 778 (1974); Angew. Chem. Int. Ed. Engl. *13*, 734 (1974); *E. Vogel, F. Hogrefe, ibid. 86*, 779 (1974) and *13*, 735 (1974); *K. Hafner, H. Diehl, H. U. Süss, ibid. 88*, 121 (1976) and *15*, 104 (1976).

[3] *J. Stegemann, H. J. Lindner*, J. Organomet. Chem. *166*, 223 (1979).

[4] Review: *A. J. Birch, I. D. Jenkins* in *H. Alper*: Transition Metal Organometallics in Organic Synthesis, Academic Press, New York 1976, Vol. 1, p. 1.

[5] *E. J. Corey, N. W. Gilman, B. E. Ganem*, J. Am. Chem. Soc. *90*, 5616 (1968).

[6] *J. Ippen*, Dissertation, Universität Köln 1975. It has meanwhile been found that the tetrachloro analog of *(6)*, obtained by reaction of the 4a,8a-epoxide of isotetralin *(5)* with chloroform and sodium hydroxide under phase-transfer conditions [m.p. 125 °C (decomp.); yield 75—80%], can be advantageously be used instead of *(6)*.

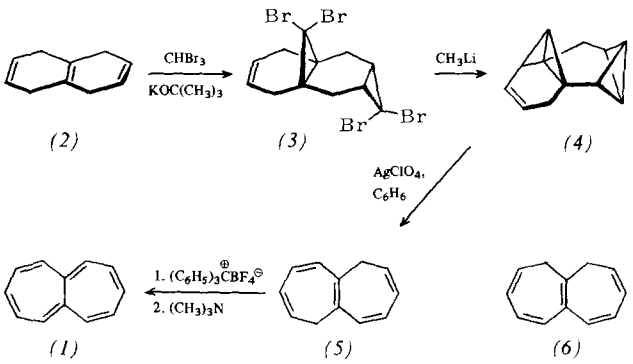
[7] The conversion of *(7)* into *(8)* is similar to the final step in the synthesis of octalene, see *E. Vogel, H.-V. Runzheimer, F. Hogrefe, B. Baasner, J. Lex*, Angew. Chem. *89*, 909 (1977); Angew. Chem. Int. Ed. Engl. *16*, 871 (1977).

[8] *L. A. Paquette, A. R. Browne, E. Chamot*, Angew. Chem. *91*, 581 (1979); Angew. Chem. Int. Ed. Engl. *18*, 546 (1979).

An Expeditious Synthesis of Heptalene from Naphthalene *via* a Bis(bicyclo[1.1.0]butane) Intermediate[**]

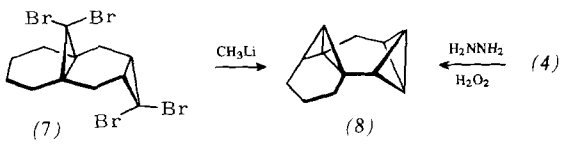
By *Leo A. Paquette, Alan R. Browne*, and *Ernest Chamot*[*]

To the present time, two syntheses of heptalene *(1)* have been reported[1,2] and access has been gained to a few derivatives. While both routes to *(1)* are elegant in their conception, they are lengthy, and the hydrocarbon has therefore remained difficultly accessible. As a result, theoretical predictions often have preceded the execution of experimental work in this field.



In this communication we describe an efficient six-step conversion of naphthalene to *(1)*. The new methodology capitalizes on the regiospecificity of two-fold intramolecular carbene insertion to give *(4)*[3] and the ability of silver(I) ions to promote the isomerization of bicyclo[1.1.0]butanes to ring-opened conjugated dienes[4].

Addition of dibromocarbene to tetrahydronaphthalene (isotetralin) *(2)*[5] using a modification[6] of *Vogel*'s procedure[7] afforded bisadduct *(3)* (38%) admixed with the corresponding mono- (12%) and tris-adducts (0.8%). These products could be efficiently separated by recrystallization; resubmission of the monoadduct to the same reaction conditions returned additional *(3)* in 72% yield. When the tetrabromide *(3)* was treated with 2 M ethereal methyllithium at 0—25 °C for 3 h, the colorless bis(bicyclo[1.1.0]butane) *(4)* was obtained in 59% yield *after molecular distillation* (80—100 °C/0.3 torr). The ^{1}H-NMR spectrum of *(4)* (C_6D_6) contains two series of multiplets at $\delta = 6.03$—5.06 (2H) and 2.46—1.11 (10H) while its ^{13}C-NMR exhibits 12 lines, thus demonstrating the isomeric homogeneity of the hydrocarbon. The definitive structural assignment follows from the Ag^+-catalyzed isomerization of *(4)* exclusively to 1,6-dihydroheptalene *(5)* and catalytic hydrogenation of this pentaene to *cis*-bicyclo[5.5.0]dodecane[2]. Whereas *(5)* belongs to the C_{2h} point group, the 1,10 isomer *(6)* has C_{2v} symmetry; a clear distinction between them becomes apparent upon ^{13}C-NMR analysis (in $CDCl_3$) which reveals the six lines ($\delta = 132.8$, 131.0, 125.6, 123.6, 123.0, and 33.6) demanded uniquely by *(5)*.



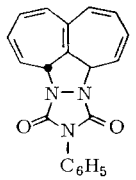
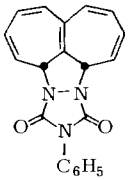
[*] Prof. Dr. L. A. Paquette, Dr. A. R. Browne, Dr. E. Chamot
Evans Chemical Laboratories, The Ohio State University
Columbus, Ohio 43210 (USA)

[**] We acknowledge the financial support of the donors to the Petroleum Research Fund, administered by the American Chemical Society, the National Cancer Institute, and an Ohio State University Graduate School postdoctoral fellowship award to *A. R. B.*

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0546 $ 02.50/0

The regiospecificity observed in the carbene insertion step to give *(4)* would appear to have its origins in the geometric constraints generated by one bicyclobutane unit upon formation of the second. Molecular models reveal that closure of either the central or peripheral carbene produces conformationally rigid intermediates in which the second insertion is forcibly directed away from the first-formed bicyclobutane ring. To establish that the double bond in *(3)* did not contribute additionally to the regiospecificity, the tetrabromide *(7)*[6] was reacted with methyllithium. Separation of *(8)* (46%) from an ether insertion product was achieved by distillation (b.p. 52—58 °C/0.2 torr). The homogeneity of hydrocarbon *(8)* was established spectroscopically and by VPC methods. As a check on the directionality of the ring closure, *(4)* was transformed into *(8)* by diimide reduction.

Although the pair of bicyclo[1.1.0]butane rings within *(4)* and *(8)* are formally conjugated, these molecules show only customary end absorption in the ultraviolet. Thus, electronic interaction between bicyclobutane orbitals becomes observable only when the connective bond is linked to the bridgehead carbon atoms[8]. A remarkable feature of these molecules is their stable nature, despite a strain energy which must be in excess of 120 kcal/mol[9].

(9)   *(10)*

The ultimate conversion of *(5)* into *(1)* was carried out according to *Dauben*'s original procedure[2]. The brownish red heptalene *(1)* entered readily into reaction with 4-phenyl-1,2,4-triazolinedione to give in good yield a 10:1 mixture of an amorphous solid and a microcrystalline substance (m.p. >310 °C). The monomeric nature of these cycloadducts was deduced by mass spectrometry (M^+ 329) and their inherent symmetry by ^{13}C-NMR spectroscopy (seven signals arising from the carbocyclic ring C atom of which two are quaternary). The closely similar ^{1}H-NMR spectra are characterized, *inter alia*, by an eight-proton olefinic multiplet and a multiplet (2H) for the allylic protons vicinal to nitrogen. Their almost superimposable ultraviolet spectra [$\lambda_{max}^{C_2H_5OH}$ 250 sh nm (ε = 11500—12000)] compare closely to that exhibited by *(8)*[2]. On this basis, the adducts are formulated as *(9)* and *(10)*, although no distinction between the C_2 and C_s forms has been made.

Received: January 30, 1979 [Z 237c IE]
German version: Angew. Chem. *91*, 581 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(1), 257-24-9; *(2)*, 493-04-9; *(2)*-monoadduct, 4578-96-5; *(2)*-trisadduct, 70528-27-7; *(3)*, 70528-28-8; *(4)*, 70562-07-1; *(5)*, 70528-29-9; *(7)*, 70528-30-2; *(8)*, 70528-31-3; *(9)*, 70528-32-4; *(10)*, 70528-33-5; 4-phenyl-1,2,4-triazolinedione, 4233-33-4; dibromocarbene, 4371-77-1

[1] *E. Vogel, J. Wassen, H. Königshofen, K. Müllen, J. F. M. Oth*, Angew. Chem. *86*, 777 (1974); Angew. Chem. Int. Ed. Engl. *13*, 732 (1974).
[2] *H. J. Dauben, Jr., D. J. Bertelli*, J. Am. Chem. Soc. *83*, 4657, 4659 (1961).
[3] *R. Vaidyanathaswamy, D. Devaprabhakara*, Chem. Ind. (London) *1968*, 515; *W. R. Moore, S. S. Hall, C. Largman*, Tetrahedron Lett. *1969*, 4353; *L. A. Paquette, G. Zon, R. T. Taylor*, J. Org. Chem. *39*, 2677 (1974); *L. A. Paquette, R. T. Taylor*, J. Am. Chem. Soc. *99*, 5708 (1977).
[4] *L. A. Paquette*, Synthesis *1975*, 347; *K. C. Bishop III*, Chem. Rev. *76*, 461 (1976).
[5] *E. Vogel, W. Klug, A. Breuer*, Org. Synth. *54*, 11 (1974).
[6] *G. L. Thompson, W. E. Heyd, L. A. Paquette*, J. Am. Chem. Soc. *96*, 3177 (1974).
[7] *E. Vogel, W. Grimme, S. Korte*, Tetrahedron Lett. *1965*, 3625.
[8] *W. R. Moore, C. R. Costin*, J. Am. Chem. Soc. *93*, 4910 (1971).
[9] *N. C. Baird, M. J. S. Dewar*, J. Am. Chem. Soc. *89*, 3966 (1967).

Tellurium-Catalyzed Reaction of Amines with Carbon Monoxide

By *Nobuaki Kambe, Kiyoshi Kondo, Hideo Ishii, Shinji Murai*, and *Noboru Sonoda*[*]

The simplest way of making urea derivatives from amine and carbon monoxide may be represented by eq. (a). In this communication, we wish to report that the reaction (a) can be catalyzed by elemental tellurium. This is the first example of activation of carbon monoxide by tellurium and of the formation of equimolar amounts of ureas and hydrogen:

$$\underset{(1)}{2\,RNH_2} + CO \xrightarrow[Te]{} \underset{(2)}{(RNH)_2CO} + H_2 \qquad (a)$$

No typical element was previously known to catalyze this reaction. Among group 6B elements, selenium catalyzes the formation of ureas from amines and carbon monoxide, but only in the presence of oxygen; moreover, water is then produced instead of hydrogen[1]. Sulfur is uneffective in catalyzing reaction (a)[2]. Various transition metal complexes have been reported to catalyze formation of ureas from amines and carbon monoxide; little is known about hydrogen formation or the exact stoichiometry of the reaction[3].

The tellurium-catalyzed carbonylation reaction (a) furnishes equimolar amounts of ureas and hydrogen; formamides appear as by-products (Table 1). The monoamines *(1a)*—*(1d)* are suitable starting materials. Ammonia, dialkylamines, and aniline failed to react under the reaction conditions reported.

Table 1. Tellurium-catalyzed carbonylation of amines *(1)* to give ureas *(2)*, hydrogen, and formamides *(3)* [*(1)*, 100 mmol; Te, 1 mmol; CO, 29 bar; *T*, 140 °C; *t*, 10 h].

	Amines *(1)*	Ureas *(2)* [mmol]	Hydrogen [mmol]	Formamides *(3)* [mmol]
a	$PhCH_2NH_2$	4.7	5.0	1.1
b	n-$C_4H_9NH_2$	7.3	7.4	15.3
c	n-$C_8H_{17}NH_2$	2.3	1.9	1.0
d	*cyclo*-$C_6H_{11}NH_2$	4.1	3.3	7.2

Experimental

Freshly distilled benzylamine (100 mmol, 10.7 g) and powdered tellurium (1 mmol, 128 mg) are placed with a magnetic stirring bar in a 50-ml stainless steel autoclave. The apparatus is then flushed several times with CO and charged with CO at 29 bar. The reaction is conducted at 140 °C for 10 h with vigorous stirring. On completion of reaction, the resulting gas (5.0 mmol H_2) is collected in gas sampler at room temperature and analyzed by gas chromatography (molecular sieve 5 Å, 3.3 m; 150 °C; carrier gas, N_2, *ca.* 1 bar). Air is introduced into the reaction mixture to precipitate tellurium. Filtration followed by evaporation gives a mixture of products; GLC analyses and comparison with authentic samples showed dibenzylurea *(2a)* (4.7 mmol) and *N*-benzylformamide *(3a)* (1.1 mmol) to be present.

[*] N. Kambe, Dr. K. Kondo [*], H. Ishii, Prof. Dr. S. Murai, Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering, Osaka University
Suita, Osaka 565 (Japan)
[*] Author to whom correspondence should be addressed.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0707-0547 $ 02.50/0*

Received: March 29, 1979 [Z 242 IE]
German version: Angew. Chem. 91, 582 (1979)

CAS Registry numbers:
(1a), 100-46-9; (1b), 109-73-9; (1c), 111-26-2; (1d), 108-91-8; (2a), 1466-67-7; (2b), 1792-17-2; (2c), 2763-88-4; (2d), 2387-23-7; (3a), 6343-54-0; (3b), 871-71-6; (3c), 2591-78-8; (3d), 766-93-8; CO, 630-08-0; Te, 13494-80-9

[1] N. Sonoda, T. Yasuhara, K. Kondo, T. Ikeda, S. Tsutsumi, J. Am. Chem. Soc. 93, 6344 (1971); K. Kondo, N. Sonoda, S. Tsutsumi, J. Chem. Soc. Chem. Commun. 1972, 307; K. Kondo, N. Sonoda, K. Yoshida, M. Koishi, S. Tsutsumi, Chem. Lett. 1972, 401.

[2] R. A. Franz, F. Applegath, J. Org. Chem. 26, 3304 (1961); R. A. Franz, F. Applegath, F. V. Morriss, F. Baiocchi, ibid. 26, 3306 (1961); R. A. Franz, F. Applegath, F. V. Morriss, F. Baiocchi, C. Bolze, ibid. 26, 3309 (1961).

[3] B. D. Dombek, R. J. Angelici, J. Organomet. Chem. 134, 203 (1977); J. Tsuji, N. Iwamoto, Chem. Commun. 1966, 380; F. Calderazzo, Inorg. Chem. 4, 293 (1965); H. Sterberg, J. Wender, R. A. Friedel, M. Orchin, J. Am. Chem. Soc. 75, 3148 (1953); J. J. Byerley, G. L. Rempel, N. Takebe, Chem. Commun. 1971, 1482; D. Durand, C. Lassau, Tetrahedron Lett. 1969, 2329; T. Saegusa, S. Kobayashi, K. Hirota, Y. Ito, Bull. Chem. Soc. Jpn. 42, 2610 (1969).

Reactions of Molybdate(VI) with Hydroxylamine and *N*-Methylhydroxylamine[**]

By *Karl Wieghardt, Wolfgang Holzbach, Johannes Weiss, Bernhard Nuber,* and *Boris Prikner*[*]

Mo^{VI} oxoanions react with hydroxylamine in alkaline or acidic aqueous solution without evolution of gas (N_2, N_2O, NO, NH_3) to give yellow products which have not yet been isolated[1,2]. The question whether Mo^{VI} is reduced[2] or whether complexes of Mo^{VI} containing an H_2NOH ligand have been formed[1] remained unsettled. On addition of 2,2'-bipyridine (bpy), we have now been able to isolate a yellow salt *(1)* from such a solution. Its IR spectrum exhibits a strong band at 1615 cm^{-1} which we assign to a $\nu(N{-}O)$ stretching vibration[3].

$$MoO_4^{2-} + 3[H_3NOH]Cl + bpy \rightarrow [Mo(bpy)(H_2NO)_2(NO)]Cl + 4H_2O + 2Cl^- \quad (1)$$

The structure of the cation of *(1)* was determined by X-ray methods[4] (Fig. 1). The central molybdenum atom has a coordination number of 7 (pentagonal pyramid); it is surrounded by one bpy and two hydroxylamido-*O,N* ligands ($H_2N{-}O^{\ominus}$), all of which are bidentate, and a nitrosyl ligand. Thus a nitrosyl complex of type $\{Mo{-}N{-}O\}^{[4]}$ has been formed; the MoNO group is approximately linear and the Mo—N5 bond is relatively short[3].

The clear-cut reaction course and the stoichiometry of formation of *(1)* suggest intramolecular two-electron oxidation of a coordinated hydroxylamine ligand to a nitrosyl ligand (formally $NO^{\ominus}$) with concomitant reduction of Mo^{VI} to Mo^{IV}. We have already proposed analogous processes to occur in the reaction of vanadium(v) with H_2NOH[5].

[*] Prof. Dr. K. Wieghardt [+], Dipl.-Chem. W. Holzbach
Institut für Anorganische Chemie der Universität
Callinstrasse 9, D-3000 Hannover 1 (Germany)
Prof. Dr. J. Weiss, Dr. B. Nuber, Dipl.-Chem. B. Prikner
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)
[+] To whom correspondence should be addressed.

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

Reaction of the weaker reducing agent *N*-methylhydroxylamine with Mo^{VI} at pH = 6 affords a colorless neutral complex *(2)*, whose structure has likewise been determined by X-ray methods[6] (Fig. 2).

$$MoO_4^{2-} + 2[MeH_2NOH]^+ \rightarrow [MoO_2(MeHNO)_2]^0 + 2H_2O$$

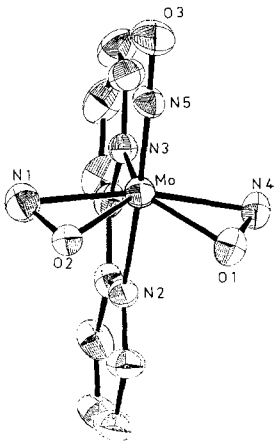


Fig. 1. Structure of the complex cation in *(1)* (without H atoms). Principal bond lengths [pm] and angles [°]:

Mo—N1	211.2(5)	N1—O2	141.2(7)	Mo—N5	177.3(4)
Mo—N4	210.3(5)	N4—O1	140.7(9)	Mo—N2	221.7(4)
Mo—O1	201.9(4)	N5—O3	121.0(6)	Mo—N3	216.1(7)
Mo—O2	204.3(6)				
N1—Mo—O2	39.7(2)	Mo—N5—O3	174.1(6)	Mo—O2—N1	72.8(4)
N4—Mo—O1	39.8(3)	Mo—N1—O2	67.5(3)	N5—Mo—N3	95.1(2)
O2—Mo—O1	92.6(2)	Mo—N4—O1	66.9(3)	N5—Mo—N2	169.6(2)
N2—Mo—N3	74.5(2)				

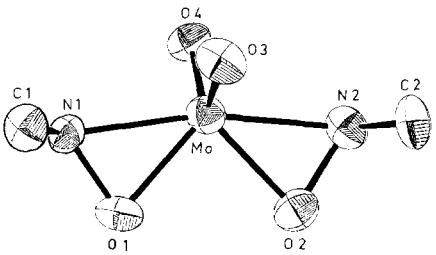


Fig. 2. Structure of the neutral complex *(2)* (without H atoms). Principal bond lengths [pm] and angles [°]:

Mo—N1	213.0(10)	Mo—O2	196.4(9)	N2—C2	148.6(18)
Mo—N2	211.9(11)	Mo—O3	170.0(8)	N1—C1	147.1(17)
Mo—O1	196.1(9)	Mo—O4	172.8(8)	O2—N2	143.1(13)
				O1—N1	142.8(13)
O3—Mo—O4	113.7(3)	O2—Mo—N2	40.8(4)	O1—Mo—O2	85.6(4)
N1—Mo—N2	166.6(5)	C1—N1—Mo	124.1(8)	O4—Mo—N1	95.1(4)
O1—Mo—N1	40.6(4)	C2—N2—Mo	123.3(8)	O3—Mo—N2	91.7(4)

In compound *(2)*, one Mo^{VI} center is surrounded by two terminal *cis*-oxo and two *N*-methylhydroxylamido-*O,N* ligands (C.N. 6). No redox process has therefore taken place in this case. To our knowledge, *(2)* is the first example of a coordination compound between a hydroxylamine derivative and molybdenum(VI).

Procedure

Synthesis of *(1)*: A solution of hydroxylammonium chloride (2.8 g, 40 mmol) in water (10 ml) is added dropwise at 60 °C to a solution of MoO_3 (0.3 g, 2 mmol) and NaOH (0.4

g) in water (20 ml). Addition of 2,2'-bipyridine (0.65 g, 4 mmol) to this clear yellow-orange solution deepens its color. Analytically pure yellow crystals are obtained (0.7 g) on slow cooling (0 °C).

Synthesis of *(2)*: *N*-Methylhydroxylammonium chloride (1.75 g, 20 mmol) is added to a solution of MoO_3 (1.5 g, 10 mmol) in 2.5 M KOH (20 ml) at 40 °C. Colorless crystals are obtained (2.1 g) on cooling (0 °C).

Received: February 13, 1979 [Z 246a IE]
German version: Angew. Chem. *91*, 582 (1979)
Publication delayed at authors' request

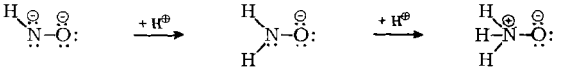
CAS Registry numbers:
(1), 70631-30-0; *(2)*, 70631-31-1; MoO_3, 1313-27-5; $[H_3NOH]Cl$, 5470-11-1; $[MeH_2NOH]Cl$, 4229-44-1

[1] *E. Lassner*, J. Less Common Met. *15*, 143 (1968); *E. Lassner, R. Püschel, H. Schedle, ibid. 15*, 151 (1968); *E. Lassner*, Talanta *19*, 1121 (1972).
[2] *H. Yaguchi, T. Kajiwara*, Jpn. Analyst *14*, 785 (1965).
[3] *S. Sarkar, A. Müller*, Angew. Chem. *89*, 189 (1977); Angew. Chem. Int. Ed. Engl. *16*, 183 (1977); Z. Naturforsch. *B 33*, 1053 (1978).
[4] *(1)* forms monoclinic crystals, space group C_c^4-Cc, $a = 911.6(1)$, $b = 1678.0(5)$, $c = 1059.2(1)$ pm, $\beta = 117.08(2)°$, $Z = 4$. Refinement with the structure factors of 2744 observed independent reflections $\{I > 3.0\sigma(I)\}$ with anisotropic temperature factors converged to an unweighted R value of 3.7%. The positions of the H atoms were not determined.
[5] *K. Wieghardt, U. Quilitzsch, B. Nuber, J. Weiss*, Angew. Chem. *90*, 381 (1978); Angew. Chem. Int. Ed. Engl. *17*, 351 (1978); *K. Wieghardt, U. Quilitzsch*, Z. Anorg. Allg. Chem., in press.
[6] *(2)* forms monoclinic crystals, space group C_{2h}^5-$P2_1/a$, $a = 637.3(1)$, $b = 1174.7(4)$, $c = 900.5(2)$ pm, $\beta = 92.47(2)°$, $Z = 4$. Refinement with the structure factors of 1251 independent reflections with anisotropic temperature factors coverged to an unweighted R value of 6.3%. The positions of the H atoms were not determined.

Synthesis of a Hydroxylamido(2−)-*O,N*-(nitrosyl)molybdenum Complex

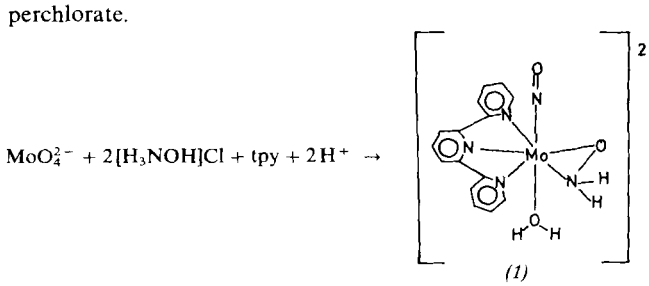
By *Karl Wieghardt* and *Wolfgang Holzbach*[*]

Transition metal complexes containing a negatively charged *O,N*-coordinated hydroxylamido ligand have recently been described by our group[1] and by other workers[2]. A uranium(VI) complex with a neutral *O*-coordinated azane oxide ligand is also known[3]. We have now accomplished the first stabilization of a doubly negatively charged hydroxylamido ligand in a nitrosylmolybdenum complex[4].



Hydroxylamide(2−) Hydroxylamide(1−) Azane oxide

Reaction of Mo^{VI} oxoanions with an excess of hydroxylamine in the presence of 2,2':6',2''-terpyridine (tpy) gives the yellow diamagnetic cation *(1)* which was isolated as the perchlorate.



(1)

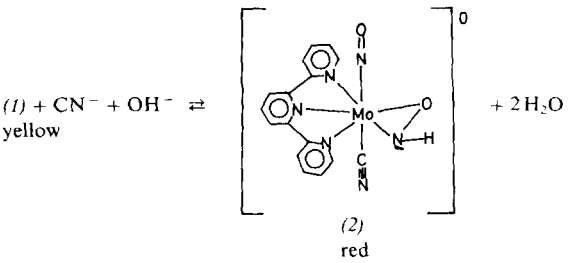
$+ 2Cl^- + 3H_2O$

The course of reaction can be interpreted as an intramolecular redox process[5]. We propose a distorted pentagonal bipyramidal environment for the Mo^{IV} center in *(1)* with one coordinated H_2O molecule[1,5]. The principal IR data are compiled in Table 1.

Table 1. IR data of the new complexes *(1)* and *(2)* (KBr discs, cm^{-1}).

(1): ν(O H): 3450 (b); ν(N H): 3220, 3030; ν(N O): 1695
ν(O D): 2570 (b); ν(N D): 2420, 2250; ν((N O): 1695
(2): ν(N H) or ν(C—H): 3080; ν(N O): 1630; ν(C N): 2138

(1) reacts with cyanide in aqueous solution at 70 °C to give the dark red neutral complex *(2)*. Treatment of *(2)* with 0.5 M perchloric acid quantitatively regenerates *(1)*.



(1) + CN^- + OH^- ⇄ yellow

(2)
red

The composition of the diamagnetic compound *(2)* has been confirmed by elemental analysis and the IR spectrum (Table 1)[6].

Procedure

A solution of $[H_3NOH]_2SO_4$ (4.10 g, 25 mmol) in H_2O (10 ml) is added at 75 °C to a solution of MoO_3 (0.30 g, 2 mmol) in 0.5 M NaOH (10 ml). 2,2':6',2''-Terpyridine (0.48 g, 2 mmol) is dissolved in the clear yellow solution; the pH is adjusted to 1 with conc. $HClO_4$, and 1 M $NaClO_4$ solution (5 ml) is added. The analytically pure crystals of $[(1)\cdot(ClO_4)_2\cdot 2H_2O]$ obtained on cooling are filtered off, washed with ethanol and ether, and dried in the air; yield 1.2 g (93%).

$[(1)\cdot(ClO_4)_2\cdot 2H_2O]$ (1.0 g, 1.6 mmol) is dissolved with stirring at 70 °C in water (45 ml). On addition of NaCN (2.7 g, 55 mmol) in H_2O (5 ml) a fine pale yellow precipitate appears, which turns into dark red crystals within 3 min. The crystals are filtered off, washed with ethanol and ether, and dried *in vacuo* over P_2O_5; yield 0.6 g (89%).

Received: April 5, 1979 [Z 246b IE]
German version: Angew. Chem. *91*, 583 (1979)

[1] *K. Wieghardt, U. Quilitzsch, B. Nuber, J. Weiss*, Angew. Chem. *90*, 381 (1978); Angew. Chem. Int. Ed. Engl. *17*, 351 (1978); *U. Quilitzsch, K. Wieghardt*, Z. Naturforsch. *B 34*, 640 (1979).
[2] *H. W. W. Adrian, A. van Tets*, Acta Crystallogr. *B 34*, 88, 2632 (1978).
[3] *H. W. W. Adrian, A. van Tets*, Acta Crystallogr. *B 35*, 153 (1979).
[4] Molybdenum(VI) complexes with *N*-phenylhydroxylamido(2−)-*O,N*-ligands are known: *L. S. Liebeskind, K. B. Sharpless, R. D. Wilson, J. A. Ibers*, J. Am. Chem. Soc. *100*, 7061 (1978); *D. A. Muccigrosso, S. E. Jacobson, P. A. Apgar, F. Mares, ibid. 100*, 7063 (1978).
[5] Cf. *K. Wieghardt, W. Holzbach, J. Weiss, B. Nuber, B. Prikner*, Angew. Chem. *91*, 582 (1979); Angew. Chem. Int. Ed. Engl. *18*, 548 (1979).
[6] An X-ray analysis of *(2)* confirms the proposed structure: *J. Weiss, B. Nuber*, unpublished results.

Simple Route to Li- or Zn-Metalated η^5-Cyclopentadienyliron-Olefin Complexes

By *Klaus Jonas* and *Ludwig Schieferstein*[*]

The method developed by us[1] for the synthesis of reactive transition metal-olefin and alkali metal-transition metal-ole-

[*] Prof. Dr. K. Wieghardt, Dipl.-Chem. W. Holzbach
Institut für Anorganische Chemie der Universität
Callinstrasse 9, D-3000 Hannover 1 (Germany)

[*] Dr. K. Jonas, Dr. L. Schieferstein
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr (Germany)

fin complexes is based upon the reaction of metallocenes with alkali metals in the presence of olefins. Starting from ferrocene the first alkali metal-olefin complexes of iron could be prepared[1a,2], which in turn are suitable precursors for the synthesis of numerous novel organoiron compounds[2].

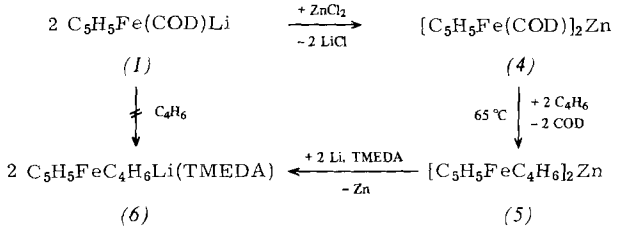
Reaction of ferrocene at low temperature (−60 to −40 °C) in dimethoxyethane (DME) or tetrahydrofuran (THF) with lithium sand and 1,5-cyclooctadiene (COD) or ethylene leads, *via* exchange of *only one* C_5H_5-ligand, to formation of the hitherto unknown iron complexes $C_5H_5Fe(COD)Li(DME)$ *(1a)* or, after addition of *N,N,N',N'*-tetramethylethylenediamine (TMEDA), to crystalline $C_5H_5Fe(COD)Li(TMEDA)$ *(1b)* or $C_5H_5Fe(C_2H_4)_2Li(TMEDA)$ *(2)* in high yields (*ca.* 80%).

$$(C_5H_5)_2Fe + 2\,Li + COD \xrightarrow[-60\text{ to }-40\,^\circ C]{\text{THF or DME}} C_5H_5Fe(COD)Li + C_5H_5Li$$
(1)

The ^{13}C-NMR spectrum[3] of *(1b)* in [D_8]toluene at −60 to −20 °C shows besides the TMEDA signals ($\delta = 56$, t; 46, q) and the C_5H_5-signal ($\delta = 75.5$, d) also two signals each for the olefinic C-atoms ($\delta = 52.5$ and 41.6, both d) and methylene C-atoms ($\delta = 35.5$ and 32.9, both t) of the COD ligand; at +80 °C only one resonance is observed for each of the two groups of signals, namely at $\delta = 47.9$ (d) and 34.1 (t). As in the case of the other alkali metal-transition metal-olefin complexes, *e.g.* $(COD)_2CoLi(THF)_2$[1b], we ascribe this equilibration of the COD signals to the increasing mobility of the cationic Li-atom bound to the anionic $C_5H_5Fe(COD)$ core in the ion pair *(1b)* with increasing temperature. In the more strongly solvating THF, *(1b)* shows a relatively high equivalent conductivity of $\Lambda = 8.7$ cm$^2/\Omega \cdot$mol (0.25 M at −30 °C).

The π-bonded olefin ligands in *(1)* and *(2)* are quantitatively replaced by carbon monoxide (1 atm) even at −78 °C: $C_5H_5Fe(CO)_2Li$ *(3)* is obtained [isolated as crystalline $C_5H_5Fe(CO)_2Li(TMEDA)$]. The corresponding sodium compound $C_5H_5Fe(CO)_2Na$ is already well-known in solution[4].

The complexes *(1)* and *(2)* can be used as precursors for preparation of the hitherto unknown polynuclear complexes *(4)*, *(5)*, and *(6)* having olefin ligands bound to iron atoms. They are obtained from *(1)* and *(2)* and metal halides such as $ZnCl_2$ or $CdCl_2$.



Replacement of the cyclooctadiene in the zinc derivative *(4)* by butadiene leads to the trinuclear complex *(5)*, which can be converted by reaction with lithium into *(6)* and metallic zinc. Under mild reaction conditions *(6)* cannot be obtained directly from *(1)* and butadiene. Reaction of *(1)* with trityl chloride affords η^5-cyclopentadienyl(η^4-1,5-cyclooctadiene)iron *(7)* in high yields (70%), which, in contrast to the dimeric $[C_5H_5Fe(CO)_2]_2$[4a,5], is obtained as the monomer with an unpaired electron.

$$(1) + (C_6H_5)_3CCl \xrightarrow[-LiCl]{} C_5H_5FeCOD\cdot + (C_6H_5)_3C\cdot$$
(7)

The iron(I) compound *(7)*, which is stable for several hours at room temperature, exhibits a wide range of interesting reactions; its structure, like that of *(2)* and *(5)*, was elucidated by X-ray crystallography[6].

Procedure

Ferrocene (50.0 g, 269 mmol) is stirred in THF (350 ml) and COD (100 ml) with Li-sand (5.2 g, 755 mmol) for 5–6 h at −50 °C. The reaction mixture is then allowed to warm to room temperature, filtered free of excess lithium, and the filtrate concentrated to 250 ml by evaporation *in vacuo*. Addition of ether (600 ml) and TMEDA (150 ml) leads to precipitation of crystalline *(1b)* (71.2 g, 75%).

Received: March 1, 1979 [Z 249a IE]
German version: Angew. Chem. *91*, 590 (1979)

CAS Registry numbers:
(1a), 69393-65-3; *(1b)*, 69393-63-1; *(2)*, 70713-55-2; *(3)*, 33361-37-4; *(4)*, 70713-56-3; *(5)*, 70713-57-4; *(6)*, 70713-59-6; *(7)*, 70713-60-9; $(C_5H_5)_2Fe$, 102-54-5

[1] a) *K. Jonas*, DOS 2724111 (1978), Studiengesellschaft Kohle mbH; b) *K. Jonas, R. Mynott, C. Krüger, J. C. Sekutowski, Y.-H. Tsay*, Angew. Chem. *88*, 808 (1976); Angew. Chem. Int. Ed. Engl. *15*, 767 (1976).

[2] *L. Schieferstein*, Dissertation, Universität Bochum 1978.

[3] We thank Dr. *R. Mynott* for recording and interpreting the ^{13}C-NMR spectra (25.2 MHz, shifts rel. to TMS, multiplicities determined by off-resonance or gated decoupling).

[4] a) *E. O. Fischer, R. Böttcher*, Z. Naturforsch. *B 10*, 600 (1955); b) *T. S. Piper, G. Wilkinson*, J. Inorg. Nucl. Chem. *3*, 104 (1956).

[5] *F. A. Cotton, G. Wilkinson*, Z. Naturforsch. *B 9*, 453 (1954); *O. S. Mills*, Acta Crystallogr. *11*, 620 (1958); *R. D. Fischer, A. Vogler, K. Noack*, J. Organomet. Chem. *7*, 135 (1967).

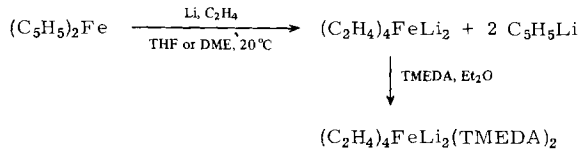
[6] *C. Krüger et al.*, unpublished work.

Tetrakis(ethylene)irondilithium and Bis(η^4-1,5-cyclooctadiene)irondilithium

By *Klaus Jonas, Ludwig Schieferstein, Carl Krüger*, and *Yi-Hung Tsay*[*]

Recently we reported the alkali metal-transition metal-ethylene complexes $(C_2H_4)_3NiLi_2$[1] and $(C_2H_4)_4CoK$[2a,3]. We have now been able to synthesize the isoelectronic iron compound $(C_2H_4)_4FeLi_2$[2a,4]. As in the case of the more electron-rich metallocenes[2] it was possible to replace systematically both C_5H_5-ligands in ferrocene *via* a similar route.

Reaction of ferrocene in tetrahydrofuran (THF) or dimethoxyethane (DME) at room temperature under slightly increased ethylene pressure (≈ 5 atm) with an excess of lithium sand and subsequent addition of a mixture of diethyl ether and *N,N,N',N'*-tetramethylethylenediamine (TMEDA) to the filtered reaction solution leads on cooling (−30 °C) to crystallization of the yellow-green colored complex $(C_2H_4)_4FeLi_2(TMEDA)_2$ *(1)* (45% yield).



[*] Dr. K. Jonas, Dr. L. Schieferstein, Priv.-Doz. Dr. C. Krüger [**], Dr. Y.-H. Tsay [**]
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr (Germany)

[**] X-ray structure analysis.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0550 $ 02.50/0

(1) reacts with acetic acid and ethylenebis(diphenylphosphane) (diphos) to give $C_2H_4Fe(diphos)_2$[5] according to:

$$(1) + 2\,\text{diphos} + 2\,CH_3COOH \rightarrow C_2H_4Fe(\text{diphos})_2 + 2C_2H_4 + C_2H_6 + 2\,CH_3COOLi$$

In the presence of stoichiometric amounts of alcohol or $ZnCl_2$, *(1)* exhibits the well-known activity of iron(0) catalysts[6] towards butadiene.

At −78 °C, *(1)* reacts with carbon monoxide (1 atm) with uptake of four equivalents of CO and liberation of four equivalents of C_4H_4. Reaction of *(1)* with 1,5-cyclooctadiene (COD) at 40—70 °C affords $(COD)_2FeLi_2$ [isolated as crystalline *(2a)* or *(2b)*],

$$(1) + 2\,\text{COD} \xrightarrow{40\text{–}70\,^\circ C} (COD)_2FeLi_2 + 4\,C_2H_4$$

$$(COD)_2FeLi_2 \xrightarrow{\text{DME}} (COD)_2FeLi_2(DME)_2 \quad (2a)$$

$$(COD)_2FeLi_2 \xrightarrow{\text{TMEDA}} (COD)_2FeLi_2(TMEDA)_2 \quad (2b)$$

thus completing the series of isoelectronic transition metal-cyclooctadiene complexes of the 3d elements of subgroup 8—namely $(COD)_2Ni$[7], $(COD)_2CoLi$[2] and $(COD)_2CoK$[2a,3], $(COD)_2FeLi_2$.

The X-ray structure analysis[8] of *(1)* shows the central Fe atom in a distorted octahedral environment with four equatorial C_2H_4 ligands and two Li atoms in the apical positions. The iron-olefin moiety has approximately the geometry expected for d^{10} systems with ethylene ligands[9]. A twofold crystallographic axis runs through the iron atom and bisects the C1 C1′ vector. Short Li C bond lengths (Li C2: 2.174, Li C3′: 2.215 Å), as in $(COD)_2CoLi(THF)_2$[2b], indicate strong iron-pair interactions between the tetrahedrally surrounded Li atom and the olefin C-atoms. The Li Fe distances are 2.619 Å.

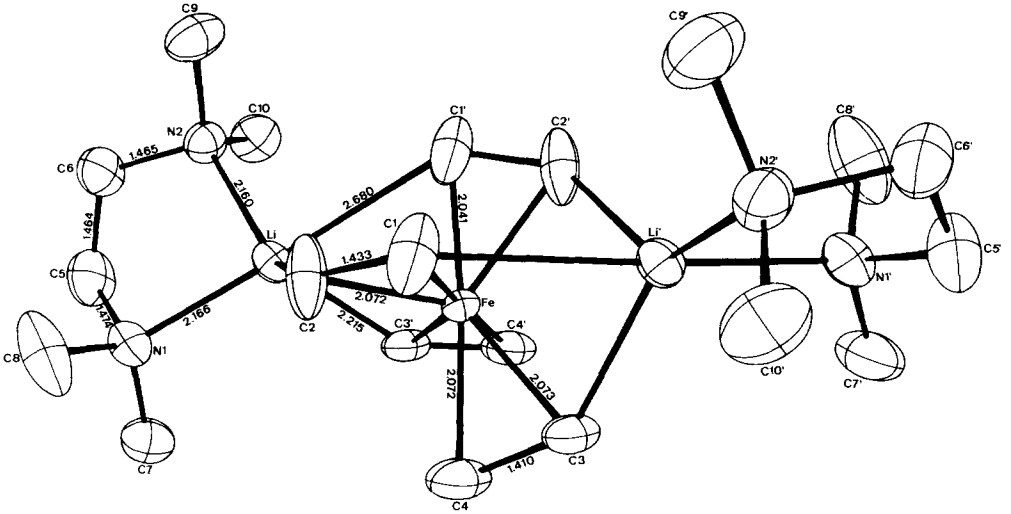


Fig. 1. Structure of $(C_2H_4)_4FeLi_2(TMEDA)_2$ *(1)* in the crystal; bond lengths in Å.

The method of reductive C_5H_5-detachment by means of alkali metal can also be used in the case of other η^5-cyclopentadienyl-transition metal compounds. It has also proved to be a useful method in the case of complexing agents other than olefins—*e.g.*, with phosphanes or molecular nitrogen.

Received: March 1, 1979 [Z 249b IE]
German version: Angew. Chem. *91*, 590 (1979)

[1] *K. Jonas*, Angew. Chem. *87*, 809 (1975); Angew. Chem. Int. Ed. Engl. *14*, 752 (1975); *K. R. Pörschke*, Dissertation, Universität Bochum 1975.
[2] a) *K. Jonas*, DOS 2724111 (1978), Studiengesellschaft Kohle mbH; b) *K. Jonas, R. Mynott, C. Krüger, J. C. Sekutowski, Y.-H. Tsay*, Angew. Chem. *88*, 808 (1976); Angew. Chem. Int. Ed. Engl. *15*, 767 (1976).
[3] *E. Deffense, K. Jonas*, unpublished work.
[4] *L. Schieferstein*, Dissertation, Universität Bochum 1978.
[5] *G. Hata, H. Kondo, A. Miyake*, J. Am. Chem. Soc. *90*, 2278 (1968).
[6] *M. Hidai, Y. Uchida, A. Misono*, Bull. Chem. Soc. Jpn. *38*, 1243 (1965); *A. Carbonaro, A. Greco, G. Dall'Asta*, Tetrahedron Lett. *1967*, 2037.
[7] *B. Bogdanović, M. Kröner, G. Wilke*, Justus Liebigs Ann. Chem. *699*, 1 (1966).
[8] Crystal data: $a = 12.279(1)$, $b = 13.069(1)$, $c = 16.336(2)$ (all values in 10^{-10} m), space group Pbcn, $Z = 4$, 2965 reflections (MoK_α) with 1477 counted as unobserved (2σ), $R = 0.078$.
[9] *N. Rösch, R. Hoffmann*, Inorg. Chem. *13*, 2656 (1974).

Structure and Reactivity of the Orthocarbonic and Orthosilicic Acid Esters of Pyrocatechol

By *Heinrich Meyer* and *Günter Nagorsen*[*]

The observation that glassy bis(*o*-phenylenedioxy)silane *(1)* and other ring-strained orthosilicic acid esters are capable of being polymerized even in the solid state[1] urged us to investigate the structure of *(1)* and the corresponding derivative of orthocarbonic acid, 2,2′-spirobi-1,3-benzodioxole *(2)*.

Zuckerman[2] believed that he had prepared monomeric *(1)*; however, the product obtained by him could very well have been a mixture of oligomers. Polymeric *(1)* is readily obtained by the following reaction:

$$2\,C_6H_4(OH)_2 + SiCl_4 \rightarrow 1/x[(C_6H_4O_2)_2Si]_x + 4\,HCl$$

Complete depolymerization takes place on transition into the gas phase—no signals were observed above the molecular peak $m/e = 244$ in the mass spectrum. From the gas phase, we were able to grow clear and colorless single crystals of monomeric *(1)* which are very sensitive to moisture and have a sharp melting point of 116 °C. We obtained monomeric—but X-ray crystallographically amorphous—*(1)* by a procedure resembling that described by *Allcock et al.*[3].

[*] Dr. H. Meyer, Dr. G. Nagorsen
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

For comparison, we prepared the orthocarbonic acid ester *(2)* as described in the literature[4]. X-ray crystallographic investigation on single crystals surprisingly showed that *(1)* and *(2)* do not crystallize isotypically.

In the structure analysis (automatic four-circle diffractometer, Siemens-AED) of *(2)* 220 of 872 measured symmetry-independent reflections could be phased by direct methods of sign determination. The positions of the hydrogen atoms were determined by difference Fourier synthesis. With anisotropic temperature factors for the carbon and oxygen atoms the structure was refined to an R_w value = 4.8%[5a].

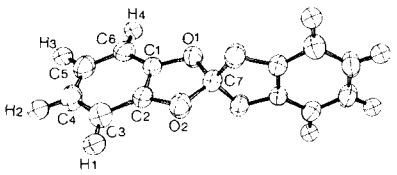


Fig. 1. Structure of the orthocarbonic acid ester *(2)*. Crystallographic data: space group Pccn; $a = 5.342$, $b = 11.496$, $c = 16.962$ Å; $\rho_{exp} = 1.48$, $\rho_{calc} = 1.46$ g/cm^3; $Z = 4$; $V = 1041.57$ Å^3.

Bond lengths [Å] and angles [°]										
C1	C2	1.366	C6	C1		1.355	O1	C1	C2	108.7
C1	C6	1.355	C6	H4		1.093	O2	C2	C1	108.8
C1	O1	1.370	C7	O1		1.396	O1	C1	C6	128.4
C2	C3	1.359	C7	O2		1.380	O2	C2	C3	128.9
C2	O2	1.378	O1	O2		2.250	C1	C2	C3	122.3
C3	C4	1.385	O1	O1′		2.285	C2	C1	C6	122.9
C3	H1	1.120	O1	C7	O2	108.3	C1	C6	C5	116.1
C4	C5	1.379	O1	C7	O1′	109.8	C2	C3	C4	115.5
C4	H2	1.012	O2	C7	O2′	111.7	C3	C4	C5	122.1
C5	C6	1.381	C7	O1	C1	107.0	C4	C5	C6	121.1
C5	H3	1.060	C7	O2	C2	107.0				

As can be seen from Figure 1 the bonding arrangement at the spiro carbon atom C7 corresponds to a very slightly distorted tetrahedron; the ring strain of the dioxole rings is evidently accommodated by the whole molecule, the valence angles at the oxygen atoms and at C1 and C2 apparently being influenced the most.

The crystal growth of the homologous orthosilicic acid ester *(1)* was extremely difficult to reproduce, in the majority of experiments only glassy products were obtained; this difficulty along with the sensitivity of the single crystals has so far thwarted satisfactorily accurate determination of the intensities of a greater number of reflections. Precession and Weissenberg photographs led to the space group $P2_1/c$ (monoclinic) with the cell data $a = 10.56$, $b = 5.60$, $c = 10.96$ Å, $\beta = 122°$, $V = 550$ Å^3. The density of the substance could not be determined, but it follows from a comparison of the volumes of the unit cells of *(1)* and *(2)* that Z must be equal to 2, since both molecules ought to have approximately the same spatial requirements. If there are only two silicon atoms in the unit cell they must be located on a special centrosymmetric equivalent position. This, however, would mean that *(1)* must be planar, at least in the solid state. Evidence for the centrosymmetric equivalent position is based on a few unobserved reflections ($0k0 \neq 2n$) for the space group determination. We consider the different space groups of *(1)* and *(2)* to be further evidence supporting the planar structure of the silicon compound—it is highly unlikely that replacement of the almost completely shielded central spiro atom C7 by Si alone causes alteration of the crystal lattice.

These conclusions are confirmed by EH calculations[5b], which for *(1)* give only slight preference for the tetrahedral arrangement (6.4 kcal/mol, using standard bond lengths) over the planar arrangement (cf. Fig. 2). A consideration of Si 3d-orbitals and experimentally determined bond lengths from the anion $[(C_6H_4O_2)_3Si]^{2-}$ (the average Si–O bond length here is 1.770 Å[6]) indicated only slight divergence in the energy differences.

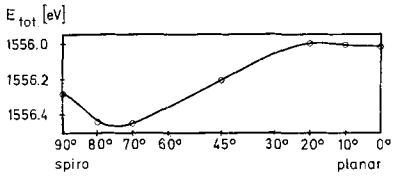


Fig. 2. Change in total energy for the "spiro- planar" transition of bis(*o*-phenylenedioxysilane) *(1)*.

In contrast, a considerable energy difference (104.5 kcal/mol) is calculated between the spirocyclic and planar orthocarbonic acid ester *(2)*.

On the other hand, there is a striking similarity in the energy level diagrams for the tetrahedral carbon and silicon compounds, the HOMO-LUMO difference in the former is only about 6 kcal/mol greater than in the latter, giving no indication of the highly reactive nature of the silicon compound, which not only forms adducts of high coordination number with donors[1b,7] but also reacts with itself. This becomes explainable only when one considers the frontier orbitals of planar *(1)* (cf. Fig. 3): At a slightly lesser HOMO-LUMO difference of about 1.7 kcal/mol, $\psi(43)$ with a distinct Si(p_z) component is obtained. In addition, a lowering of the energy gives $\psi(47)$ as a further orbital with a large eigenvalue coefficient for Si(p_z). If 3d-orbitals are taken into consideration then a further orbital, very similar to $\psi(47)$—but at higher level and having a very large Si(d_{z^2}) component—is obtained.

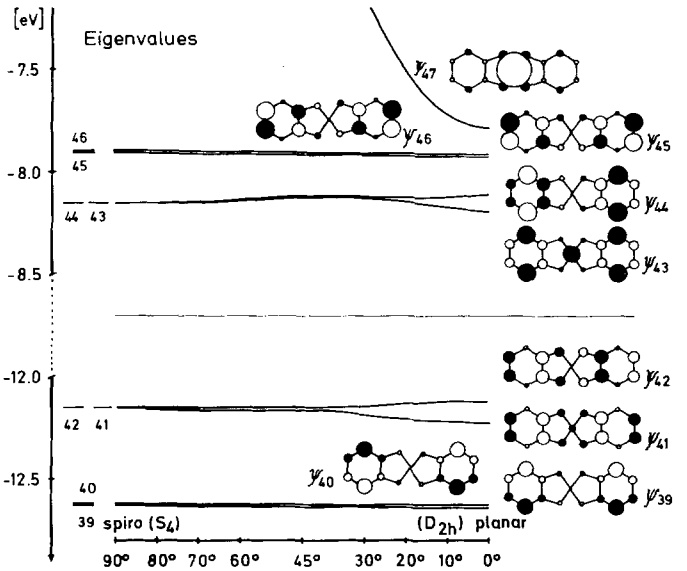


Fig. 3. Section from the correlation diagram for the spiro-to-planar transition of bis(*o*-phenylenedioxy)silane *(1)*.

It appears perfectly possible to stabilize the planar arrangements by sufficient interaction with donor orbitals. We assume this to take place in the crystal lattice, and the resulting coordination can thus also be regarded as pseudooctahedral. Each molecule in the crystal functions simultaneously as donor and acceptor.

From the total energy curve it can be seen that the spirocyclic compound ($\alpha = 90°$) does not lie at the energy minimum; this occurs at an angle $\alpha \approx 75°$ between the planes of the rings. According to the conservation of orbital symmetry

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0552 $ 02.50/0

the "spiro-planar" transition of *(1)* is thermally permissible. The π system of the benzene rings is important for easy planarization of the tetrahedral bonds on the silicon: calculations for bis(vinylenedioxy)silane favor the tetrahedral form by about double the energy difference (13.1 kcal); here also the HOMO-LUMO gap for the tetrahedral arrangement is about 4.8 kcal greater.

It is still unclear whether the ease of planarization and associated generation of low-lying acceptor orbitals is a widely applicable principle. Should this be so, then current ideas on the course of substitution reactions at silicon will have to be further reviewed. In our opinion an essential point is that our explanation of the reactivity of *(1)* without implication of Si-3d-orbitals is perfectly possible.

Calculations on the orthocarbonic acid esters *(2)* show that the small C7 O bond length restricts planarization; approximation of the four oxygen atoms, as in the square planar arrangement, is energetically strongly disfavored (on the problem of planar carbon compounds cf. [8]).

Solutions of monomeric *(1)* are not stable, oligomerization or polymerization takes place. This is true in particular for non-polar solvents, which favor association of the polar molecules. Solvents having good donor properties often form adducts. Dipolar or ambidentate solvents ought to form associates with *(1)* and render oligomerization difficult. In fact this reaction can be suppressed in nitromethane to such an extent that solutions are stable at $-15\,^{\circ}C$ for about a day, thus enabling molecular weight determinations to be carried out ($M_{obs}=243\pm3$, average of five measurements; $M_{calc}=244$[9]). The recording of ^{13}C- and ^{29}Si-NMR spectra is difficult because of sparing solubility and the oligomerization that takes place during prolonged measuring times, even at low temperatures.

Received: November 27, 1975
Supplemented: December 28, 1978 [Z 251a IE]
German version: Angew. Chem. *91*, 587 (1979)
Publication delayed at authors' request

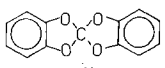
CAS Registry numbers:
(1), 181-88-4; *(2)*, 181-82-8

[1] a) *M. G. Woronkow, J. Romadam, I. B. Mascheika*, Z. Chem. *8*, 252 (1968); *M. G. Voronkov, V. P. Davydova, B. N. Dolgov*, Bull. Acad. Sci. USSR *1958*, 677; b) *H. Meyer*, Dissertation, Universität München 1971.
[2] *J. J. Zuckerman*, J. Chem. Soc. *1962*, 837.
[3] *H. R. Allcock, T. A. Nugent, L. A. Smeltz*, Synth. Inorg. Met.-Org. Chem. *2*, 97 (1972).
[4] *H. Cross, A. Rieche, E. Höft*, Chem. Ber. *94*, 544 (1961).
[5] a) Program XTAN, *G. M. Sheldrick*, Cambridge; b) we thank Dr. *J. Kroner* for his EH-program.
[6] *J. J. Flynn, F. P. Boer*, J. Am. Chem. Soc. *91*, 5756 (1969).
[7] *C. M. Silcox Yoder, J. J. Zuckerman*, Inorg. Chem. *6*, 163 (1967).
[8] *J. B. Collins, J. D. Dill, E. D. Jemmis, Y. Apeloig, P. v. R. Schleyer, R. Seeger, J. A. Pople*, J. Am. Chem. Soc. *98*, 5419 (1976); *T. Clark, P. v. R. Schleyer, J. A. Pople*, J. Chem. Soc. Chem. Commun. *1978*, 137. *E. V. Würthwein, P. v. R. Schleyer*, Angew. Chem. *91*, 588 (1979); Angew. Chem. Int. Ed. Engl. *18*, 553 (1979).
[9] *D. W. Schacht*, Diplomarbeit, Universität München 1978.

Planar Tetracoordinate Silicon[**]

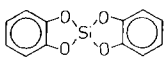
By *Ernst-Ulrich Würthwein* and *Paul von Ragué Schleyer*[*]

X-ray crystallographic investigations on the orthocarbonic *(1)* and orthosilicic *(2)* acid esters led *Meyer* and *Nagorsen*[1] to a startling conclusion. While the bond angles at the central carbon atom of *(1)* are essentially tetrahedral *(1a)*, the completely different space group adopted by *(2)* ($P2_1/c$, monoclinic) indicates a planar structure *(2b)*. *(2b)* may be regarded as the first example of planar tetracoordinate silicon.



(1)

(1a): perpendicular (D_{2d})
(1b): planar (D_{2h})



(2)

(2a): perpendicular (D_{2d})
(2b): planar (D_{2h})

Because of our continuing interest in non-tetrahedral four-coordination involving elements of the second and third periods[2], we have studied this problem theoretically by means of quantum mechanical calculations in order to clarify the electronic basis for the difference between *(1)* and *(2)*.

We began by examining CH_4 and SiH_4 in tetrahedral (T_d) and artificially constrained square planar (D_{4h}) geometries. Standard calculational methods[3] were employed (Table 1).

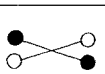
Table 1. Differences in total energies E (*ab initio*)/heats of formation ΔH_f^0 (MNDO) between perpendicular and planar structures (kcal/mol) [a].

	STO-3G	4-31 G	STO-3G*	MNDO
CH_4	240.0 [b, c]	168 [b]	—	140.7 [d]
SiH_4	152.2 [c]	—	114.1 [c]	82.2 [e]
CH_3OH	230.8 [f]	200 [b]	—	130.1 [g]
SiH_3OH	108.2 [h]	—	84.3 [i]	68.5 [j]
(1)	—	—	—	116.3 [k]
(2)	—	—	—	32.9 [l]
(3)	—	—	38.9 [m]	30.7 [n]

[a] All structures were fully optimized (ref. [3]); D_{4h} or D_{2h} symmetry was imposed on the planar species.
[b] Ref. [2a].
[c] Ref. [2b].
[d] $\Delta H^0_{perp} = -11.9$ kcal/mol; $\Delta H^0_{pl} = 128.8$ kcal/mol.
[e] $\Delta H^0_{perp} = 11.5$ kcal/mol; $\Delta H^0_{pl} = 93.7$ kcal/mol.
[f] $E_{perp} = -113.54598$ a.u.; $E_{pl} = -113.17811$ a.u.
[g] $\Delta H^0_{perp} = -57.4$ kcal/mol; $\Delta H^0_{pl} = 72.7$ kcal/mol.
[h] $E_{perp} = -361.77187$ a.u.; $E_{pl} = -361.59937$ a.u.
[i] $E_{perp} = -361.88011$ a.u.; $E_{pl} = -361.74579$ a.u.
[j] $\Delta H^0_{perp} = -65.2$ kcal/mol; $\Delta H^0_{pl} = 3.3$ kcal/mol.
[k] $\Delta H^0_{perp} = -97.2$ kcal/mol; $\Delta H^0_{pl} = 19.1$ kcal/mol.
[l] $\Delta H^0_{perp} = -211.9$ kcal/mol; $\Delta H^0_{pl} = -179.0$ kcal/mol.
[m] STO-3G*-single-point-calculation on fully optimized MNDO geometries.
$E_{perp} = -733.18633$ a.u.; $E_{pl} = -733.12430$ a.u.
[n] $\Delta H^0_{tetr} = -228.8$ kcal/mol; $\Delta H^0_{pl} = -198.1$ kcal/mol.

All theoretical levels show clearly that the tetrahedral-planar energy difference is much smaller with SiH_4 than with CH_4. Planar tetracoordination is fundamentally easier to realize with silicon than with carbon.

There is an even more important *qualitative* distinction between planar CH_4 and planar SiH_4: the preferred hybridization is different[2b]! The highest occupied orbital (HOMO) in CH_4 (a_{2u}) has pure p character; in SiH_4 this orbital is unoccupied (LUMO). The HOMO in SiH_4 (the LUMO in CH_4) is a sigma orbital (b_{1g}) with d-type symmetry. This orbital ordering is found even when no d-orbitals are included in the Si basis set (MNDO and STO-3G); inclusion of d-orbitals (STO-3G*), as expected, favors the planar forms even more[2b].

		
orbital symmetry	a_{2u}	b_{1g}
CH_4 (D_{4h})	HOMO	LUMO
SiH_4 (D_{4h})	LUMO	HOMO

[*] Dr. E.-U. Würthwein [+], Prof. Dr. P. v. R. Schleyer
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)
[+] Author to whom correspondence should be addressed.

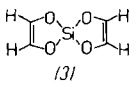
[**] This work was supported by the Fonds der Chemischen Industrie (Liebig-Stipendium to E.-U. W.) and benefited from discussions with Dr. *J. Chandrasekhar* and Dr. *T. Clark*.

This interchange of orbital ordering has fundamental consequences for the stabilization of planar structures: π-acceptor-σ-donor substituents (*e.g.* Li, Be, and B[2a]) preferentially stabilize planar tetracoordinate carbon, but silicon requires π-donor-σ-acceptor groups (*e.g.* F, OR and NR_2).

Model calculations on methanol H_3COH and silanol H_3SiOH illustrate these predictions: the effect of the OH group in stabilizing planar silanol is much greater than in planar methanol (Table 1). Additional electronegative, π-donor substituents should lower the energy difference between planar and tetrahedral forms of silicon compounds even more.

Since the large size of *(2)* precludes *ab initio* calculations, our investigation was carried out at the semiempirical MNDO[3b] level. Comparisons in Table 1 indicate that MNDO and STO-3G* *ab initio* trends are in good agreement. Although the perpendicular arrangement *(2a)* is still preferred, a drastic reduction in the planar-perpendicular energy difference (to 32.9 kcal/mol) is indicated by MNDO calculations on *(2)*.

This result was checked by examining the closely related model compound *(3)*. The MNDO difference is 30.6 kcal/mol; single point STO-3G* calculations on the MNDO geometries of planar *(3b)* and perpendicular *(3a)* gave $\Delta E = 38.9$ kcal/mol, thus confirming the semiempirical result. A planar structure for the orthocarbonic ester *(1b)* is out of the question. According to MNDO, the perpendicular form *(1a)* should be 116.3 kcal/mol more stable.

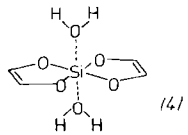


(3)

(3a): perpendicular (D_{2d})
(3b): planar (D_{2h})

Meyer and *Nagorsen*[1] suggest that the planar structure *(2b)* in the crystal was favored by additional intermolecular interactions of silicon with two oxygen atoms of neighboring molecules (pseudooctahedral coordination). This suggestion is supported by our model calculations on *(4)* which simulate the postulated coordination by placing water molecules above and below silicon as shown. The total energy of coordination to the water molecules in going from planar *(3b)* to *(4)* is 47.3 kcal/mol, 16.7 kcal/mol more than necessary to overcome the residual preference of *(3)* for the perpendicular geometry *(3a)* in the absence of such additional coordination. In *(4)* the MNDO Si O distances involving the water molecules are 1.94 Å in comparison with the 1.75 Å value for the four covalently bound oxygens[4].

Since we are dealing with a known substance[1], it would be exciting not only to ascertain the full crystal structure of *(2)* for comparison with our calculated geometries, but also to determine its conformation in solution as a function of solvent character. The barrier to planar inversion of *(2a)* may well be low enough for experimental measurements, *e.g.*, by determination of the rate of racemization of chiral analogs of *(2a)*.



(4)

We conclude that silicon is inherently better suited than carbon for the detection and observation of planar tetracoordinate structures. Classical compounds, such as the orthosilicic acid esters, should exhibit reduced energy differences between planar and tetrahedral forms, which may be small enough to permit experimental observation of planar inversion. The additional possibility of silicon six-fold coordination in the solid phase or in suitable solvents may render planar arrangements more stable than the tetrahedral.

Received: March 26, 1979 [Z 251b IE]
German version: Angew. Chem. *91*, 588 (1979)

[1] *H. Meyer, G. Nagorsen*, Angew. Chem. *91*, 587 (1978); Angew. Chem. Int. Ed. Engl. *18*, 551 (1979); we thank the authors for the communication of their results prior to publication.

[2] a) *J. B. Collins, J. D. Dill, E. D. Jemmis, Y. Apeloig, P. v. R. Schleyer, R. Seeger, J. A. Pople*, J. Am. Chem. Soc. *98*, 5419 (1976) and references cited therein. b) For detailed studies on non-tetrahedral structures of AH_4-molecules see: *M.-B. Krogh-Jespersen, J. Chandrasekhar, P. v. R. Schleyer, E.-U. Würthwein*, in preparation.

[3] a) *Ab initio* methods: All calculations were performed using the Gaussian 70 and Gaussian 76 series of programs (*W. J. Hehre, W. A. Lathan, R. Ditchfield, M. D. Newton, J. A. Pople*, program No. 236 from the Quantum Chemistry Program Exchange, Indiana Univ., Bloomington, Ind.; *J. S. Binkley, R. A. Whiteside, P. C. Hariharan, R. Seeger, J. A. Pople, W. J. Hehre, M. D. Newton*, program No. 368, *ibid.*); *W. J. Hehre, R. F. Stewart, J. A. Pople*, J. Chem. Phys. *51*, 2657 (1969) (STO-3G minimal basis set); *J. B. Collins, P. v. R. Schleyer, J. S. Binkley, J. A. Pople*, J. Chem. Phys. *64*, 5142 (1976) (STO-3G*, minimal basis set with inclusion of d-functions); *R. Ditchfield, W. J. Hehre, J. A. Pople*, J. Chem. Phys. *54*, 724 (1971) (4-31 G; split valence basis set). b) Semiempirical method (MNDO): *M. J. S. Dewar, W. Thiel*, J. Am. Chem. Soc. *99*, 4899, 4907 (1977); *M. J. S. Dewar, M. L. McKee, H. S. Rzepa, ibid. 100*, 3607 (1978).

[4] This comparison is not quite fair; *(2a)* might also be stabilized, if only slightly, by interaction with solvent oxygen.

Electronic Structure of μ-Methylene-Transition Metal Complexes[**]

By *Peter Hofmann*[*]

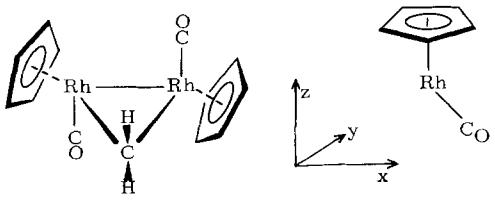
Apart from classical transition metal carbene complexes of type *(1)*, μ-methylene complexes containing M_2C (MM'C) structures such as *(2a)*—*(2d)* have been synthesized and their geometries analyzed[1]. They warrant theoretical and practical interest as intermediate members in the series cyclopropane (C_3 ring) ... metal-olefin complexes (MC_2 ring) ... trinuclear metal clusters (M_3 ring).



(1) *(2)*

Examples of molecules of general type *(2)* whose structures have been confirmed by X-ray methods

ML_n	X	
$(\eta^5\text{-}C_5H_5)Rh(CO)$	CH_2	*(2a)*
$(\eta^5\text{-}C_5H_5)Co(CO)$	CHCOOR	*(2b)*
$(\eta^5\text{-}C_5H_5)Mn(CO)_2$	CH_2	*(2c)*
$Fe(CO)_3$(olefin)	CHR	*(2d)*
$(\eta^5\text{-}C_5H_5)Rh(CO)$	CO	*(2e)*
$Fe(CO)_4$	$C{=}C(C_6H_5)_2$	*(2f)*
$(\eta^5\text{-}C_5H_5)Mn(CO)_2$	$C{=}CHC_6H_5$	*(2g)*
$(\eta^5\text{-}C_5H_5)Ir(CO)$	C_6H_4	*(2h)*



(3) *(4)*

[*] Priv.-Doz. Dr. P. Hofmann
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)

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

MO calculations[3] on the rhodium complex *(2a)*, whose geometry[2] as established by X-ray methods is shown in *(3)*, provide typical data regarding the electronic structure of such singly methylene-bridged compounds. A particularly simple description[4] of the bonding in *(2a)* can be constructed from the interaction of the MOs of one CH_2 group and two d^8-(η^5-C_5H_5)Rh(CO) sixteen electron fragments.

The valence orbitals of *(4)* (Fig. 1, left) can be readily interpreted in terms of the MOs already described[5] for a half-sandwich complex such as $CpRh(CO)_2$ and the perturbational consequences of the absence of a CO ligand: the disappearance of σ antibonding and the loss of π back bonding lead, with appropriate energetic modifications, to the HOMO 2a″ and LUMO 3a′ of *(4)* (both MOs hybridized towards the missing ligand) and to the d levels 2a′, 1a′, and 1a″ of CpRh(CO) separated energetically from the frontier orbitals[6a].

Two identical units *(4)* make up the partial skeleton *(5)* for bonding the μ-methylene group in *(2a)*. Calculations on *(5)* assuming a geometry like that found for the $Cp_2Rh_2(CO)_2$ moiety in the complex[6b], lead to the MO scheme shown in Figure 1 (right).

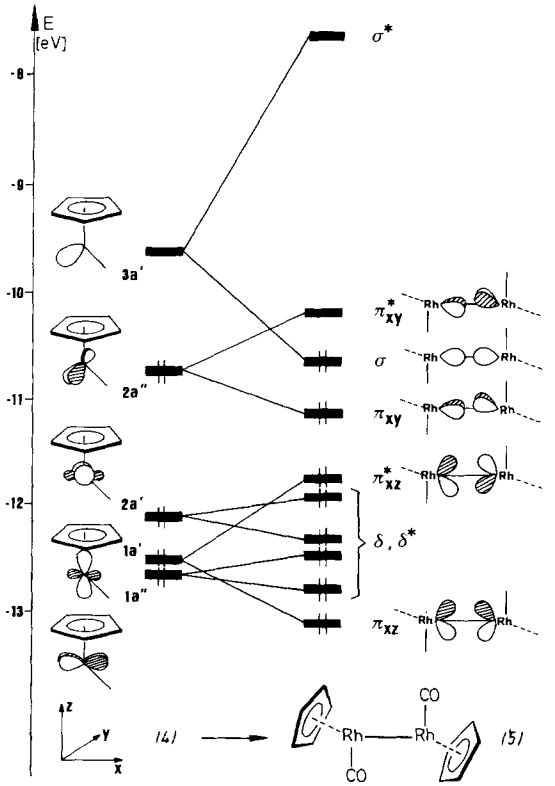


Fig. 1. Energy level scheme of fragment *(5)* as derived from the interaction of two sixteen-electron fragments *(4)*. Only the contributions to the wave function at the metal center are shown in the case of *(4)*, and only those in the Rh Rh region for *(5)* (taken from the corresponding contour diagrams).

Given a choice of axes suitable for *(5)*, the molecular orbital π^*_{xy} [which is π-antibonding in the *xy* plane] becomes the lowest acceptor function, and the bonding linear combination (σ) of two 3a′ orbitals of *(4)* emerges as the highest occupied orbital. Pronounced splitting is also caused by interaction of the two 1a′ functions so that the π^*_{xz} orbital, which is "orthogonal" to π^*_{xy}, appears at relatively high energy and the corresponding bonding combination π_{xz} is the lowest MO of the d group of *(5)*. Interaction involving 1a″ and 2a′ is much less extensive; the four resulting molecular orbitals are δ bonding or δ antibonding and do not play a significant role

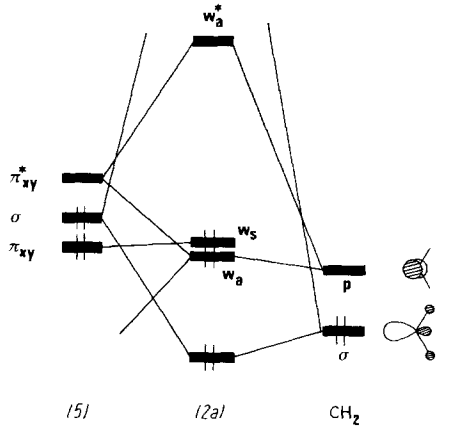


Fig. 2. Scheme for construction of MOs of *(2a)* from *(5)* and CH_2 (section).

here. In the d^8 case, the energy levels (Fig. 1) formally resemble those of a Rh Rh double bond.

The valence MOs of the CH_2 bridge, p and σ, acquire symmetrically suitable partners in the frontier orbitals π^*_{xy} and σ. Apart from the σ-type bonding between the methylene group and *(5)*, the qualitative interaction scheme (Fig. 2) demonstrates the existence of a situation corresponding exactly to the Walsh description of cyclopropane, derived on the basis of an ethylene and a methylene structural unit. The two highest occupied MOs (w_a and w_s) of the μ-CH_2-rhodium complex are accordingly regarded as an essentially unperturbed π_{xy} orbital of *(5)* (w_s) and as a bonding linear combination of π^*_{xy} with p of the CH_2 unit (w_a). The LUMO of the three-membered ring is the antibonding counterpart of w_a. Contour diagrams of w_a, w_s, and w^*_a in the plane of the three-membered ring (Fig. 3) clearly underline the relationship with the Walsh orbitals of a cyclopropane.

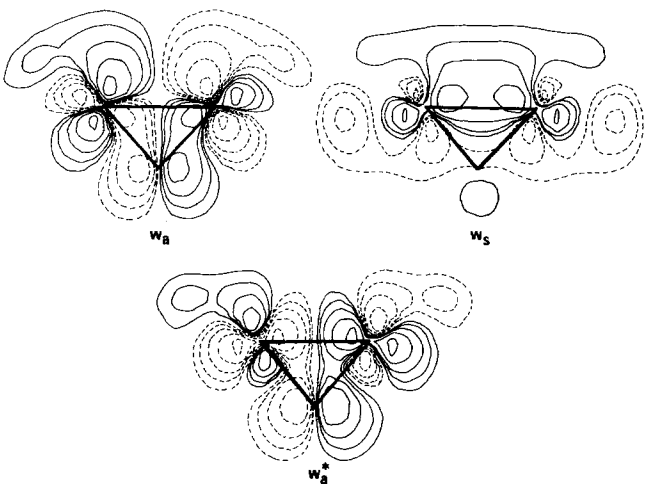


Fig. 3. Contour diagrams of the MOs of the three-membered ring w_a, w_s, w^*_a (values of wave functions: ±0.2, ±0.1, ±0.05, ±0.025, ±0.0125).

The w_a orbital appears slightly destabilized with respect to p, in spite of its bonding interaction with π^*_{xy}, because one of the δ* levels mixes in an antibonding manner with w_a and plays a role in determining its energy. Like π_{xy}, π^*_{xz} cannot avail itself of a symmetrically suitable orbital on the bonding ligand and remains essentially unaffected; π_{xz} experiences a small repulsive interaction with the low-lying π_{CH_2} orbital of the methylene group, giving rise to interesting consequences with regard to the H C H angle in such systems[7].

The most important result of the occupation of w_a is an electron transfer from the Rh Rh σ-bond into an orbital

containing a π^*_{xy} component and to the carbon atom. The formal metal-metal double bond in fragment *(5)* becomes a "single bond". In accord with NMR data, the C atom exhibits a far greater charge density than in complexes of type *(1)*[1a]. Electrophilic attack at the bridging carbon atom should take place in addition to reactions at the electron-rich rhodium centers[8]. "Carbene rotation" as in molecules *(1)*, *via* a geometry with the carbon in a planar ligand environment in the present case is clearly unattainable for energetic reasons: the π^*_{xy}/p interaction would be supplanted by the far weaker π_{xz}/p interaction and a very high energy occupied orbital with p character would result[9]. As in the situation known for cyclopropane, μ-methylene complexes can be expected to adopt preferred conformations of "single-faced" π-acceptor substituents ($CH_2^{\oplus}$, COR, ...) in which the stabilizing donor property of w_a on electron-deficient centers comes into operation[10].

This bonding situation is not limited to the specific case of *(2a)* but is valid for *(2b)*—*(2h)* in which the CpRh(CO) fragment is replaced by other isolobal units ML_n or the CH_2 group by other bridges[11]. Predictions concerning concomitant changes are possible. Thus it becomes understandable that an additional π* acceptor orbital of bridging ligands such as CO orthogonal to the plane of the three-membered ring should have hardly any effect on the overall geometry of *(2e)* relative to that of *(2a)*; the additional interaction with π_{xz} is small and weakens the metal-metal bond only slightly. A similar situation is encountered in *(2f)*—*(2h)*.

Further interesting consequences of this MO model come to mind in molecules of the general type *(2)* with regard to questions of reactivity, structure, and possible intramolecular dynamic processes[12].

Received: December 22, 1978;
revised: February 20, 1979 [Z 250 IE]
German version: Angew. Chem. *91*, 591 (1979)

[1] a) *W. A. Herrmann*, Angew. Chem. *90*, 855 (1978); Angew. Chem. Int. Ed. Engl. *17*, 800 (1978) and references cited therein.—b) μ-$CH_2[\eta^5$-$C_5H_4Me)Mn(CO)_2]_2$: *I. Bernal, M. Creswick, W. A. Herrmann*, unpublished; μ-$CH_2[(\eta^5$-$C_5H_5)Mn(CO)_2]_2$: *A. D. Redhouse, W. A. Herrmann*, unpublished; μ-$CR_2[(\eta^5$-$C_5H_5)Co(CO)]_2$: *M. Creswick, I. Bernal, W. A. Herrmann, I. Steffl*, Chem. Ber., in press; *W. A. Herrmann, I. Schweizer, M. Creswick, I. Bernal*, J. Organomet. Chem. *165*, C17 (1979).—c) *T. V. Ashworth, J. A. K. Howard, F. G. A. Stone*, J. Chem. Soc. Chem. Commun. *1979*, 42; *T. V. Ashworth, M. Berry, J. A. K. Howard, M. Laguna, F. G. A. Stone, ibid. 1979*, 43; *M. Green, A. Laguna, J. L. Spencer, F. G. A. Stone*, J. Chem. Soc. Dalton Trans. *1977*, 1010.—d) *R. Aumann, H. Wörmann, C. Krüger*, Angew. Chem. *88*, 640 (1976); Angew. Chem. Int. Ed. Engl. *15*, 609 (1976) [complex type *(2d)*].—e) *R. B. Calvert, J. R. Shapley*, J. Am. Chem. Soc. *99*, 5225 (1977); *R. B. Calvert, J. R. Shapley, A. J. Schultz, J. M. Williams, S. L. Suib, G. D. Stucky, ibid. 100*, 6240 (1978).

[2] *W. A. Herrmann, C. Krüger, R. Goddard, I. Bernal*, J. Organomet. Chem. *140*, 73 (1978); Angew. Chem. *89*, 342 (1977); Angew. Chem. Int. Ed. Engl. *16*, 334 (1977).

[3] Extended Hückel calculations: *R. Hoffmann*, J. Chem. Phys. *39*, 1397 (1963); parameters for Rh: *R. Summerville, R. Hoffmann*, J. Am. Chem. Soc. *98*, 7240 (1976); H_{ii} matrix elements: *J. A. Ammeter, H.-B. Bürgi, J. C. Thibeault, R. Hoffmann, ibid. 100*, 3686 (1978).

[4] For methodology cf. *H. Fujimoto, R. Hoffmann*, J. Phys. Chem. *78*, 1167 (1974); *T. A. Albright, R. Hoffmann, P. Hofmann*, J. Am. Chem. Soc. *99*, 7546 (1977).

[5] *P. Hofmann*, Angew. Chem. *89*, 551 (1977); Angew. Chem. Int. Ed. Engl. *16*, 536 (1977); *T. A. Albright, R. Hoffmann*, Chem. Ber. *111*, 1578 (1978).

[6] a) CpM(CO) and CpML sixteen-electron fragments are themselves interesting experimentally observed intermediates: *K. P. C. Vollhardt, J. E. Bercaw, R. G. Bergman*, J. Am. Chem. Soc. *97*, 4998 (1974); *W. S. Lee, H. Brintzinger*, J. Organomet. Chem. *127*, 87 (1977); *H. Werner, K. Leonhard*, Angew. Chem. *89*, 656 (1977); Angew. Chem. Int. Ed. Engl. *16*, 649 (1977). Their electronic structure, geometry, and bonding capacity will be reported elsewhere: *P. Hofmann*, to be published.—b) $Cp_2Rh_2(CO)_2$ is isoelectronic with the known species $Cp_2Co_2(CO)_2$, which contains two μ-CO bridges: *N. E. Schore, C. S. Ilenda, R. G. Bergman*, J. Am. Chem. Soc. *99*, 1781 (1977).

[7] The repulsive π_{xy}/π_{CH_2} interaction for various ML_n ML_n fragments will depend upon the H C H angle, which in turn determines the energy of the π_{CH_2} MO: *P. Hofmann*, to be published.

[8] Thus *(2d)* undergoes H/D exchange with CF_3COOD: *R. Aumann, H. Wörmann, C. Krüger*, Chem. Ber. *110*, 1442 (1977).

[9] However, calculations on *(2a)* show that the H C H plane may not be exactly perpendicular to the plane of the three-membered ring, as a consequence of the resulting better overlap of p with the π^*_{xy} MO, which (as indicated in Fig. 1) is not symmetrical with respect to the plane of the three-membered ring (C_2 symmetry).

[10] Cf. also clusters such as $[Co(CO)_3]_3C$ $CH_2^{\oplus}$: *R. Hoffmann, B. Schilling*, J. Am. Chem. Soc. *100*, 6274 (1978).

[11] *A. N. Nesmejanov, G. G. Aleksandrov, A. B. Antonova, K. N. Anisimov, N. E. Kolobova, Yu. T. Struchkov*, J. Organomet. Chem. *110*, C36 (1976); *O. S. Mills, A. D. Redhouse*, J. Chem. Soc. *A 1968*, 1282; *E. Keller, H. Vahrenkamp*, Z. Naturforsch. *B 33*, 537 (1978); *M. D. Rausch, R. G. Gastinger, S. A. Gardner, R. K. Brown, J. S. Wood*, J. Am. Chem. Soc. *99*, 7870 (1977).

[12] Interest attaches to barriers for CO exchange phenomena (cf. point made in ref. [1a]). In the ground state, two μ-CO groups are present in the anion $[Cp_2Rh_3(CO)_4]^-$ (CH_2 in *(2a)* replaced by the isolobal moiety $Rh(CO)_2$): *W. D. Jones, M. A. White, R. G. Bergman*, J. Am. Chem. Soc. *100*, 6770 (1978). The terminal CO ligands in *(2a)* do not exchange sites: *W. A. Herrmann*, personal communication.

Spectroscopic Identification of Polymethyl-Substituted 2,4-Cyclohexadienones[**]

By *Gerhard Quinkert, Gerd Dürner, Erna Kleiner, Erhard Haupt*, and *Dieter Leibfritz*[*]

Ultraviolet spectra should be used whenever one has to distinguish between 2,4- and 2,5-cyclohexadienones[1]. By and large it is accepted that close correlations of those spectra with structure are not possible within the class of linearly conjugated cyclohexadienones[2]. In actual fact there is a notable relationship, however, between the location of the maximum of the relatively strongly absorbing π*,π-band (in nm, alcoholic solution) and the number and position of additional methyl groups in 6-acetoxy-6-methyl-2,4-cyclohexadienones: If the absorption maximum of *(1a)* (298 nm) is ad-

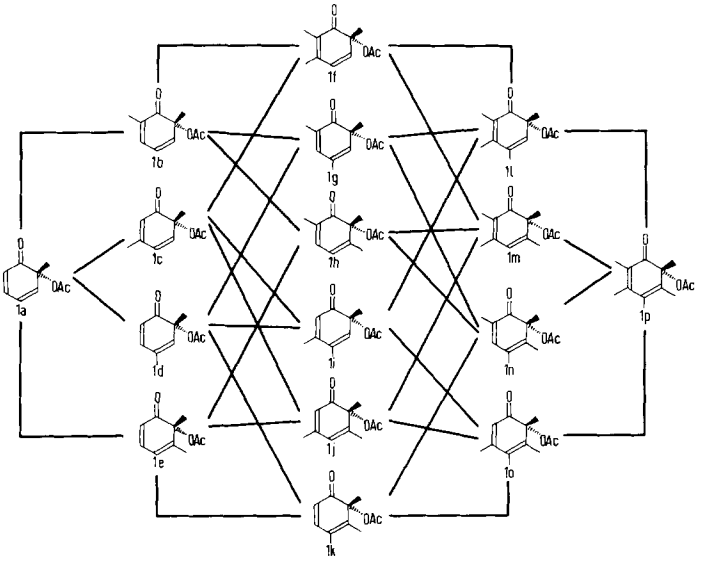


Fig. 1. Family tree of all 6-acetoxy-6-methyl-2,4-cyclohexadienones *(1)* having 0 to 4 methyl-substituents in positions 2 to 5 (the designations of compounds *(1a)* to *(1p)* deviate from those in the text in that they are not printed in italics).

[*] Prof. Dr. G. Quinkert, Dr. G. Dürner, Dr. E. Kleiner
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. D. Leibfritz, Dipl.-Chem. E. Haupt
Studienbereich 3 der Universität
D-2800 Bremen 33 (Germany)

[**] 19th Communication of Light-Induced Reactions. This work was supported by Deutsche Forschungsgemeinschaft, Fonds der Chemischen Industrie, and Hoechst AG. 18th Communication: *W.-D. Stohrer, G. Wiech, G. Quinkert*, Angew. Chem. *86*, 200 (1974); Angew. Chem. Int. Ed. Engl. *13*, 200 (1974).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0556 $ 02.50/0

opted as the basic value, each successive methyl substituent in positions 2, 3, 4 or 5 [according to *(1b)* to *(1e)*] generates increments of 6, 1, 7, and 9, respectively (cf. Table 1)[3].

The observed and calculated UV maxima are found to exhibit good agreement for those members of the family of methylated *o*-quinol acetates having 0 to 4 methyl substituents in positions 2 to 5 (see Fig. 1) whose constitution is known *a priori*[4] (Table 2: data in normal print) or whose constitution is to be determined[5] (Table 2: data in bold-face type).

Table 1. Non- and mono-methylated *o*-quinol acetates whose π^*,π absorption maxima in alcohol provide the basic value and positional increments (in nm) for more highly methylated derivatives.

Dienone	UV Maximum recorded
1a	298 nm
1b	304.5nm
1c	299 nm
1d	305.5nm
1e	307.5nm

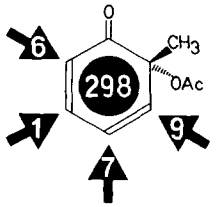


Table 2. π^*,π absorption maxima (in nm) calculated with the parameters found for *o*-quinol acetates (Table 1) and experimental values recorded in alcoholic solution.

Dienone	UV Maximum calculated	recorded
1f	**305**	**306**
1g	311	311
1h	**313**	**313**
1i	306	307
1j	308	308
1k	314	317
1l	**312**	**313**
1m	314	314
1n	**320**	**320**
1o	315	316
1p	321	321

The assignment receives further support from an analogous correlation of chemical shifts of ^{13}C-NMR-spectra with the number and position od additional methyl groups at unsaturated ring carbon atoms[6]. Table 3 shows the corresponding basic figures and positional increments for all the ring carbon atoms. Table 4 indicates, by means of a selection including the interesting cases *(1f)* and *(1h)*, as well as *(1l)* and *(1n)*, how reliably the individual members of the family studied can be recognized.

Table 3. Basic values and positional increments for calculation of ^{13}C-NMR shifts for methyl-substituted 6-acetoxy-6-methyl-2,4-cyclohexadienones *(1f)* to *(1p)*.

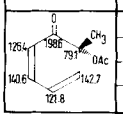
δ	Methyl position	Shift [ppm] of the ring carbon atoms on methyl substitution C-1	C-2	C-3	C-4	C-5	C-6
	C-2	+0.5	+7.7	-3.8	+0.1	-2.8	-0.1
	C-3	-0.9	-2.8	+12.0	+3.8	-1.2	-1.1
	C-4	-0.3	-0.7	+4.1	+8.1	-6.1	-0.8
	C-5	+1.1	-2.6	+1.2	-2.7	+10.1	+3.2

Table 4. ^{13}C-NMR shifts calculated with the parameters found for *o*-quinol acetates (Table 1) and experimental values recorded in $CDCl_3$.

Dienone \ Carbon		C-1	C-2	C-3	C-4	C-5	C-6
1f	calc.	198.2	131.3	148.8	125.7	138.7	77.9
	exp.	198.0	129.6	146.2	127.0	138.2	77.9
1g	calc.	198.8	133.5	140.9	130.0	133.8	78.2
	exp.	198.7	133.1	141.0	129.9	133.9	78.3
1h	calc.	200.2	131.5	138.0	119.2	150.0	82.2
	exp.	199.9	131.4	137.9	118.8	149.3	82.1
1j	calc.	198.8	121.0	153.8	122.9	151.6	81.2
	exp.	198.6	121.5	153.5	123.1	151.3	81.2
1l	calc.	197.9	130.6	152.9	133.8	132.6	77.1
	exp.	198.2	129.5	148.2	131.6	134.2	78.2
1n	calc.	199.9	130.8	142.1	127.3	143.9	81.4
	exp.	199.9	130.4	143.8	124.3	141.8	81.9

The values for *(1f)* and *(1h)* and for *(1l)* and *(1n)* differ sufficiently to permit unambiguous identification.

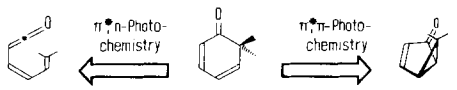
Received: March 21, 1979 [Z 248a IE]
German version: Angew. Chem. 91, 584 (1979)

[1] *J. Derkosch, K. Kalvegger*, Monatsh. Chem. *88*, 778 (1957).
[2] *A. J. Waring*, Adv. Alicyclic Chem. *1*, 188 (1966); Oesterr. Chem. Ztg. *68*, 232 (1967).
[3] If carbon of coordination number 4 is the central atom of both ligands attached to C-6 then the basic value is 301 and the positional increments amount to 7, 0, 10, and 16.
[4] 12 members of the family expressed by the graph of Fig. 1 leave no doubt as to their constitution, provided the constitution of each of the phenolic reactants is known. In the case of *(1a)*, *(1c)*, *(1d)*, *(1e)*, *(1i)*, *(1j)*, *(1h)*, *(1o)* only one of the *ortho* positions is substituted; the acetoxy ligand must enter that site if an *o*-quinol acetate is to be formed. In the case of *(1b)*, *(1g)*, *(1m)*, *(1p)*, the parent phenols exhibit homotopic methyl ligands at C-2 and C-6; the same *o*-quinol acetate always results regardless of which *o*-position the acetoxy ligand enters.
[5] 2,3,6-Trimethylphenol and 2,3,4,6-tetramethylphenol are each linked to a pair of constitutionally isomeric *o*-quinol acetates.
[6] It has already been demonstrated that chemical shifts of ^{13}C-NMR spectra are suitable for determining the number and position of methyl ligands in linearly conjugated cyclohexadienones: *R. Hollenstein, W. von Philipsborn*, Helv. Chim. Acta *55*, 2030 (1972).

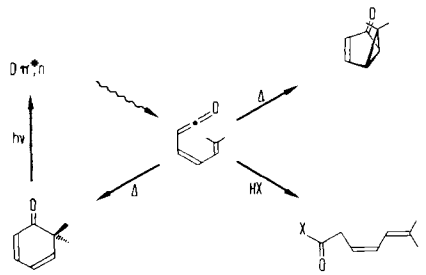
The Question of π^*,n- and π^*,π Selective Photochemistry of 2,4-Cyclohexadienones[**]

By *Gerhard Quinkert, Franz Cech, Erna Kleiner*, and *Dieter Rehm*[*]

Electro isomers[2] differ fundamentally in their structure, energy content, and chemical reactions. Linearly conjugated cyclohexadienones are often cited as relevant examples[3]. It is generally accepted that electro isomeric 2,4-cyclohexadienones having mainly π^*,n-character afford constitutionally isomeric dienylketenes[4] while electro isomeric 2,4-cyclohexadienones having predominantly π^*,π-character furnish constitutionally isomeric bicyclo[3.1.0]hex-3-en-2-ones[5]:



The $\pi^*\pi$ photochemistry of linearly conjugated cyclohexadienones originally postulated by *Griffiths* and *Hart*[5a], and initially accepted in our laboratory[2,4b,6], does not stand up to experimental scrutiny. In fact, the bicyclic ketones are also undoubtedly products of π^*,n photochemistry[7]. They arise by bicyclization of the dienylketene transients. This process principally competes with recyclization[8] and/or addition of protic nucleophiles:



[*] Prof. Dr. G. Quinkert, Dr. F. Cech, Dr. E. Kleiner, Prof. Dr. D. Rehm
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)

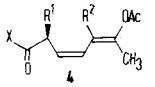
[**] 20th Communication on Light-Induced Reactions. This work was supported by Deutsche Forschungsgemeinschaft, Fonds der Chemischen Industrie, and Hoechst AG.—Part 19: ref. [1].

The relative ratio in which the dienylketene in a given case partitions itself between the three reaction channels depends upon the reaction medium and the pattern of substitution[9]. Table 1 selects prototypes from the family of methylated *o*-quinol acetates[1] whose photoproducts are leveled in methanol and are individualized in 2,2,2-trifluoroethanol (TFE).

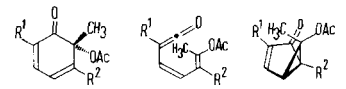
Table 1. The effects of methanol and TFE (leveling and individualizing, respectively) on photoreactions, shown for prototype reactants *(1a)*—*(1c)* (the formulas—not printed in italics as in the text—stand for racemates and for the ligand orientation at the individual CC double bonds or three-membered rings).

Reactant	Methanol		Trifluoroethanol	
	Product	Reaction	Product	Reaction
1a	4a	A	4d	A
1b	4b	A	3b	B+R
1c	4c	A	1c	R

A: Adduct formation
B: Bicyclization
R: Recyclization



4



1 2 3

a: $R^1 = R^2 = H$; b: $R^1 = CH_3$, $R^2 = H$; c: $R^1 = H$, $R^2 = CH_3$

a: $R^1 = R^2 = H$, $X = OCH_3$
b: $R^1 = CH_3$, $R^2 = H$, $X = OCH_3$
c: $R^1 = H$, $R^2 = CH_3$, $X = OCH_3$
d: $R^1 = R^2 = H$, $X = OCH_2CF_3$

Dienone *(1b)* demonstrates that the dienylketene transient *(2b)* can be clearly identified by flash spectroscopy in cyclohexane, methanol, or TFE.

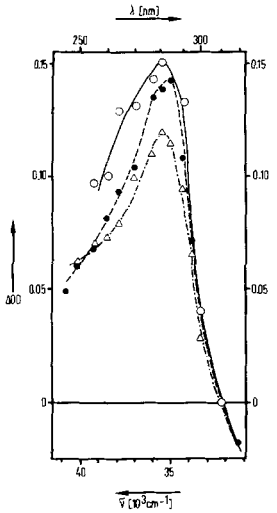


Fig. 1. Spectra of absorption differences of flash photolysis of *(1b)* at room temperature in cyclohexane (- -, 5.15×10^{-5} M), methanol (---, 9.03×10^{-6} M), and TFE ----, 3.32×10^{-5} M).

The transmission/time plot of Figure 2 shows that in TFE *(2a)* gives exclusively the 1,2-adduct *(4d)*, that *(2b)* partly recyclizes to *(1b)* and partly bicyclizes to *(3b)*, and that *(2c)* undergoes recyclization only, affording *(1c)*[9].

A chemical pathway which starts on the $\pi^*\pi$ energy surface is still open to *o*-quinol acetates. This is the light-induced dienone/phenol rearrangement leading to resorcinol monoacetates[4a]. Thus, *e.g.*, *(1b)* isomerizes to 3-acetoxy-2,6-dimethylphenol on direct irradiation in anhydrous ether.

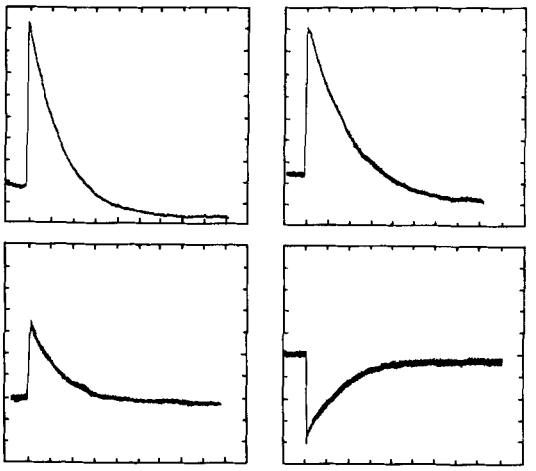


Fig. 2. Flash photolysis (*ca.* 300 J of electrical energy per flash) at room temperature in TFE.—Above left: *(1a)* [1.04×10^{-5} M, $\lambda = 280$ nm, $TB = 2$ s/scale unit, sens./scale unit. = 0.05 V, $Vo = 1.00$ V] reacts completely to *(4d)* *via (2a)* [*(4d)* absorbs less than *(1a)* at 280 nm] without any recyclization being observed [only *(1a)* effectively absorbs at 325 nm].—Above right: *(1b)* [3.32×10^{-5} M, $\lambda = 283$ nm, $TB = 1$ s/scale unit, sens./scale unit. = 0.10 V, $Vo = 3.17$ V] reacts *via (2b)* to give both *(3b)* [*(3b)* absorbs less than *(1b)* at 283 nm] and *(1b)* [only *(1b)* effectively absorbs at 370 nm]. Bottom left: The transient *(2c)* formed from *(1c)* [1.37×10^{-5} M, $\lambda = 250$ nm, $TB = 50$ ms/scale unit, sens./scale unit = 0.05 V, $Vo = 1.35$ V] exhibits neither adduct formation nor bicyclization [*(3c)* and the corresponding adduct would absorb more strongly than *(1c)* at 250 nm].—Bottom right: The transient *(2c)* formed from *(1c)* [1.37×10^{-5} M, $\lambda = 325$ nm, $TB = 50$ ms/scale unit, sens./scale unit = 0.05 V, $Vo = 2.53$ V] recyclizes completely to *(1c)* [only *(1c)* effectively absorbs at 325 nm].

This rearrangement also occurs on warming of *(1b)* in the presence of the "depot sensitizer" tetramethyl-1,2-dioxetane as well as on photosensitization. Since sensitizers are effective down to a triplet energy of 42 kcal/mol, only the energetically lowest-lying triplet spin isomer of the electro isomeric 2,4-cyclohexadienone with $\pi^*\pi$ character has to be taken into account (see footnote [27a] in ref. [2]).

Received: March 21, 1979 [Z 248b IE]
German version: Angew. Chem. *91*, 585 (1979)

[1] *G. Quinkert, G. Dürner, E. Kleiner, E. Haupt, D. Leibfritz*, Angew. Chem. *91*, 584 (1979); Angew. Chem. Int. Ed. Engl. *18*, 556 (1979).
[2] Cf. *G. Quinkert*, Angew. Chem. *87*, 851 (1975); Angew. Chem. Int. Ed. Engl. *14*, 790 (1975). We replace the clumsy expression "isomers which differ in their electronic structure" by the more expedient term "electro isomers".
[3] *J. A. Barltrop, J. D. Coyle*: Excited States in Organic Chemistry. Wiley. London 1975; *D. O. Cowan, R. L. Drisko*: Elements of Organic Photochemistry. Plenum Press, New York 1976; *W. M. Horspool*: Aspects of Organic Photochemistry. Academic Press, London 1976.
[4] a) *D. H. R. Barton, G. Quinkert*, J. Chem. Soc. *1960*, 1; b) *G. Quinkert*, Pure Appl. Chem. *33*, 285 (1973).
[5] a) *J. Griffiths, H. Hart*, J. Am. Chem. Soc. *90*, 5296 (1968); b) *H. Hart*, Pure Appl. Chem. *33*, 247 (1973).
[6] *G. Quinkert, B. Bronstert, K. R. Schmieder*, Angew. Chem. *84*, 638 (1972); Angew. Chem. Int. Ed. Engl. *11*, 637 (1972); *G. Quinkert, ibid. 84*, 1157 (1972) and *11*, 1072 (1972); respectively.
[7] Initially adopted by *Griffiths* and *Hart* [J. Am. Chem. Soc. *90*, 3297 (1968)], this view was soon extended to include the untenable π^*,π route [5a, b].
[8] *G. Quinkert, H. Englert, F. Cech, A. Stegk, E. Haupt, D. Leibfritz, D. Rehm*, Chem. Ber. *112*, 310 (1979).
[9] This can be justified by conformational analysis with due consideration of the rotamers of the various transients: *G. Quinkert et al.*, to be published.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0707-0558 $ 02.50/0

Phase Transfer Catalysis in Organic Chemistry. By *W. P. Weber* and *G. W. Gokel*. Springer Verlag, Berlin—Heidelberg—New York 1977. 280 pp., bound, DM 64.70.—**Phase Transfer Catalysis. Principles and Techniques.** By *C. M. Starks* and *C. Liotta*. Academic Press, New York—San Francisco—London 1978. 365 pp., bound, $ 38.00.

Phase transfer catalysis is a term characterizing an essential advance in chemical synthesis techniques over the last decade. Several review articles have already appeared[*], and now we have the first two monographs (there is already a publisher's announcement of a third[**]). They are written by authors who have taken active part in the development of the technique, *Starks* even coining the term "phase transfer catalysis". The books have been conceived and printed in a pleasantly readable manner, and the number of printing errors has been kept within limits. Both books have been slightly inflated by the repetition of the same subject matter in several chapters and by the tabulation of every compound treated, together with yields, which seems unnecessary in the case of homologous or analogous series with little difference between the individual members. In each book the material in the synthesis section is arranged by the type of reaction: simple substitutions, alkylations and condensations, methods for carbene production, ylide reactions, oxidations and reductions, miscellaneous further phase transfer catalysis reactions (this is the arrangement in *Starks* and *Liotta*). Efforts have been made to cover the literature as comprehensively as possible. *Weber* and *Gokel* cover it to the end of 1976, and there is an appendix with further references from 1976—77, arranged by chapter, giving a total of 650 references. *Starks* and *Liotta* cover just 700 of the 900 references known to them to the end of 1977. The field is developing rapidly; for the period 1978—79, the present reviewer already has more than 200 new references in his file!

There are marked differences in the way that the two books deal with the theoretical foundations (*Starks* and *Liotta* take three chapters with 90 pages, *Weber* and *Gokel* one chapter with 17 pages), and in their printing of typical preparative details (lacking in the case of *Weber* and *Gokel*). While *Weber* and *Gokel* deal briefly with general, mechanistic, and theoretical problems, *Starks* and *Liotta* have put a lot of effort into collecting data on the extraction of anions and cations into organic solvents, on the reactive behavior in different media, and on other fundamental questions. Kinetics, limiting conditions, and possible mechanistic alternatives are discussed, and hints are given on the choice of the catalyst and the solvent and also of the conditions for a new reaction. *Weber* and *Gokel* do give all this material as well, but in a very summary form. Although we are still far from being able to predict the catalyst activity or the exact course of a new phase transfer catalysis process, *Starks* and *Liotta* give the essential starting points for a general theory, and in the case of substitution reactions a fair amount of progress has been made. Difficulties arise in the explanation of alkylation and carbene production in the presence of concentrated caustic soda. *Starks* and *Liotta*'s critical approach, which is otherwise impeccable, breaks down here, for example, in the use of different values for the selective extraction of OH^- (p. 173: Br^- is 10^5 times more readily extracted than OH^-, in Table 7, p. 24, however, it is only 1650 times. Although in other places the difficulty of dissolving tetrabutylammonium hydroxide in benzene is mentioned, the extraction value given in Table 3 on p. 18 is obviously wrong). Notwithstanding these minor blemishes, this is a very good book. Despite the better layout and better paper in *Weber* and *Gokel*, *Starks* and *Liotta*'s book must still be the first choice for anyone who cannot wait for further developments.

Ekkehard V. Dehmlow [NB 471 IE]

[*] For example Angew. Chem. *86*, 187 (1964), *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974), *16*, 493 (1977).

[**] Phase Transfer Catalysis. By *E. V.* and *S. S. Dehmlow*; Verlag Chemie International, New York and Weinheim, in press.

Principles of Chemical Kinetics. By *G. G. Hammes*. Academic Press, New York 1978, x, 268 pp., bound, $ 19.50.

Despite some pleasing recent publications, there is still a lack of introductory books on reaction kinetics that deal with the fundamentals of formal kinetics and at the same time lead on to the major areas of current research. The present book partly fills this gap. Based on the book by *Amdur* and *Hammes*, it has now been revised by *Hammes* after *Amdur*'s death. It contains chapters on formal kinetics, collision theory, and the theory of the transition state. After examples of bimolecular and unimolecular gas reactions and the more recent theories concerned with them, the author discusses molecular beam experiments and experiments on energy transfer (including recent work with lasers). Shock-wave techniques are dealt with in an appendix. Next comes a survey of reactions in solution, first on the basis of electrochemical relationships and then oriented toward more recent techniques such as relaxation methods and NMR spectroscopy. After a survey of protolytic reactions and acid-base catalysis, the book closes with a chapter on enzyme kinetics.

The author has succeeded in producing a lively and compact presentation of selected topics in modern reaction kinetics. Because it is only a selection, a number of areas have obviously been touched on only lightly if at all. Because of its choice of topics of current interest, the book can be highly recommended as an introduction to some major areas of modern research in reaction kinetics, and as a supplement to the basic lectures of a course on kinetics for advanced students.

Jürgen Troe [NB 466 IE]

Inorganic Polymers. By *N. H. Ray*. Academic Press, London 1978. viii, 174 pp., £ 8.40.

The book gives a concise account of the current stage of development of inorganic polymers, which are defined here as large molecules with no carbon in the main chain and with mainly covalent bonds. Polyphosphoric acid esters, and in particular silicones, which come under this definition, are not dealt with because of their high proportion of organic side groups. There is a brief discussion of the most important physical parameters: modulus of elasticity, tensile strength, brittleness, solubility, and glass transition temperature. From the fact that most inorganic polymers, even if they are highly cross-linked, can be heated beyond the glass transition temperature without decomposition (which is generally not true of organic polymers) and can be processed in this way, the author deduces that the earlier assumption that linear inorganic polymers could be produced by reducing the functionality of elements like B, Si, or P is fundamentally false.

Inorganic polymers may be classified as follows on the basis of the coordination number of the element(s) making up the polymer skeleton:

CN 2: Linear polymers: S, Se, Te, linear metaphosphates, polycarboranes, and the currently much discussed polyphosphazenes and SN polymers.
CN 3: Chalcogenide glasses such as As_2S_3 and ultraphosphates.
CN 3—4: Borate and boron phosphate glasses.
CN 4: Quartz glass, alkali metal silicates, borosilicate glasses, glass ceramics, BeF_2, phosphorus oxide nitride, crystalline silicates such as ladder and layer silicates, three-dimensional networks such as felspars and zeolites, and boron and aluminum phosphate.
CN >4: Titanium, zirconium and tin phosphate, SiP_2O_7.

The main emphasis of the work is on glasses.

Next comes a section on inorganic fibers, *e.g.* on the basis of Al_2O_3 and ZrO_2; there is no discussion of glass fibers, but the reactions involved in the setting of cement are mentioned. There is no reference to enamels.

The author's opinions on the need to replace organic polymers by inorganic ones—for example because of the increasing shortage of oil—are highly debatable.

For whom is the book intended? It will certainly stimulate the thinking of chemists involved in research and development. To evaluate it critically, however, the author assumes that the reader has a very good grounding in inorganic, organic, and polymer chemistry.

Reinhard Schliebs [NB 463 IE]

The Donor-Acceptor Approach to Molecular Interactions. By *V. Gutmann*, Plenum Press, New York 1978, xvi, 279 pp., bound, £ 33.00.

Over the last ten years the author has won considerable respect with a series of papers in which he has attempted to extend the donor-acceptor model of coordination chemistry into a unified concept for the description of all types of molecular interactions. The present monograph contains a detailed presentation of this approach.

The approach is described in two relatively short introductory chapters. The essential effects of a donor-acceptor interaction between two subsystems (two molecules, molecule and solvent, *etc.*) on the properties of these subsystems in the complex can be summarized in three rules concerning the change in bond lengths (the bond-length variation rules). The ability of the subsystems to form donor-acceptor bonds is characterized by empirical parameters specific to the molecule (donor number, acceptor number), and these may be determined by calorimetric, kinetic, or NMR measurements.

In the next fifteen chapters this concept is applied to a wide variety of chemical phenomena, from the formation of simple coordination compounds between isolated molecules, such as $H_3N \cdot BF_3$, *via* solvent effects to enzyme reactions. In each case the donor and acceptor numbers of the subsystems are related to the properties of the complex formed, such as geometric structure, partial charges, stability, chemical behavior, reaction mechanisms, *etc.*

The author has succeeded in discussing a wealth of widely scattered material from all fields of chemistry under one unified viewpoint, and has summarized a large number of different reactions in one concept. Sometimes the approach seems too simple, and sometimes it is also not very satisfactory to have a concept constructed purely upon empirical parameters without any attempt being made to understand the details of a chemical bond and to discuss them. Be that as it may, we must agree with the author when he states in the foreword that the donor-acceptor model is a useful general concept that enables a number of phenomena to be explained and predicted.

Volker Staemmler [NB 472 IE]

Thin Films—Interdiffusion and Reactions. Edited by *J. M. Poate et al.* John Wiley & Sons, London 1978. 1st edit., x, 578 pp., bound, £ 25.00.

The title does not give much indication of the book's great relevance for current problems in semiconductor technology. The work contains information on almost every aspect of interfacial reactions between two solids: interdiffusion, diffusion across the grain boundaries, formation of intermetallic phases, and—in the case of the silicides—formation of chemical compounds.

The techniques and the scope of analytical methods for the characterization of films are described, as are the methods of depth profile analysis, and are illustrated with examples of successful applications. Contact between metals and semiconductors is discussed for the cases of Schottky barriers and ohmic contacts. There is also a chapter on electron migration, *i.e.* on material transport in metal films. The section on solid phase epitaxy may, at first, seem to be of less immediate relevance, but this is not the case, because, for example, recrystallization after ion implantation falls within this field. Finally the effects of ion implantation in metal films on the properties of the metals are considered.

The editors have shown great skill in their choice of topics and authors, but have not intervened to coordinate the contents of the various sections. For example, electron migration appears in two different places in the book.

The unifying element of this book is the relevance of the theme for the further development of semiconductor technology. An understanding of the fundamental physical and chemical processes in the interface and in the metal film itself will result in ideas that may help to solve important problems in the development of new generations of semiconductor components. The book is not a textbook, nor is it a reference book. One should read it for its wealth of information.

Konrad Eisele [NB 455 IE]

The Spectrum in Chemistry. By *J. E. Crooks.* Academic Press, London 1978. 1st edit., x, 313 pp., bound, £ 12.60.

Dozens of monographs, summarizing reports, handbook articles, *etc.* appear every year on various individual aspects of chemical spectroscopy. What is lacking is a monograph or an introductory textbook that would present the chemist with an authoritative guide to the whole range of spectroscopy in chemistry. The present book is directed toward this requirement and meets it well.

The various subfields of spectroscopy with electromagnetic waves are dealt with in 14 chapters. A short introduction is followed by sections on the microwave region, NQR, IR, VIS, UV, Raman, NMR, EPR, fluorescence and phosphorescence, circular dichroism, photoelectron spectroscopy, and Mössbauer spectroscopy. Relevant literature references are appended to each chapter. The use of SI units is dealt with in an appendix. The reader can acquaint himself with the questions raised by means of worked examples. There is a good subject index.

The author assumes a certain knowledge of the fundamentals of physical chemistry, as he makes clear in the introduction.

The requirements are low—even a less advanced student should be able to meet them. In general, the weight of the individual chapters is matched to the importance of the method concerned in the field of chemistry. One or two readers would certainly have wished for a stronger emphasis on the theoretical relationships in contrast to the experimental aspects. Experimental details can sometimes quickly become obsolete (*e.g.* on p. 214 the resolution for a Si solid state detector is given as ≈ 1 keV at 10 keV. However, there are already X-ray detectors on the market that can resolve about 250 eV at 6 keV and 600 eV at 120 keV).

There are a few printing errors that will need correcting in the next edition, *e.g.* Table 6.1 (S incorrectly given for d^2) or p. 44 (the boiling point of nitrogen is 77 K and not 70 K). The reviewer would have preferred a rather more general treatment of the Beer-Lambert Law. The chapter on Mössbauer spectroscopy is perhaps kept too qualitative.

In all, however, the book constitutes a very good introduction to chemical spectroscopy, which will bring both the advanced student and the practising chemist closer to the problems, show them how the techniques are applied, and prepare them for reading specialist monographs. It can be recommended to any scientist requiring a survey of this branch of physical chemistry.

Alarich Weiss [NB 456 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Frontiers in Physicochemical Biology. Edited by *B. Pullman.* Academic Press, New York 1978. xvi, 503 pp., bound, $ 45.00.—ISBN 0-12-566960-7

Characterisation of Protein. Conformation and Function. Edited by *F. Franks.* Symposium Press, London 1978. 157 pp., paper, £ 9.25.—ISBN 0-905927-05-2

Topics in Stereochemistry, Vol. 10. Edited by *E. L. Eliel* and *N. L. Allinger.* John Wiley & Sons, London 1978. xiii, 349 pp., bound, £ 27.50.—ISBN 0-471-04344-3

General Chemistry, Principles and Structure. By *J. E. Brady* and *G. E. Humiston.* John Wiley & Sons, London 1978. 2nd Edit., xiv, 786 pp., bound, £ 12.65.—ISBN 0-471-01910-0

Metal Alkoxides. By *D. C. Bradley, R. C. Mehrotra,* and *D. P. Gaur.* Academic Press, New York 1978. viii, 411 pp., bound, $ 58.00.—ISBN 0-12-124250-1

Jahrbuch für den Praktiker. Edited by Verlag für Chemische Industrie H. Ziolkowsky KG, Augsburg 1979. 22nd Edit., 497 pp., paper, DM 36.00.—ISBN 3-87846-140-2

Marine Natural Products. Chemical and Biological Perspectives, Vol. 2. Edited by *P. J. Scheuer.* Academic Press, New York 1978. xiii, 392 pp., bound, $ 38.00.—ISBN 0-12-624002-7

Luftverunreinigungen durch Vinylchlorid (VC) aus PVC-Erzeugnissen. By *E.-G. Kohl* and *D. Pruggmeyer.* Erich Schmidt Verlag, Berlin 1978 (Umweltforschungsplan des Bundesministers des Innern—Luftreinhaltung—). 23 pp., paper, DM 14.60.—ISBN 3-503-01737-2

Physical Methods in Modern Chemical Analysis, Vol. 1. Edited by *T. Kuwana.* Academic Press, New York 1978. x, 320 pp., bound, $ 33.00.—ISBN 0-12-430801-5

Catalysis, Vol. 2. Senior Reporters: *C. Kemball* and *D. A. Dowden.* The Chemical Society, London 1978. xi, 276 pp., bound, DM 95.00.—ISBN 0-85186-544-5.—A volume in the series, "Specialist Periodical Reports"

Proceedings of the 5th European Symposium on Polymer Spectroscopy. Edited by *D. O. Hummel.* Verlag Chemie, Weinheim 1979. xi, 332 pp., paper, DM 88.00.—ISBN 3-527-25777-2

Analytical Methods for Coal and Coal Products, Vol. 2. Edited by *C. Karr, Jr.* Academic Press, New York 1978. xvi, 669 pp., bound, $ 55.00.—ISBN 0-12-399902-2

Erkennen von Kunststoffen. By *D. Braun.* Carl Hanser Verlag, München 1978. 94 pp., bound, DM 26.00.—ISBN 33-446-12673-2

Organometallic Mechanisms and Catalysis. By *J. K. Kochi.* Academic Press, New York 1978. xviii, 623 pp., bound, $ 59.50.—ISBN 0-12-418250-X

Contemporary Topics in Polymer Science, Vol. 1. Macromolecular Science. Retrospect and Prospect. Edited by *R. D. Ulrich.* Plenum Press, New York 1978. ix, 284 pp., bound, $ 35.40.—ISBN 0-306-36261-9

Emulsions, Latices, and Dispersions. Edited by *P. Becher* and *M. H. Yudenfreund.* Marcel Dekker, New York-Basel 1978. x, 329 pp., bound, SFr. 64.00.—ISBN 0-8247-6797-7

Topics in Applied Physics, Vol. 29. Hydrogen in Metals II. Application-Oriented Properties. Edited by *G. Alefeld* and *J. Völkl.* Springer-Verlag, Berlin 1978. xxii, 387 pp., bound, DM 86.00.—ISBN 3-540-08883-0

Studies in Soviet Science. The Siloxane Bond. By *M. G. Voronkov, V. P. Mileshkevich,* and *Yu. A. Yuzhelevskii.* Consultants Bureau, New York 1978. xii, 493 pp., bound, $ 78.00.—ISBN 0-306-10940-9

Contemporary Topics in Analytical and Clinical Chemistry, Vol. 3. Edited by *D. M. Hercules, G. M. Hieftje, L. R. Snyder,* and *M. A. Evenson.* Plenum Press. New York 1978. xi, 306 pp., bound, $ 32.50.—ISBN 0-306-33523-9

Advances in Laser Chemistry. Edited by *A. H. Zewail.* Springer-Verlag, Berlin 1978. x, 463 pp., bound, DM 69.00.—ISBN 3-540-08997-7

Dünger und Düngung. By *A. Finck.* Verlag Chemie, Weinheim 1979. xiv, 442 pp., paper, DM 58.00.—ISBN 3-527-25805-1

Chemistry and Physics of Carbon, Vol. 14. Edited by *Ph. L. Walker* and *P. A. Thrower.* Marcel Dekker, New York-Basel 1978. ix, 309 pp., bound, SFr. 78.00.—ISBN 0-8247-6746-2

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 8
August 1979
Pages 563 – 640

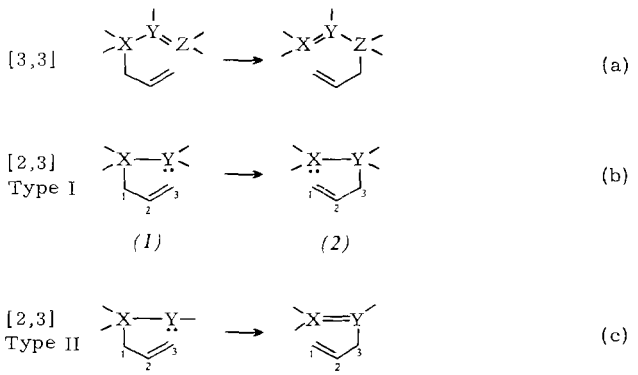
Stereochemistry of [2,3]Sigmatropic Rearrangements

By Reinhard W. Hoffmann[*]

Stereoselective synthesis is attracting more and more attention. Successful stereoselective syntheses require the availability of reactions of known stereochemistry which give maximum yields of the desired products. This is particularly so with reactions proceeding *via* cyclic transition states. Of these, the stereochemistry of [3,3]sigmatropic processes has long been known. This article now summarizes the factors determining the stereoselectivity of [2,3]sigmatropic rearrangements.

1. Introduction

[3,3]Sigmatropic rearrangements (a) (Scheme 1; Claisen, Cope, oxy-Cope, hetero-Cope rearrangement)[1-4] have been thoroughly studied with regard to their stereochemical course[5,6] and belong to the standard repertoire of stereoselective syntheses of olefins[3-7] or centers of chirality[8-11]. Recent outstanding applications can be seen in a juvenile hormone synthesis[12], transformation of sugars into prostaglandins[13], or the synthesis of tocopherol[14].



Scheme 1. Survey of [3,3]- and [2,3]sigmatropic rearrangements. The suggested valences may be bonds to other atoms or lone pairs. Formal charges follow from the nature and the bonding situation of atoms X, Y, Z.

[*] Prof. Dr. R. W. Hoffmann
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg (Germany)

Among the [2,3]sigmatropic rearrangements there is a great variety of reactions of types I and II [Scheme 1, eq. (b) and (c)][15-21] which frequently occur at lower temperatures than the [3,3]sigmatropic rearrangements. The five-membered cyclic transition state of [2,3]sigmatropic rearrangements shows greater conformational "flexibility" than the six-membered transition state of [3,3]sigmatropic rearrangements and should therefore be far more susceptible to the effects of stereochemical control by substituents[22]. In view of this synthetic potential it was most appropriate that studies on [2,3]sigmatropic rearrangements should have been accompanied by a thorough examination of their stereochemistry which began almost simultaneously[23]. It is thus all the more surprising that the starting materials for the preparative investigation of [2,3]sigmatropic rearrangements were (purposely?) chosen in such a way that no stereochemical problems occurred. However, this meant forgoing stereochemical information.

The following compilation of results should provide an insight into the stereochemistry of [2,3]sigmatropic rearrangements.

1.1. Stereochemical Observables

The rearrangements (b) and (c) lead to formation of a new double bond between C-1 and C-2. Given two different substituents on C-1 this double bond may result in an *E* or *Z* configuration. Hence the factors determining the configuration of the new double bond are of interest.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0563 $ 02.50/0

The centers X and C-1 of the reactants of rearrangements (b) and (c) are chiral if they each bear two different substituents. A lone pair will also be regarded as a substituent in these considerations. C-3 [rearrangements (b) and (c)] and Y [rearrangements (b)] are prochiral if the substituents on these centers are different. In the course of rearrangement, the chirality of X and C-1 disappears and new chiral centers are created at C-3 and Y. Interest attaches here to the factors determining the extent to which chirality is transferred to C-3 and Y.

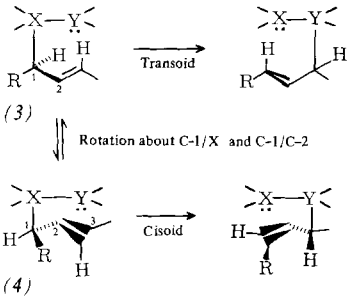
This article will consider only reactions whose products are formed by kinetic control, and reactions which are concerted, *i.e.* no reactions proceeding *via* a dissociation-recombination mechanism[24-27].

2. Configuration of the New Double Bond

[3,3]Sigmatropic rearrangements are often employed for the stereoselective construction of di- and tri-substituted olefins. The [2,3]sigmatropic rearrangements considered here exhibit a stereoselectivity comparable with, or even higher than, similar [3,3]sigmatropic rearrangements.

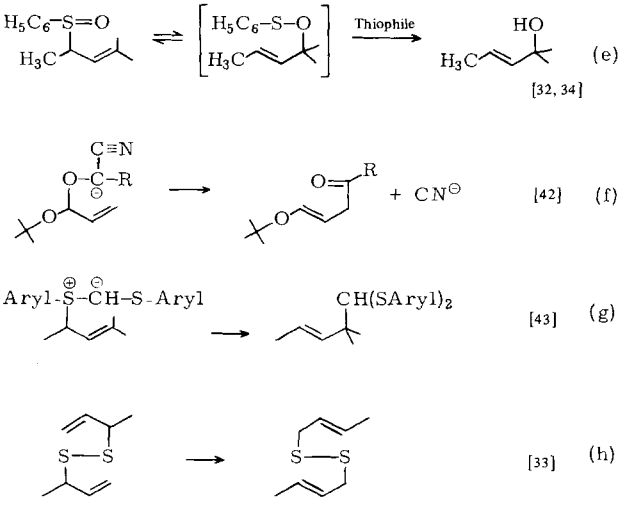
2.1. 1,2-Disubstituted Double Bonds

In the case of a 1-monosubstituted derivative of *(1)* (Scheme 1), rearrangement starting from *(3)* and *(4)* can proceed *via* two transition states, designated as transoid and cisoid by *Mislow*[23] [eq. (d)].



(3) (4) (d)

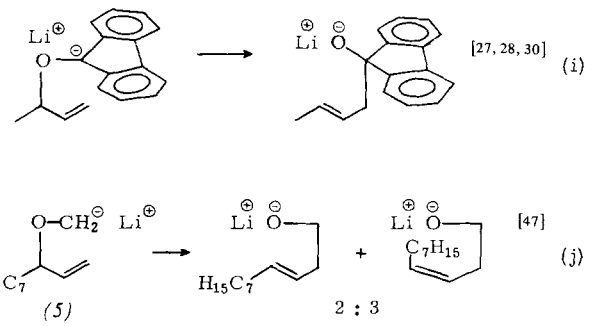
Examples (e)—(h) show that the rearrangement generally leads with a high degree of selectivity *via* the transoid transition state to *E* olefins[27-45] (R = *i*-butyl, *n*-hexyl, Aryl = phenyl).



(e) [32, 34] (f) [42] (g) [43] (h) [33]

Formation of the *E* double bond can be rationalized by assuming the substituent R to preferentially adopt an equatorial position in a five-membered cyclic transition state, *versus* a pseudoaxial position leading to the *Z* double bond. This amounts to saying that the substituents on C-1, C-2, and C-3 come to rest in a plane during the rearrangement. In the cisoid transition state, a destabilizing 1,3-allyl interaction[46] would become operative between R and the hydrogen atom on C-3; in the transoid transition state only a 1,3-hydrogen-hydrogen interaction will occur.

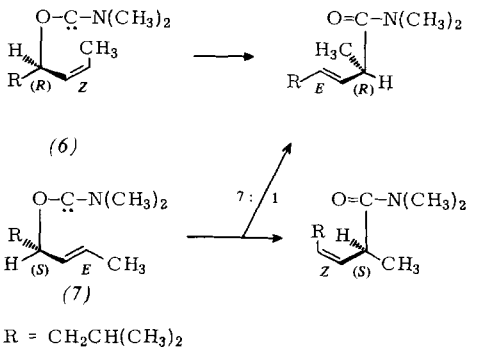
The regularity with which *E* olefins are formed serves to underscore exceptional behavior: while Wittig rearrangement (i)[*][27,28,30] proceeded entirely *E*-selectively according to these rules, reaction (j)[47] followed an exceptional course, giving mainly the *Z* olefin.



(i) (j) (5)

In contrast to reaction (i), reaction (j) is probably strongly exothermic. This would indicate an early transition state and hence diminished selectivity[48]. The charge distribution in reactant *(5)* also suggests the migrating allyl group to have considerable carbanion character. This could favor formation of the *Z* olefin owing to the greater stability of a *Z*-substituted allyl anion[49]. The regioselectivity of the rearrangement rules out dissociation[50] to formaldehyde and an allyllithium derivative.

A low stereoselectivity was also found in a rearrangement of type II[51,52]. The species *(6)* and *(7)* are reactive intermediates; this fact and the high reaction temperature (130 °C) would offer a reasonable explanation of the diminished selectivity.



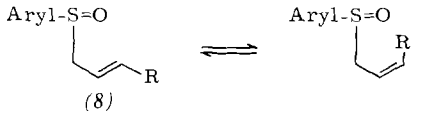
(6) (k) (7)

R = $CH_2CH(CH_3)_2$

These exceptions show that the energy difference between the transoid and the cisoid transition state cannot be large. In full accord with this conclusion, *E*/*Z* isomerization of the double bond was found to occur in reversible sigmatropic

[*] Designations such as Wittig or Stevens rearrangement are used in the widest sense.

rearrangements, such as that of *(8)*[23,53,54] (Aryl = *e.g. p*-tolyl; R = methyl, *n*-pentyl).

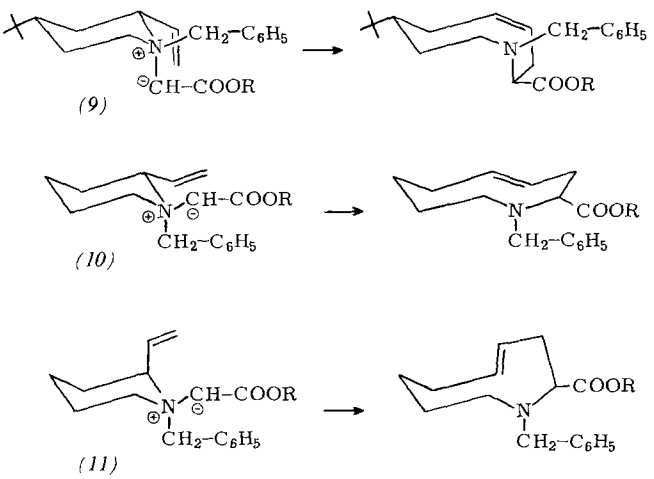


(8)

In the irreversible allyl sulfoxide/allyl sulfenate rearrangement of type (e), the *E*-allyl sulfoxide reacts nine times as fast as the *Z* isomer[55]. This result and the position of equilibrium between *E* and *Z*-allyl sulfoxide permit us to estimate the cisoid transition state for *(8)*, Aryl = phenyl, *p*-tolyl, R = *n*-pentyl, to be only *ca.* 1.5 kcal/mol less stable than the transoid transition state. This estimate does not include interactions with the substituents on X or Y [see eq. (d)]. Moreover, these values are also in agreement with data reported for the [3,3]sigmatropic Claisen rearrangement according to which *E*-allyl ethers react three- to nine times as fast as their *Z* isomers[56,57].

The slight energy difference between cisoid and transoid transition states also explains why [2,3]sigmatropic rearrangements proceed readily *via* cisoid transition states if they are constrained to occur by incorporation of the double bond into a ring[51,58,62].

[2,3]Sigmatropic rearrangements have also been used to advantage for ring enlargement[63]. The new endocyclic double bond is formed with high stereoselectivity: if Y (CH COOR in this case) in a reactant such as *(9)* is in an axial arrangement a *Z* olefin will be formed; if Y assumes an equatorial position as in *(10)* and *(11)* an *E* olefin will result, regardless of the arrangement (equatorial or axial) of the vinyl group in the reactant (R = ethyl).

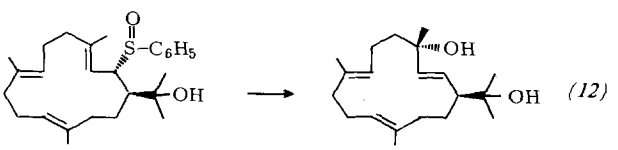


(9)

(10)

(11)

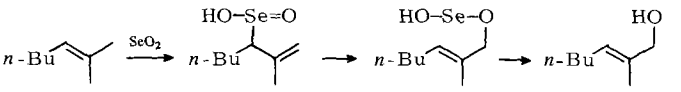
According to what has been said so far, [2,3]sigmatropic rearrangements are just as suitable as [3,3]sigmatropic rearrangements[3] for the stereoselective construction of 1,2-disubstituted double bonds, with *E* olefins generally being formed. A further example may be seen in the *E* selective introduction of a double bond into the cembrene derivative *(12)*[44].



(12)

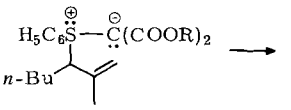
2.2. Trisubstituted Double Bonds

If a substituent is introduced into compounds such as *(3)* at C-2, this will have no effect on the cisoid transition state but should destabilize the transoid transition state by way of an additional 1,2-allyl interaction[46] between the substituents on C-1 and C-2. Nevertheless, as in the case of [3,3]sigmatropic rearrangements[3], the tendency to form an *E* double bond is retained: in the allyl sulfoxide/allyl sulfenate rearrangement of type (e) the products were found to have exclusively an *E* double bond[64,65] or to show pronounced *E* preference (20:1)[66]. This also applies to the corresponding allyl selenoxide rearrangement[67]; the *E* selective oxidation of isopropylidene groups as in *(13)* by selenium dioxide can probably be attributed to the stereoselectivity of the [2,3]sigmatropic rearrangement[67].

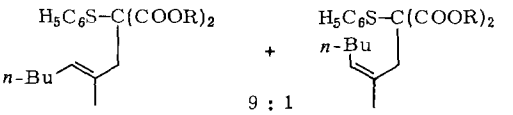


(13)

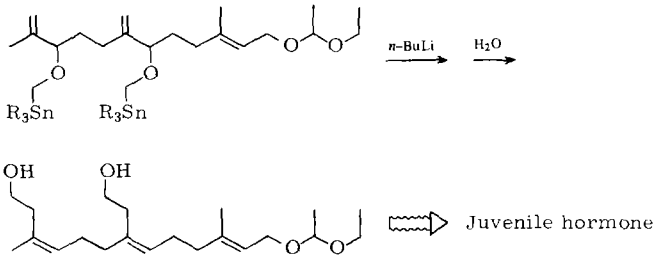
The Stevens rearrangement [eq. (l)][68] gave less *E* olefin than the reactions just considered, and the Wittig rearrangement [eq. (j)] of 2-methyl-substituted *(5)* was unexpectedly



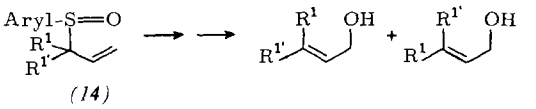
(1)



completely *Z* selective[47]. This unusual *Z* selectivity found an ideal application in a new juvenile hormone synthesis[69].



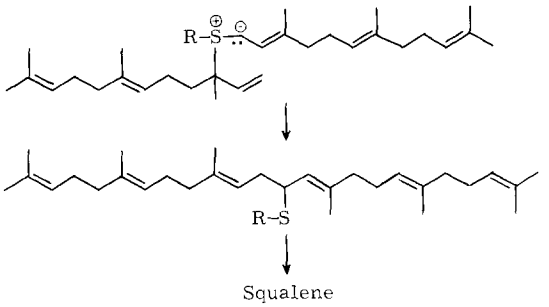
Trisubstituted olefins also result from the rearrangement of 1,1-disubstituted derivatives of *(1)*. The *E* or *Z* stereoselectivity depends upon the relative sizes of the substituents attached to C-1. Thus *E* preferences ranging from 3[66] *via* 10[66]



(14)

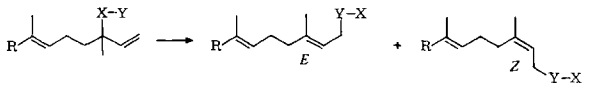
to > 20[70,71] were found in the rearrangement of 1,1-disubstituted allyl sulfoxides of type *(14)*. A corresponding rearrangement of a sulfonium ylide is presumably involved in

the *E* stereospecific biochemical linkage of two farnesyl units to give squalene[72,73]. The reaction can be accomplished *in vitro* with $R = C_6H_5$.



Model studies on comparable systems show that the Stevens rearrangement is *E* stereospecific[73] whereas Wittig rearrangements and carbene rearrangements of type II eq. (c) show a considerably diminished selectivity towards formation of an *E* double bond. Examples are shown in Table 1.

Table 1. Stereoselectivity in [2,3]sigmatropic rearrangements.



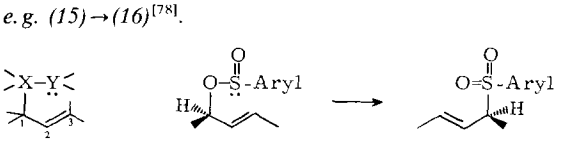
R	X	Y	*T* [°C]	Result	Ref.
$(CH_3)_2CH$ ^{f} $C(CH_3)_2$	$C_6H_5S^{\oplus}$	$\ddot{C}H$ $[CH=^f C(CH_3)(CH_2)_2]_2CH=C(CH_3)_2$	65	only *E*	[73]
H	$C_6H_5S^{\oplus}$	$\dot{O}^{\ominus}$	25	*E*:*Z* = 9:1	[66]
H	S	$\ddot{C}H$ $CH=C(CH_3)_2$	−30	*E*:*Z* = 3:2	[74]
H	O	$\ddot{C}H$ C_6H_5	−20	*E* and *Z*	[24]
H	O	$\ddot{S}(O)$ $CH_2CH=C(CH_3)(CH_2)_2CH=(CH_3)_2$	110	*E* and *Z*	[75]
CH_3	O	$\ddot{C}$ $N(CH_3)_2$	139	*E* and *Z*	[51]

In some cases[70-74], the [2,3]sigmatropic rearrangement of 1,1-disubstituted allyl derivatives thus exhibits a significantly greater stereoselectivity than the corresponding [3,3]sigmatropic rearrangement[6].

3. Transfer of Chirality

3.1. 1→3 Chirality Transfer

On rearrangement of 1,3-disubstituted derivatives of *(1)*, the chiral center at C-1 is eliminated and a new one created at C-3. The term "self-immolative" asymmetric synthesis has been introduced to describe syntheses of this kind[21,76]. Provided that the reactant has a uniform configuration of the C-2/C-3 double bond, quantitative 1→3 chirality transfer will follow from the suprafacial[18,77] course of rearrangement, *e.g. (15)→(16)*[78].

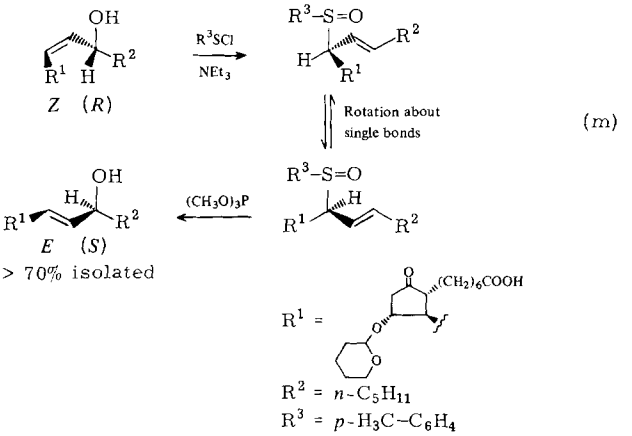


(1) *(15)* *(16)*

This has been repeatedly confirmed by experiment[52,78,79] and accords with experience gained in [3,3]sigmatropic rearrangements[80]. Homogeneous products can be obtained directly if the new double bond is formed stereoselectively (see Section 2.1). Only Wittig rearrangement[18] or carbene rearrangement [eq. (k)][52] gave mixtures of *E*/*Z* isomers in which the stereochemistry at C-3 nevertheless results from complete chirality transfer. The example of a prostaglandin synthesis [eq. (m)] illustrates how the *E* preference is exploited on formation of the new double bond in order to invert both the double bond geometry and the chirality of an allyl alcohol at one stroke by a series of [2,3]sigmatropic rearrangements[37]; for the chemical aspects, cf. eq. (e) and (n).

3.2. X→3 Chirality Transfer

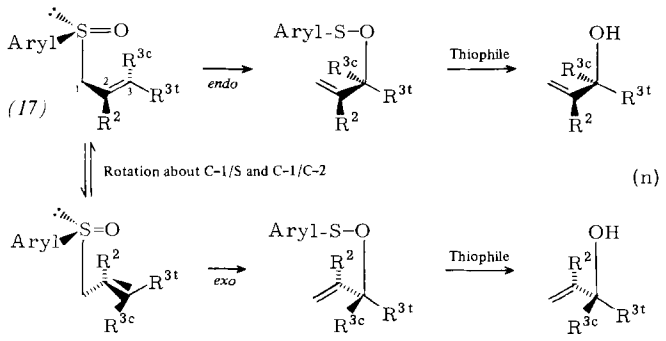
For preparative reasons, the reactants of [2,3]sigmatropic rearrangements are usually obtained by linking the allyl system with the X–Y fragment. In the case of 1→3 chirality transfer, the chirality is shifted by two carbon atoms along the same synthon (the allyl component). In contrast, an X→3 chirality transfer permits the preparatively more useful transfer of chirality from one synthon—the X–Y fragment—to another (achiral) synthon, specifically to C-3. Rational utilization of this chirality transfer requires that the prochiral center C-3 has a uniform configuration[55] (*i.e.* that the double bond in *(1)* has either *E* or *Z* configuration)—a requirement that leads to further preparative complications.



The fundamental stereochemical concepts concerning the transition states of [2,3]sigmatropic rearrangements are due to *Mislow*[23], who developed them for the example of allyl sulfoxide/allyl sulfenate rearrangement. This rearrangement can proceed *via* two diastereomeric transition states, *viz.* *"exo"* and *"endo"*[27], which interconvert by rotation about the C-1/C-2 and the C-1/C–S bond [eq. (n)].

Since the different enantiotopic sides of the C-2/C-3 double bond are attacked in the *exo* and the *endo* transition state, a reactant of uniform chirality will give enantiomeric products *via* the *exo* and the *endo* transition state. The extent of chirality transfer therefore depends upon the relative energy of the two transition states.

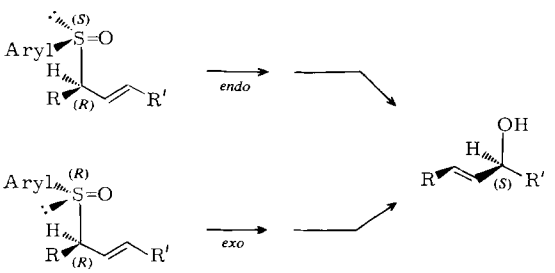
In similar manner, the energy difference between the transition states having chair and boat conformation determines the degree of a corresponding 1→3′ chirality transfer in [3,3]sigmatropic rearrangements[5]. Owing to the energy difference of *ca.* 3 kcal/mol, extensive (>94%) 1→3′ chirality transfers are observed in these cases[11,81]. Thus the transition states with chair and boat conformation in [3,3]sigmatropic rearrangements correspond to the *exo* and *endo* transition states of [2,3]sigmatropic rearrangements with regard to the stereochemical results.



(n)

The situation is most readily discussed in which the two "freely available" ligands on the chiral X atom of *(1)* differ considerably in size, as with *(17)* whose X ligands are an aryl group and a lone pair. It may then be assumed that the energy difference between the two transition states is determined by the extent of aryl-R^2 interaction (destabilizing the *endo* transition state) and aryl-R^{3c} interaction (destabilizing the *exo* transition state).

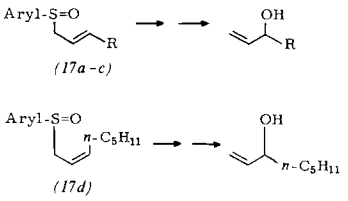
These interactions must first be examined in relation to other substituent effects for they are considerably weaker than those between a 1-substituent and R^2 and R^{3c} [cf. eq. (l) and eq. (k)]. Thus experience shows that a substituent on C-1—if present—will determine the stereochemistry of rearrangement. This is why we were able to discuss the controlling influence of such a substituent in Section 2 without paying the slightest attention to the chirality at centers X and Y. Even when both diastereomeric reactants were present[44,64], allyl sulfoxide/allyl sulfenate rearrangement gave the *E* olefin. This means that under the influence of the substituent on C-1 one diastereomer reacts selectively *via* the *exo* transition state and the other selectively *via* the *endo*-transition state [eq. (o)].



(o)

Hence, any attempt to establish the influence of the chirality of center X on the stereochemistry of rearrangement must be undertaken with derivatives of *(1)* which are unsubstituted at C-1 or bear two identical substituents at that site. We therefore first examined C-1-unsubstituted derivatives of *(17)* with $R^2 = R^{3c} = H$. Examples are shown in Table 2[55].

Table 2. X→3 chirality transfer for sulfoxides *(17)*. Aryl = *p*-CH_3-C_6H_4.



Cpd.	R	Reaction *via* *exo* transition states [%]	*endo* [%]	Chirality transfer [%]
(17a)	*n*-C_5H_{11}	30±5	70±5	40±10
(17b)	*t*-C_4H_9	≈50	≈50	5
(17c)	C_6H_5	50	50	0
(17d)	*n*-C_5H_{11}	< 5	>95	>90

The modest transfer of chirality reveals that the energies of the *exo*- and *endo* transition states hardly differ for the *E*-allyl sulfoxides *(17a—c)*. In contrast, the *exo* transition state can be selectively destabilized by the R^{3c} substituent in the *Z*-allyl sulfoxide *(17d)*. In this case the rearrangement proceeds largely *via* the *endo* transition state and is therefore, close to stereospecific.

The relative energies of the four conceivable diastereomeric transition states could be estimated from the rate and the stereochemical course of rearrangement of *(17a)* and *(17d)* (Fig. 1)[55].

A number of earlier observations can be discussed with the aid of Figure 1: *Mislow et al.*[23] found that at room tempera-

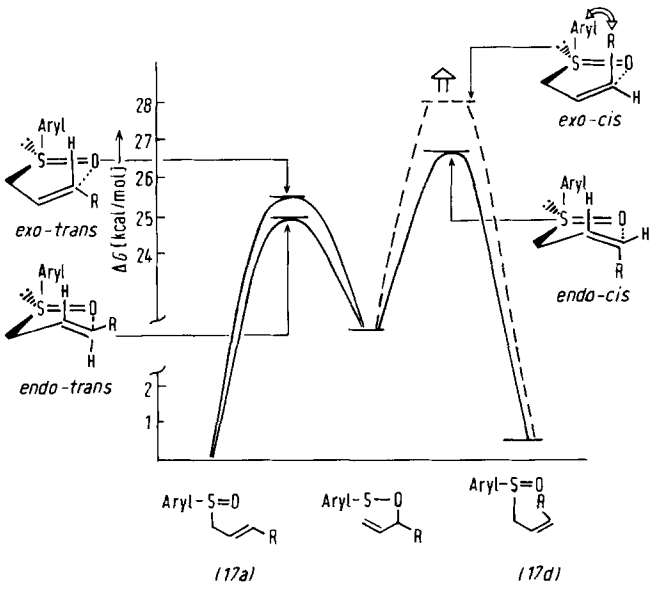
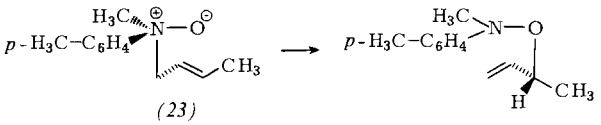


Fig. 1. Relative energies of the four conceivable transition states of the [2,3]sigmatropic rearrangement of *(17a)* and *(17d)* (see text for details). R = *n*-pentyl, Ar = *p*-tolyl.

ture allyl sulfoxides undergo fast racemization [at the asymmetric S atom, see eq. (o)] and slow *E/Z* isomerization. Racemization of, say, the *E*-configurated allyl sulfoxide *(17a)* requires that it must rearrange *via* the *exo-trans* and the *endo-trans* transition state. *E/Z* isomerization additionally requires that the *endo-cis* transition state be transversed, which is rate-determining for this isomerization. The *Z*-configurated allyl sulfoxide *(17d)* can also racemize: to this end it first transforms *via* the *endo-cis* transition state into the *E* isomer *(17a)*, which undergoes fast racemization so that racemic *(17d)* is ultimately regenerated *via* the *endo-cis* transition state. Thus only three of the four possible diastereomeric transition states are necessary for the stereoisomerizations observed by *Mislow*. The least favorable *exo-cis* transition state (greatest steric interaction) therefore probably fails to play any significant role. On suitable destabilization of the *endo-cis* transition state, slow rearrangements *via* the *exo-cis* transition state have been observed[101].

In the same way as an R^{3c} substituent destabilizes the *exo-cis* transition state, and thus compells reaction *via* the *endo-cis* transition state, an R^2 substituent should, depending upon its size, hinder rearrangements *via* the *endo* transition states[79b,81a] and thus lead to reactions *via* the *exo* transition state. This was examined in the case of the aryl-1-cycloalkenylmethyl sulfoxides *(18)*—*(22)* (Table 3)[82].

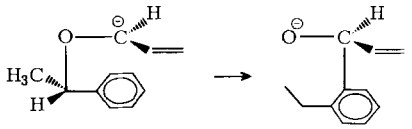
The annelated secondary alkyl group R^2 [see eq. (n)] leads to preferential rearrangement of the cyclopentene derivative *(18) via* the *exo* transition state. This tendency is further enhanced with the cyclohexene derivatives *(19)* and *(20)*; and in the case of compounds *(21)* and *(22)*, which contain a tertiary and a quaternary group R^2, respectively, reaction proceeds exclusively *via* the *exo* transition state. The allyl sulfoxide/allyl sulfenate rearrangement [eq. (e)] can therefore be employed for complete transfer of chirality from X to C-3 provided that a R^{3c} substituent or a bulky group R^2 is present. Also in the case of the *N*-oxide *(23)* with two substituents attached to X not differing much in bulk a remarkable transfer of chirality (>81%) was observed[21].



(23)

It is rather unclear, however, why the *exo* transition state should be preferred in this instance.

Complementary to X→3 chirality transfer is a transfer of chirality from C-1 to Y. Wittig rearrangement of *(24)* is an example[83] (cf. also ref. [18]); it proceeds selectively *via* one of the four diastereomeric transition states (cf. Fig. 1). However, secondary reactions mask which transition state is actually preferred.



(24)

3.3. X→Y Chirality Transfer

X→Y chirality transfer in the diatomic element of [2,3]sigmatropic rearrangement correspond to 1→3 chirality transfer in the triatomic element. Most accounts of such effects have been reported for rearrangements of sulfur ylides; however, stereochemical assignments are not given [Table 4, *(25)*—*(27)*].

Chirality transfer has recently also been found in Pummerer rearrangements, although it is not clear whether a competing dissociation into two fragments might be respon-

Table 3. X→3 chirality transfer for sulfoxides *(18)*—*(22)*, Aryl = *p*-CH_3 C_6H_4.

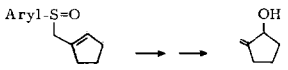
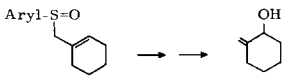
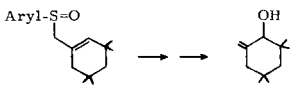
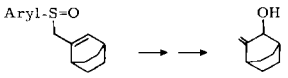
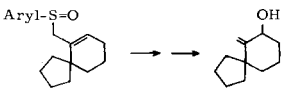
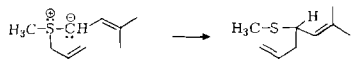
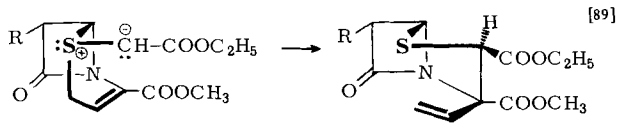
Cpd.	Reaction	Reaction *via* *exo* transition state [%]	Reaction *via* *endo* transition state [%]	Chirality transfer [%]
(18)		72	28	44
(19)		80	20	60
(20)		84	16	68
(21)		>95	<5	>90
(22)		>95	<5	>90

Table 4. X→Y chirality transfer for sulfur ylides *(25)—(28)*.

Cpd.	Reaction	Chirality transfer [%]	Ref.
(25)	 Ad = 1-Adamantyl	>94	[84]
(26)		[a]	[85]
(27)		<25	[86]
(28)			
(28a)	R = CN, Aryl = *p*-CH_3 C_6H_4	29	[87]
(28b)	R = $P(OCH_3)_2$, Aryl = *p*-CH_3 C_6H_4	24	[88]

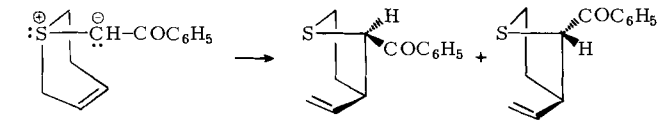
sible for the slight degree of chirality transfer [Table 4 *(28ab)*].



[89]

(29)

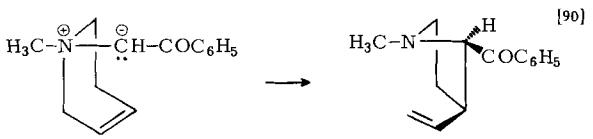
R = $C_6H_5CH_2$–CO–NH



[90]

(30)

25 : 1



[90]

(31)

A considerably higher selectivity was observed in the reactions of the ylides *(29)—(31)* in which not only the chirality of the center X is a controlling factor, but probably also the diastereoselectivity on linkage of the C-3/Y bond.

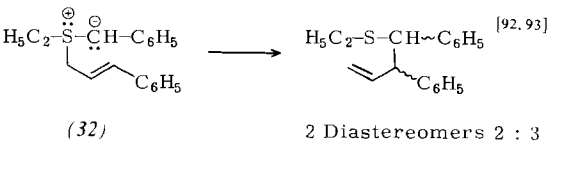
4. Diastereoselectivity in Bond Formation

4.1. Diastereoselective C-3/Y Bond Formation

On rearrangement of the ylides *(29)-(31)*, pronounced diastereoselectivities were found on linkage of the C-3/Y bond. However, exclusive formation of one diastereomer[27,91] is not the general rule. Only modest diastereoselectivity was frequently observed for conformationally mobile substrates[18,27,92-94].

In these cases, the diastereoselectivity is determined primarily by the relative energies of the *exo* and *endo* transition state.

The fact that a reciprocal diastereomeric ratio is established starting from *(34)* or *(35)* shows the influence of *exo* or *endo* folding (cf. Section 2.1) of the allylic moiety in the transition state to be the determining factor in this case. In contrast, the rearrangement (q)[18,27] leads to different diastereomeric ratios starting from the *E* or the *Z* reactant—a sign that the energy difference between the *threo* and *erythro* arrangement on formation of the new bond cannot generally be neglected. In the rearrangement (p) a further controlling

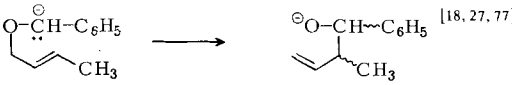


[92,93]

(p)

(32)

2 Diastereomers 2 : 3

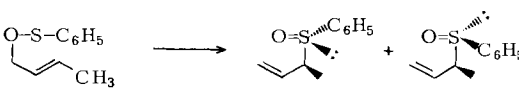


[18,27,77]

(q)

(33)

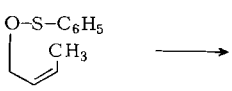
2 Diastereomers



[95]

(34)

7 : 1



1 : 7

(35)

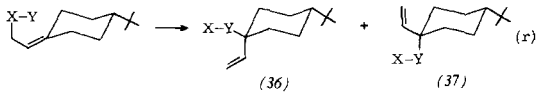
influence of unknown magnitude is exerted by the chirality at the center X.

Thus, while in [3,3]sigmatropic rearrangements the new C-3/C-3′ bond is formed with high diastereoselectivity owing to the comparatively large energy difference between the chair and boat conformation in the transition state[5,57,96], only slight diastereoselectivity is generally encountered in [2,3]sigmatropic rearrangements owing to the smaller energy differences between the *exo* and the *endo* transition state.

4.2. Diastereoselectivity on Formation on Other Stereocenters

The stereoselective formation of quaternary carbon centers is of importance in terpene syntheses, particularly with regard to the construction of spiro linkages. Results available so far suggest that the use of [2,3]sigmatropic rearrangements is of particular advantage for this purpose[22]. Examples are shown in Table 5.

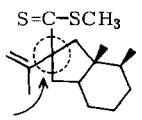
Table 5. Diastereoselectivity in reactions according to eq. (r).



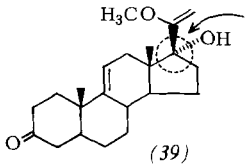
(36) (37)

X	Y	T [°C]	(36):(37)	Ref.
$C_6H_5S^{\oplus}$	$\overset{\ominus}{C}Cl_2$	25	97:3	[97]
$C_5H_5S^{\oplus}$	$\overset{\ominus}{O}$	25	92:8	[98]
$C_6H_5S^{\oplus}$	$\overset{\ominus}{C}H\ COOC_2H_5$	25	91:9	[97]
$\overset{\oplus}{N}$	$\overset{\ominus}{C}H\ CN$	−10	90:10	[99]

In contrast to these reactions, the corresponding [3,3]sigmatropic Claisen rearrangement[100] at 200 °C proceeded with very low stereoselectivity. It is also remarkable that the stereoselectivity in reactions (r) is largely independent of the nature of X and Y. This enhances the preparative flexibility in the use of [2,3]sigmatropic rearrangements for diastereoselective syntheses. Formation of the stereocenters marked in *(38)*[22] and *(39)*[101] serves as example.



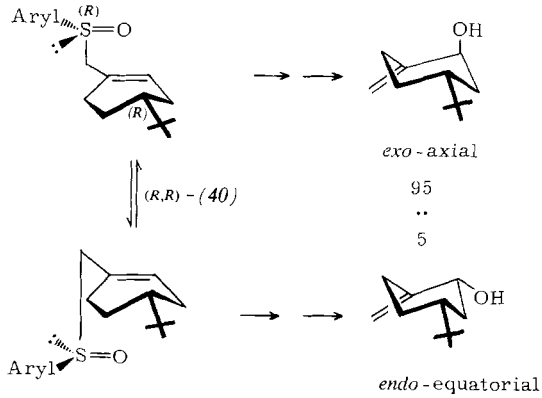
(38)



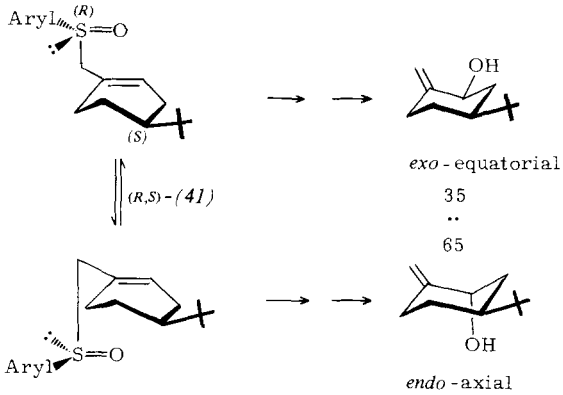
(39)

Diastereoselectivities with regard to another ring substituent are also found in the rearrangement of allyl sulfoxides *(40)* having an endocyclic double bond[102]. For example, the *R,R*-diastereomer *(40)* showed a pronounced tendency to rearrange *via* the *exo*-axial transition state. The *R,S*-diastereomer *(41)* reacts preferentially *via* the *endo*-axial transition state (Aryl = *p*-tolyl).

This situation can be interpreted[102] by assuming a 3.1-fold preference for rearrangement *via* the *exo* as against the *endo* transition state (cf. Section 3.2) and, moreover, a 6.2-fold preference for formation of an axial as against an equatorial bond[*]. These effects reinforce each other in the case of the diastereomer *(40)* and oppose each other in that of the diastereomer *(41)*. This striking preference for formation of



axial bonds has parallels in [3,3]sigmatropic rearrangements[6] and is in accord with general stereoelectronic principles[103].

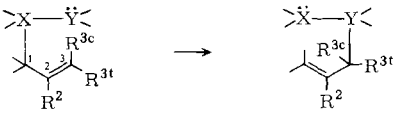


5. Conclusion

The *clou* of the stereochemistry of [2,3]sigmatropic rearrangements and of the corresponding [3,3]sigmatropic rearrangements, discussed in this article, lies in the mutual transformation of potentially chiral groups into prochiral ones, and prochiral groups into chiral centers—as is adequately illustrated by reactions (k) and (m). Its importance in stereoselective synthesis is apparent from fact that the stereochemical situation at an sp^3 center is transformed into a defined configuration of the resulting double bond and *vice versa*.

An attempt has been made in this article to draw up the rules governing transformation of chirality into prochirality and prochirality into chirality in [2,3]sigmatropic rearrangements. In preparative applications particular importance attends those factors which determine the degree of stereoselectivity in these reactions.

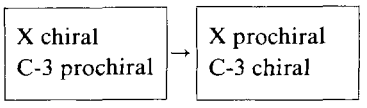
The stereochemical consequences of [2,3]sigmatropic rearrangements of type I [see eq. (b)] are recapitulated in Scheme 2.



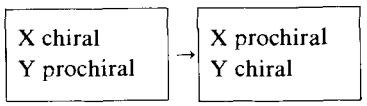
C-1 chiral C-3 prochiral	→	C-1 prochiral C-3 chiral

high stereoselectivity due to suprafacial reaction course

[*] Values calculated in the following manner: $95:5 \approx (3.1 \times 6.2):1$; $35:65 \approx 3.1:6.2$.



slight to pronounced stereoselectivity depending upon R^2 and R^{3c}



variable stereoselectivity since it has generally not been possible to simultaneously ensure chirality at X and homogeneous prochirality at Y

Scheme 2

Of the above-cited studies performed by our research team, the major contributions were made by Dr. S. Goldmann alongside those of R. Gerlach and Dr. N. Maak. Generous support from the Deutsche Forschungsgemeinschaft, the Verband der Chemischen Industrie, and the Doktor-Konrad-Adenauer-Stiftung is gratefully acknowledged.

Received: April 9, 1979 [A 279 IE]
German version: Angew. Chem. *91*, 625 (1979)

[1] *G. B. Bennett*, Synthesis *1977*, 589.
[2] *S. J. Rhoads, N. R. Raulins*, Org. React. *22*, 1 (1975).
[3] *D. J. Faulkner*, Synthesis *1971*, 175.
[4] *E. Winterfeldt*, Fortschr. Chem. Forsch. *16*, 75 (1970).
[5] *H. J. Hansen, H. Schmid*, Tetrahedron *30*, 1959 (1974).
[6] *F. E. Ziegler*, Acc. Chem. Res. *10*, 227 (1977).
[7] *J. Reucroft, P. Sammes*, Q. Rev. Chem. Soc. *25*, 135 (1971).
[8] *W. Sucrow, B. Schubert, W. Richter, M. Slopianka*, Chem. Ber. *104*, 3689 (1971); *W. Sucrow, P. P. Caldeira, M. Slopianka, ibid. 106*, 2236 (1973).
[9] *R. K. Hill, R. Soman, S. Sawada*, J. Org. Chem. *37*, 3737 (1972).
[10] *Y. Yamamoto, H. Shimoda, J. Oda, Y. Inouye*, Bull. Chem. Soc. Jpn. *49*, 3247 (1976).
[11] *R. K. Hill, H. N. Khatri*, Tetrahedron Lett. *1978*, 4337.
[12] *D. J. Faulkner, M. R. Petersen*, J. Am. Chem. Soc. *95*, 553 (1973).
[13] *G. Stork, T. Takahashi, I. Kawamoto, T. Suzuki*, J. Am. Chem. Soc. *100*, 8272 (1978).
[14] *K. K. Chan, A. C. Specian, G. Saucy*, J. Org. Chem. *43*, 3435 (1978).
[15] *G. A. Russell, G. J. Mikol*, Mech. Mol. Migr. *1*, 157 (1968).
[16] *R. A. W. Johnstone*, Mech. Mol. Migr. *2*, 249 (1969).
[17] *U. Schöllkopf*, Angew. Chem. *82*, 795 (1970); Angew. Chem. Int. Ed. Engl. *9*, 763 (1970).
[18] *J. E. Baldwin, J. E. Patrick*, J. Am. Chem. Soc. *93*, 3556 (1971).
[19] *R. W. Hoffmann, R. Hirsch, R. Fleming, M. T. Reetz*, Chem. Ber. *105*, 3532 (1972).
[20] *B. M. Trost, L. S. Melvin, Jr.*: Sulfur Ylides. Academic Press, New York 1975.
[21] *M. Moriwaki, Y. Yamamoto, J. Oda, Y. Inouye*, J. Org. Chem. *41*, 300 (1976).
[22] *D. A. Evans, C. L. Sims, G. C. Andrews*, J. Am. Chem. Soc. *99*, 5453 (1977).
[23] *P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller, K. Mislow*, J. Am. Chem. Soc. *90*, 4869 (1968).
[24] *J. E. Baldwin, J. DeBernardis, J. E. Patrick*, Tetrahedron Lett. *1970*, 353.
[25] *J. E. Baldwin, R. E. Hackler*, J. Am. Chem. Soc. *91*, 3646 (1969); *J. E. Baldwin, J. E. Brown, R. W. Cordell*, Chem. Commun. *1970*, 31; *J. E. Baldwin, M. C. H. Armstrong, ibid. 1970*, 631.
[26] *J. E. Baldwin, F. J. Urban*, Chem. Commun. *1970*, 165.
[27] *V. Rautenstrauch*, Chem. Commun. *1970*, 4.
[28] *U. Schöllkopf, K. Fellenberger*, Justus Liebigs Ann. Chem. *698*, 80 (1966).
[29] *W. Kirmse, M. Kapps, R. B. Hager*, Chem. Ber. *99*, 2855 (1966).
[30] *Y. Makisumi, S. Notzumoto*, Tetrabedron Lett. *1966*, 6393.
[31] *J. E. Baldwin, G. Höfle, S. C. Choi*, J. Am. Chem. Soc. *93*, 2810 (1971).
[32] *D. A. Evans, G. C. Andrews, C. L. Sims*, J. Am. Chem. Soc. *93*, 4956 (1971).
[33] *G. Höfle, J. E. Baldwin*, J. Am. Chem. Soc. *93*, 6307 (1971).
[34] *D. A. Evans, G. C. Andrews, T. T. Fujimoto, D. Wells*, Tetrahedron Lett. *1973*, 1385.
[35] *D. A. Evans, G. C. Andrews*, Acc. Chem. Res. *7*, 147 (1974).
[36] *S. Bravermann, H. Mechoulam*, Tetrahedron *30*, 3883 (1974).
[37] *J. G. Miller, W. Kurz, K. G. Untch, G. Stork*, J. Am. Chem. Soc. *96*, 6774 (1974).
[38] *H. J. Reich*, J. Org. Chem. *40*, 2570 (1975).
[39] *P. Metzner, J. Vialle, A. Vibet*, Tetrahedron Lett. *1976*, 4295.
[40] *B. B. Snider, N. J. Hrib, L. Fuzesi*, J. Am. Chem. Soc. *98*, 7115 (1976).
[41] *H. J. Reich, S. K. Shah*, J. Am. Chem. Soc. *99*, 263 (1977).
[42] *B. Cazes, S. Julia*, Bull. Soc. Chim. Fr. *1977*, 931.
[43] *C. Huynh, V. Ratovelomanana, S. Julia*, Bull. Soc. Chim. Fr. *1977*, 710.
[44] *M. Kodama, K. Shimada, S. Itô*, Tetrahedron Lett. *1977*, 2763.
[45] *D. F. Taber*, J. Am. Chem. Soc. *99*, 3513 (1977); *K. Kondo, T. Umemoto, Y. Takahatake, D. Tunemoto*, Tetrahedron Lett. *1977*, 113; *D. Tunemoto, Y. Takahatake, K. Kondo*, Chem. Lett. *1978*, 189; *K. Kondo, T. Umemoto, K. Yako, D. Tunemoto*, Tetrahedron Lett. *1978*, 3927; *B. M. Trost, J. H. Rigby*, J. Org. Chem. *43*, 2938 (1978).
[46] *F. Johnson*, Chem. Rev. *68*, 375 (1968).
[47] *W. C. Still, A. Mitra*, J. Am. Chem. Soc. *100*, 1928 (1978).
[48] *B. Giese*, Angew. Chem. *89*, 162 (1977); Angew. Chem. Int. Ed. Engl. *16*, 125 (1977).
[49] *M. Schlosser, J. Hartmann*, J. Am. Chem. Soc. *98*, 4674 (1976).
[50] *P. T. Lansbury, V. A. Pattison*, J. Org. Chem. *27*, 1933 (1962).
[51] *G. Büchi, M. Cushman, H. Wüest*, J. Am. Chem. Soc. *96*, 5563 (1974).
[52] *K. K. Chan, G. Saucy*, J. Org. Chem. *42*, 3828 (1977).
[53] *D. Barnard, T. H. Houseman, M. Porter, B. K. Tidd*, Chem. Commun. *1969*, 371.
[54] *Y. Gaoni*, Eighth International Symposium of Organic Sulphur Chemistry, Portorož (Yugoslavia) 1978, Abstracts of Papers p. 90.
[55] *S. Goldmann, R. W. Hoffmann, N. Maak, K. J. Geueke*, Chem. Ber., in press.
[56] *P. Cresson, S. Bancel*, C. R. Acad. Sci. Ser. *C 266*, 409 (1968).
[57] *P. Vittorelli, T. Winkler, H. J. Hansen, H. Schmid*, Helv. Chim. Acta *51*, 1457 (1968).
[58] *D. A. Evans, C. A. Bryan, C. L. Sims*, J. Am. Chem. Soc. *94*, 2891 (1972).
[59] *P. T. Lansbury, J. E. Rhodes*, Chem. Commun. *1974*, 21.
[60] *D. A. Evans, T. C. Crawford, T. T. Fujimoto, R. C. Thomas*, J. Org. Chem. *39*, 3176 (1974).
[61] *B. Cazes, S. Julia*, Bull. Soc. Chim. Fr. *1977*, 925.
[62] *M. Isobe, H. Iio, T. Kawai, T. Goto*, J. Am. Chem. Soc. *100*, 1940 (1978); *M. Isobe, H. Iio, M. Kitamura, T. Goto*, Chem. Lett. *1978*, 541.
[63] *E. Vedejs, M. J. Arco, J. M. Renga*, Tetrahedron Lett. *1978*, 523; *E. Vedejs, M. J. Arco, D. W. Powell, J. M. Renga, S. P. Singer*, J. Org. Chem. *43*, 4831 (1978); *R. Schmid*, Dissertation, Universität Zürich 1978.
[64] *P. Brownbridge, S. Warren*, J. Chem. Soc. Perkin Trans. I *1977*, 1131; *A. Ogiso, E. Kitazawa, M. Kurabayashi, A. Sato, S. Takahashi, H. Noguchi, H. Kuwano, S. Kobayashi, H. Mishima*, Chem. Pharm. Bull. Jpn. *26*, 3117 (1978).
[65] *K. Kosugi, H. Uda, S. Yamagiwa*, J. Chem. Soc. Chem. Commun. *1975*, 192; *Y. Masaki, K. Hashimoto, K. Kaji*, Tetrahedron Lett. *1978*, 4539, 5123.
[66] *D. A. Evans, G. C. Andrews, T. T. Fujimoto, D. Wells*, Tetrahedron Lett. *1973*, 1389; cf., however: *P. R. Ortiz de Montellano, C. K. Hsu, ibid. 1976*, 4215; *S. Yamagiwa, H. Sato, N. Hoshi, H. Kosugi, H. Uda*, J. Chem. Soc. Perkin Trans. I *1979*, 570; *P. Blatcher, S. Warren*, Tetrahedron Lett. *1979*, 1247.
[67] *K. B. Sharpless, R. F. Lauer*, J. Am. Chem. Soc. *94*, 7154 (1972).
[68] *P. A. Grieco, D. Boxler, K. Hiroi*, J. Org. Chem. *38*, 2572 (1973).
[69] *W. C. Still, J. H. McDonald III, D. B. Collum, A. Mitra*, Tetrahedron Lett. *1979*, 593.
[70] *P. A. Grieco*, J. Chem. Soc. Chem. Commun. *1972*, 702.
[71] *P. A. Grieco, R. S. Finkelhor*, J. Org. Chem. *38*, 2245 (1973).
[72] *J. E. Baldwin, R. E. Hackler, D. P. Kelly*, J. Am. Chem. Soc. *90*, 4758 (1968).
[73] *G. M. Blackburn, W. D. Ollis*, Chem. Commun. *1968*, 1261; *G. M. Blackburn, W. D. Ollis, S. Smith, I. O. Sutherland, ibid. 1969*, 99.
[74] *V. Rautenstrauch*, Helv. Chim. Acta *54*, 739 (1971).
[75] *G. Büchi, R. M. Freidinger*, J. Am. Chem. Soc. *96*, 3332 (1974).
[76] *K. Mislow*: Introduction to Stereochemistry. Benjamin, New York 1966, p. 131; Einführung in die Stereochemie. Verlag Chemie, Weinheim 1967, p. 121.
[77] *U. Schöllkopf, K. Fellenberger, M. Rizk*, Justus Liebigs Ann. Chem. *734*, 106 (1970).
[78] *S. Bravermann*, Int. J. Sulfur Chem. *C6*, 149 (1971).
[79] a) *Y. Yamamoto, J. Oda, Y. Inouye*, J. Org. Chem. *41*, 303 (1976); b) *D. N. Jones, J. Blekinsopp, A. F. C. Edwards, E. Helms, R. J. K. Taylor*, J. Chem. Soc. Perkin Trans I *1973*, 2602.
[80] *S. Valentine, Jr., J. W. Scott*, Synthesis *1978*, 329.
[81] *R. K. Hill, N. W. Gilman*, Tetrahedron Lett. *1967*, 1421; Chem. Commun. *1967*, 619.
[81a] *H. E. Zimmerman, D. R. Diehl*, J. Am. Chem. Soc. *101*, 1841 (1979), footnote 8.
[82] *R. W. Hoffmann, S. Goldmann, R. Gerlach, N. Maak*, Chem. Ber., in press.
[83] *H. Felkin, C. Frajerman*, Tetrahedron Lett. *1977*, 3485.
[84] *B. M. Trost, R. F. Hammen*, J. Am. Chem. Soc. *95*, 963 (1973).
[85] *B. M. Trost, W. G. Biddlecom*, J. Org. Chem. *38*, 3438 (1973).
[86] *S. J. Campbell, D. Darwish*, Can. J. Chem. *54*, 193 (1976).
[87] *T. Numata, S. Oae*, Tetrahedron Lett. *1977*, 1337.
[88] *M. Mikołajczyk, A. Zatorski, S. Grzejszczak, B. Costisella, W. Midura*, J. Org. Chem. *43*, 2518 (1978).

[89] M. Yoshimoto, S. Ishihara, E. Nakayama, N. Soma, Tetrahedron Lett. 1972, 2923.
[90] S. Mageswaran, W. D. Ollis, I. O. Sutherland, J. Chem. Soc. Chem. Commun. 1973, 656.
[91] S. Mageswaran, W. D. Ollis, I. O. Sutherland, Y. Thebtaranonth, Chem. Commun. 1971, 1494.
[92] R. W. C. Cose, A. M. Davies, W. D. Ollis, C. Smith, I. O. Sutherland, Chem. Commun. 1969, 293.
[93] K. Kondo, I. Ojima, J. Chem. Soc. Chem. Commun. 1972, 62.
[94] L. Leger, M. Saquet, A. Thuillier, S. Julia, J. Organomet. Chem. 96, 313 (1975).
[95] V. Rautenstrauch, Chem. Commun. 1970, 526.
[96] R. E. Ireland, R. H. Mueller, A. K. Willard, J. Am. Chem. Soc. 98, 2868 (1976).
[97] G. Andrews, D. A. Evans, Tetrahedron Lett. 1972, 5121.
[98] D. A. Evans, G. C. Andrews, J. Am. Chem. Soc. 94, 3672 (1972).
[99] L. N. Mander, J. V. Turner, J. Org. Chem. 38, 2915 (1973).
[100] H. O. House, J. Lubinowski, J. H. Good, J. Org. Chem. 40, 86 (1975).
[101] V. H. van Rheenen, K. P. Shephard, J. Org. Chem. 44, 1582 (1979).
[102] R. W. Hoffmann, R. Gerlach, S. Goldmann, Tetrahedron Lett. 1978, 2599; Chem. Ber., in press.
[103] O. Eisenstein, J. Klein, J. M. Lefour, Tetrahedron 35, 225 (1979), and references cited therein.

Adiabatic Photoreactions of Organic Molecules

By Nicholas J. Turro, Jeffrey McVey, V. Ramamurthy, and Peter Lechtken[*]

An adiabatic photoreaction is a chemical process that occurs entirely on a single excited electronic energy surface. As a rule, most photoreactions of organic molecules start on an excited electronic surface but "jump" to a lower surface somewhere along the reaction coordinate. There are, however, exceptions to this general rule. For example, photoreactions involving small structural changes and minor alterations in covalent bonding (*e.g.*, proton transfers and complex formation) are commonly found to occur adiabatically. The purpose of this review is to survey examples of more complicated adiabatic photoreactions such as fragmentations, electrocyclic rearrangements, and geometrical isomerizations. The concepts employed are presented in an introductory discussion.

1. Introduction

What is an "adiabatic photoreaction"? According to *Förster*[1]: *an adiabatic photoreaction is a chemical process that occurs entirely on a single excited electronic energy surface.* The notion of electronic excitation is a key ingredient in any *photochemical* process and the notion of passage along a *single energy surface* is the essence of an *adiabatic* process. In this spirit, most thermal reactions are adiabatic because they tend to occur entirely on a ground state electronic surface. *Every overall photoreaction,* on the other hand, is diabatic (or nonadiabatic) since it is initiated with molecules on excited electronic surfaces, but terminates with (isolated) products in their ground states. In order to visualize more precisely what is happening at the molecular level, let us first discuss the "three state" and the "energy surface" concepts.

2. The Three State Concept: S_0, T_1, and S_1

An important paradigm of organic photochemistry is the *three state concept,* or the rule that understanding the mechanisms of most organic photoreactions in solution requires explicit consideration of only three electronic states: S_0, the electronic ground state, T_1, the lowest energy triplet state, and S_1, the lowest energy excited singlet state. The postulate that T_1 and/or S_1 are the starting points of all chemically significant photochemical processes is an extension of *Kasha*'s rule[2] that electronic emission from organic molecules (in the condensed phase) generally occurs only from S_1 (fluorescence) or from T_1 (phosphorescence).

The three state concept is a good starting point for analyses of the electronic spectroscopy of organic molecules, which involves (more or less) "vertical" radiative or radiationless jumps between surfaces at geometries similar to the initial equilibrium geometry of S_0. A useful extension of the three state concept to photochemistry involves the S_0, T_1, and S_1 *surfaces* that occur along a reaction pathway. We now briefly review the key features of the energy surface concept.

3. The Energy Surface Concept[3]

A molecule in a particular electronic state may exist with various spatial configurations of its nuclei, each nuclear configuration corresponding to a definite potential energy (*i.e.*, kinetic energy due to nuclear motion equals zero) of the molecule. A map of a molecule's potential energy in a given electronic state *versus* nuclear configuration is termed a *potential energy surface.* It is important to realize that for any given nuclear change (say, from nuclear structure R, corresponding to an initial reactant structure, to a nuclear structure P, corresponding to a final product structure) a different potential energy surface exists for *each electronic state.*

[*] Prof. Dr. N. J. Turro
Department of Chemistry, Columbia University
New York, NY 10027 (USA)
Prof. Dr. J. McVey
Chemistry Department, Princeton University
Princeton, NJ 08540 (USA)
Prof. Dr. V. Ramamurthy
Department of Organic Chemistry, Indian Institute of Science
Bangalore 560012 (India)
Dr. P. Lechtken
BASF AG, D-6700 Ludwigshafen/Rhein (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0572 $ 02.50/0

Imagine now a nuclear configuration that happens to be of interest to you and label the initial nuclear structure R and the final nuclear structure P. Now imagine proceeding from structure R to structure P *via* a number of different specific molecular choreographies. Each of these "pathways" from R to P will possess a set of energy surfaces corresponding to the change in potential energy of each initial state of R as a function of nuclear configuration. However, for a given electronic state there will generally exist a unique lowest energy surface. Schematically, a given R→P pathway may be visualized in terms of *energy curves* (a topological simplification of an energy surface) as shown in Figure 1.

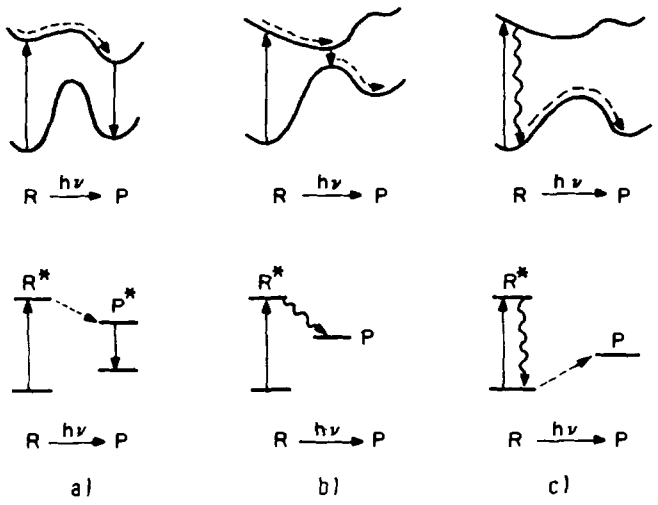


Fig. 1. Schematic representation of (a) an adiabatic photoreaction, (b) a diabatic photoreaction, and (c) a "hot" ground state reaction. The upper drawings provide a surface description and the lower drawings provide a state level description. →, radiative "jump"; - - →, motion on surface; ⇝, radiationless "jump".

The important points to remember when employing such structure-energy diagrams are: (1) they are too good to be true, *i.e.*, they are oversimplified; (2) they contain very general, qualitative topological information only; (3) the surfaces corresponding to many configurational transformations which take R→P may possess common topological features.

3.1. The Trajectory of a "Representative Point" on an Energy Surface

An adiabatic photoreaction occurs when an electronically excited reactant R* is converted into an electronically excited product P* on a single energy surface. We may discuss this interconversion in terms of the trajectory of a "representative point" on an energy surface. The "point" represents the state of the molecule and contains information on the molecule's energy and nuclear, electronic, and spin structure. The trajectory of the point on a given energy surface corresponds to motion along a reaction coordinate with the molecule in a given (S_0, T_1, or S_1) electronic state. Thus,the overall conversion of structure R to structure P may be viewed as occurring on the S_0, T_1, or S_1 surfaces. Although the choreography of the nuclei in space may be similar (or nearly identical) for the overall R→P transformation on each surface, the actual shape of the S_0, T_1, or S_1 surface traversed may be quite different.

A representative point on an excited surface is always subjected to a force that attracts it to a lower surface. The origin of this force is the electrostatic interactions of nuclei and electrons. If, for a given nuclear configuration, the electronic configuration is excited, there will always exist an attracting force to produce states of lower energy. Thus, during its trajectory along *any* excited surface, the representative point is being inexorably "attracted" to lower surfaces and jumps from upper surfaces to lower energy surfaces will occur spontaneously and inevitably. However, the *rates* (and efficiencies) of spontaneous surface jumps, in analogy to spontaneous chemical reactions, depend on *available mechanisms* open to the representative point as it surveys various nuclear configurations during its motion on a given surface.

If an adiabatic photoreaction is to occur on the T_1 or S_1 surface, then along the reaction coordinate there can occur no nuclear geometries from which the representative point can efficiently "jump" to a lower surface. Jumps between surfaces are most efficient when the representative point finds itself in a fairly stable energy minimum (a large energy barrier exists for further motion along the same energy surface) or when the representative point approaches a nuclear geometry for which two surfaces (one of which it is on) become close in energy (potential for strong mixing of states).

Thus, if the representative point is on an excited surface which is "far away" from all lower energy surfaces for the entire trajectory corresponding to the structural conversion R→P, in the absence of energetic restraints, the adiabatic photoreaction R*→P* should be efficient. In the absence of dynamic effects, there is one important exception to the expectation that a surface jump by the representative point will occur efficiently when two surfaces come close to each other. The jump will be inefficient if the two approaching surfaces differ substantially in electronic or spin structure[3c].

For example, "zero order" crossings of singlet surfaces and triplet surfaces remain as crossings unless a very strong spin orbit coupling force exists when the representative point is in the "crossing region."

3.2. Adiabatic, Diabatic, and "Hot" Ground State Photoreactions[3c]

It is convenient to classify photoreactions in terms of three types which are based on the distinction as to whether electronic de-excitation occurs (a) when the nuclear configuration is essentially that of the primary product(s); (b) when the nuclear configuration is intermediate between that of the reactant(s) or primary product(s); (c) when the nuclear configuration is that of the reactant(s). Case a is an adiabatic photoreaction. Although both case b and case c are diabatic photoreactions, we shall term case b as a "diabatic photoreaction" and c as a "hot" ground state photoreaction.

To illustrate these distinctions consider Figure 1, in which three energy surface situations for an overall R→P conversion are shown schematically (for simplicity just one excited surface is shown).

In each case light is employed to take the representative point from the ground surface to the excited surface ($R + h\nu \rightarrow R^*$). Thermal energy will when "propel" the repre-

sentative point (dotted line indicates the trajectory) along the reaction coordinate.

For case (a) the representative point is imagined to move over a relatively small energy barrier from R* to P*. Since the surfaces are "far apart" at all nuclear geometries along the reaction coordinate, a surface jump is improbable over the entire reaction coordinate. The photoreaction, therefore, is *adiabatic*. Commonly, energy barriers separating reactant geometry from product geometry are *smaller* on the excited surface for the *same reaction coordinate*. In favorable cases the occurrence of an adiabatic reaction is manifested by the observation of emission of light as a result of the radiative transition $P^* \rightarrow P + h\nu$. If the excited-state barrier is too high for the representative point to progress from R* to P*, emission from R* to R may occur instead of emission from P* to P.

In case (b) an excited surface and a ground surface approach one another at some geometry that is intermediate between that of R and P. Near this geometry, radiationless jumps from the excited surface to S_0 are favored. However, with respect to the maximum on the S_0 surface we can imagine jumps leading to geometries "to the left" (return to R and a net photophysical process) or "to the right" (formation of P and a net photochemical process). For case (b), it is clear that the terms photophysical and photochemical may become blurred when one is discussing processes occurring for the nuclear geometries in which the two surfaces *come close*. When the representative point proceeds "to the right" after the surface jump, it does so on the ground state surface until the nuclear geometry of P is achieved. Since the photoreaction involves a surface jump between structures R and P it is *diabatic*.

As a third example, in case (c) we suppose that a vertical jump from the excited surface puts the representative point on the ground surface with a *large excess of thermal energy*. As a result the minimum on the ground surface (corresponding to an intermediate on the ground surface) cannot "hold" onto the representative point and the latter escapes from the minimum (corresponding to the vertical jump) to a second minimum corresponding to P. We suppose that by the time the representative point reaches P its excess energy has been removed (say, by collisions with molecules in its environment) and eventually settles into the $v = 0$ level of P. Case (c) is a special kind of diabatic reaction and is called a "hot" ground state reaction.

It appears that most organic photoreactions conform to case (b). As a result, a knowledge of both photophysical and photochemical radiationless processes is crucial for an understanding of the molecular photochemistry of organic compounds. Of special importance is knowing when surfaces "get close" and what mechanisms are available to allow the representative point to make its jump to another surface.

Classically, we may view radiationless transitions as occurring from a "hole" or "funnel" in an upper surface at critical molecular geometries[3f]. When the representative point must search for a considerable time for the correct geometry required for a surface jump (thermal equilibrium), we speak of a "hole" on the excited surface at that geometry. When the representative point makes a surface jump nearly every time it achieves a certain geometry, we speak of a "funnel" on the excited surface of that geometry.

From the preceding discussion it is clear that energetically allowed adiabatic photoreactions can be anticipated when the following features of the surfaces are known:

1) the location of the minima in S_0, S_1, and T_1;
2) the location of maxima in S_0, S_1, and T_1;
3) the electronic interactions which cause the separation of the surfaces;
4) the geometries for which two surfaces come "close together";
5) the mechanisms which mix electronic states when the representative point is in an excited state minimum or near a geometry for which surfaces come "close together".

3.3. Typical Surface Topologies

Scrutiny of a broad range of photoreactions reveals that several "surface topologies" suffice to serve as a starting point for mechanistic analysis. For simplicity, we shall consider the following categories:

(a) "orbital symmetry allowed" ground state reactions;
(b) "orbital symmetry forbidden" ground state reactions;
(c) reactions producing diradical products.

Surface topologies typical of each of these categories are shown in Figure 2. In case (a) the ground surface and the excited surfaces are generally "far apart" along the reaction coordinate (small ground state barrier).

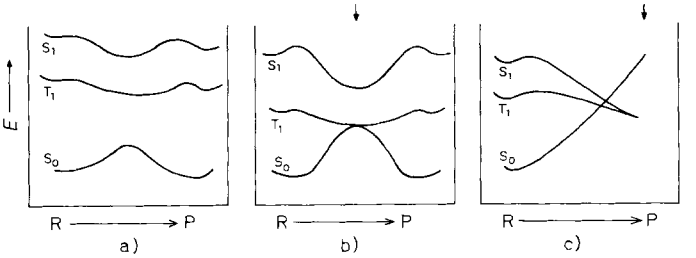


Fig. 2. Three commonly encountered surface topologies for the conversion of R into P. (a) Orbitally allowed ground state reaction; no diradical structure along the reaction coordinate; (b) orbitally forbidden ground state reaction; diradical structure between reactant and product (arrow); (c) reaction producing a diradical product (arrow).

In case (b) the ground and excited surfaces come "close together" at the geometry of the transition state for the ground state reaction. The important features of this topology are:

(1) the occurrence of minima in the S_1 and T_1 surface near the geometry corresponding to the transition structure;
(2) the diradical electronic character of the transition structure;
(3) the close approach of the S_0 and T_1 surfaces at the transition structure.

In case (c) the ground surface and excited surfaces come "close together" and as the primary photochemical product is formed at this diradical geometry the S_1 and T_1 surfaces essentially "touch".

4. Examples of Adiabatic Organic Photoreactions

Several years ago *Förster* pointed out[1] that adiabatic organic photoreactions involving protolytic processes (acid-base reactions)[4a] and weak complexation (excimer and exciplex

formation)[4b] are well known, but that documented examples of adiabatic organic photoreactions involving carbon-carbon bond breaking and making were almost unknown[5]. During the past five years this situation has changed. We now review the several classes of photoreactions for which there is substantial evidence for an adiabatic step involving an electronically excited surface.

4.1. Adiabatic Photochemical Electrocyclic Reactions

Several important examples of adiabatic photoreactions have been found in the electrocyclic ring opening and ring closing reactions of aromatic compounds. In particular, aromatic systems based on "Dewar" structures [*e.g.*, *(1)*, *(2)*, and *(3)*] undergo smooth electrocyclic ring opening to the corresponding aromatic hydrocarbon upon heating or photochemical excitation[6-9]. The thermal rearrangement of *(1)* to produce benzene is chemiluminescent[10]. Significantly, there is evidence that each "Dewar" compound undergoes a photochemical adiabatic ring opening on a S_1 and/or T_1 surface.

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

In the case of *(1)*, excitation of S_1 does not lead to formation of S_1 of benzene[7]. The experimental support for this conclusion is based on the observation of a "quantum chain" process involving T_1 of benzene upon triplet photosensitized excitation of *(1)* [confirming the occurrence of a *(1)* (T_1)→benzene (T_1) pathway] and the failure to observe fluorescence of benzene upon direct photoexcitation of *(1)* [denying the occurrence of a *(1)* (S_2)→benzene (S_1) pathway].

(1) S_1 T_1

The quantum chain pathway involves the reaction of triplet benzene with *(1)* to yield benzene (S_0) plus benzene (T_1)[7]. The process is formally catalytic and, since a benzene triplet is produced, a chain propagation sequence is possible. Indeed, the limiting quantum yields for photosensitized ring opening of *(1)* are considerably greater than unity.

T_1 *(1)* S_0 T_1

In the case of *(2)*, the situation is a bit more interesting since both *(2)* (S_1) and *(2)* (T_1) undergo adiabatic ring opening to naphthalene S_1 and T_1, respectively[8] (Fig. 3).

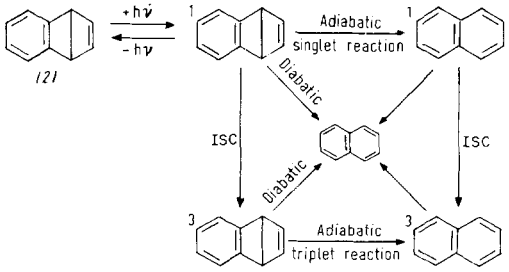


Fig. 3. Summary of the photochemistry and photophysics of Dewar naphthalene *(2)*.

The experimental support for the reactions shown in Figure 3 is derived from the following studies. The photochemical conversion of *(2)* into naphthalene was examined in solution at room temperature and at 77 K in EPA matrices[8]. Excitation of *(2)* in *n*-hexane solution at 300 K results in two emission bands. One of the emissions (290 nm, $\Phi_f = 0.001$) was that of normal fluorescence of *(2)* whereas the second structured emission (310–380 nm, $\Phi_f = 0.095$) was identical to that of naphthalene fluorescence. The naphthalenic emission was shown not to be due to small amounts of naphthalene contaminants by doping experiments and analysis of excitation spectra. The fluorescence lifetime of this emission was measured as 110 ± 5 ns, identical to that of photoexcited naphthalene fluorescence. No phosphorescence was observed in fluid solutions.

At 77 K in an EPA matrix, excitation of *(2)* at 268 nm leads to fluorescence of *(2)* ($\Phi_f = 0.11$) and to both a naphthalenic fluorescence (310–380 nm, $\Phi_f = 0.14$) and a naphthalenic phosphorescence (460–560 nm, $\Phi_p = 0.04$). The lifetime of the phosphorescence was 2.3 ± 0.25 s, identical to that of photoexcited naphthalene phosphorescence. Triplet sensitization of *(2)* in EPA at 77 K with acetophenone also leads to naphthalenic phosphorescence[8].

At 300 K, the adiabatic conversion of singlet Dewar naphthalene into singlet naphthalene is 49% efficient and the adiabatic path to ground state naphthalene is 34% efficient. At 77 K the efficiency of the adiabatic triplet state conversion, triplet *(2)* into triplet naphthalene, may approach unity.

It appears that *(3)* (S_1) undergoes adiabatic ring opening to anthracene (S_1), but no data relevant to the behavior of *(3)* (T_1) are available at the present time[9].

(3) (S_1) S_1

The conversion of Dewar anthracene *(3)* into anthracene was studied in solution at 300 K[9]. The fluorescence emission spectra of *(3)* consist of the fluorescence of *(3)* and an anthracene-like emission. Doping experiments and excitation spectra indicate that the anthracene emission is derived directly from *(3)* and not from energy transfer to trace anthracene contaminants. The emission lifetime was 24.5 ± 0.3 ns, considerably longer than that of photoexcited anthracene (4.9 ns). This means that some precursor of anthracene S_1, *i.e.*, *(3)* (S_1), persists for about 25 ns and that the emission from anthracene (S_1) is fast relative to the *(3)* (S_1) → anthra-

cene (S_1) rearrangement. Quantitative analysis showed that the adiabatic conversion in the singlet state, *(3)* (S_1) → anthracene (S_1) accounts for 10% in the overall decay kinetics of *(3)* (S_1).

These adiabatic photoreactions may be analyzed in terms of the surface topology for an orbital symmetry forbidden ground state reaction, since each is formally a disrotary electrocyclic ring opening[11, 15]. Ground state forbidden electrocyclic reactions possess a characteristic S_0, T_1, and S_1 surface topology, related to that for simple *cis-trans* isomerization of an ethylene *via* twisting about the C C bond (Fig. 4). The latter serves as a prototype for ground state forbidden pericyclic reactions[3]. The important features of this simple surface topology are:

(1) the presence of a maximum in the ground state surface corresponding to an antiaromatic or diradical transition structure;
(2) the presence of a minimum on the S_1 surface near the structure corresponding to the diradical structure;
(3) the occurrence of a "touching" or close approach of the T_1 and S_0 surfaces at the diradical structure.

The reaction coordinate is that of the rehybridization of the 1-C and 4-C orbitals to sp^2 geometry. The presence of a lower state maximum at the S_0 equilibrium geometry and upper state minimum on S_1 corresponding to the diradical structure provides for a very effective deactivation. A jump from the excited state surface to the ground state surface, a diabatic process, is possible and evidently occurs when S_1 of *(1)* is excited, *i.e.*, *(1)* (S_1) → benzene (S_0).

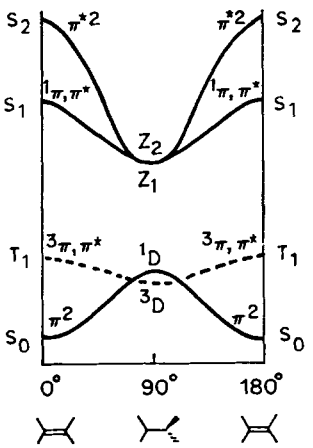


Fig. 4. The surface topology for *cis-trans* isomerization about a carbon-carbon double bond. This topology is a prototype for ground state forbidden pericyclic reactions. Z = zwitterionic states, D = diradical states.

In the case of Dewar compounds *(2)* and *(3)* the high exothermicity of the conversion of Dewar into aromatic species may distort the normal energy surfaces and tilt[15] the excited state surface, theoretically allowing for the production of excited state products (Fig. 5). The close approach of S_0 and T_1 at the diradical geometry will provide an efficient pathway for a $T_1 \rightarrow S_0$ jump only if the diradicaloid structure possesses strong spin-coupling. This is *not* the situation in general for any hydrocarbon structure. As a result, the conversions of the triplets of *(1)*, *(2)*, and *(3)* to the T_1 states of the corresponding aromatic hydrocarbons are efficient.

Should thermolysis follow the reaction coordinate of Figure 5, a low yield of *triplets* is expected in a *chemiluminescent*

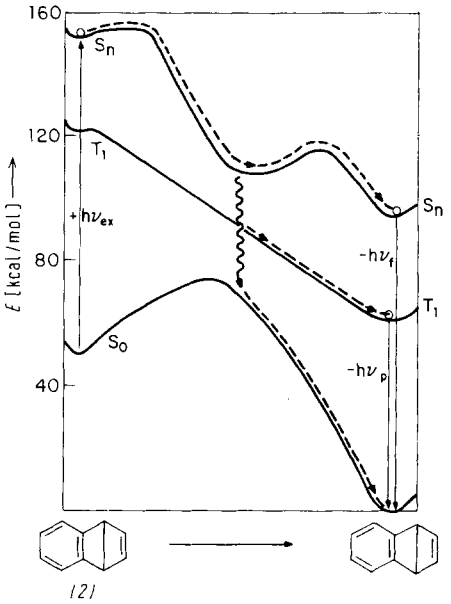


Fig. 5. Interpretation of the conversion of Dewar naphthalene *(2)* to naphthalene in terms of the surface topology for a ground state forbidden pericyclic reaction.

diabatic process, as is found to be the case for the parent of the series, Dewar benzene *(1)*.

The benzvalene structure [*e.g.*, *(4)* and *(5)*] has also been found to be involved in adiabatic photoreactions. In analogy to Dewar benzene, *(4)* was found to undergo adiabatic ring



(4) *(5)*

opening to benzene on the triplet surface but not on the singlet surface[16].

In the case of *(5)*, the conversion of *(5)* (T_1) → naphthalene (T_1)[17] occurs very efficiently. No evidence for a significant efficiency of the *(5)* (S_1) → naphthalene (S_1) reaction has been obtained.

As in the case of *(1)*, the evidence for the triplet adiabatic reaction *(4)* (T_1) → benzene (T_1) stems from the occurrence of a triplet photosensitized "quantum chain" sequence[16]. In this case, benzene triplets interact with benzvalene to yield benzene (S_0) and benzene (T_1).

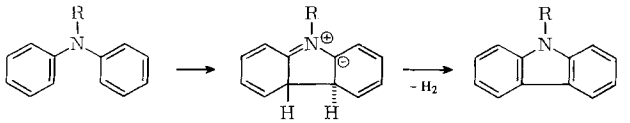


T_1 *(4)* S_0 T_1

The occurrence of such a quantum chain was found to depend on the energy of the triplet sensitizer. It was found that if the sensitizer triplet energy was >63 kcal/mol, the formation of benzene (T_1) was efficient, whereas if the sensitizer triplet energy was <63 kcal/mol, the formation of benzene (T_1) was inefficient. These observations were interpreted in terms of excitation of *two* triplets of *(4)*. Sensitized excitation of the lower energy triplet of *(4)* ($E <$ 63 kcal/mol) does not result in adiabatic ring opening to benzene (T_1), whereas excitation of the higher energy triplet of *(4)* ($E >$ 63 kcal/mol)

results in adiabatic electrocyclic ring opening to benzene triplet.

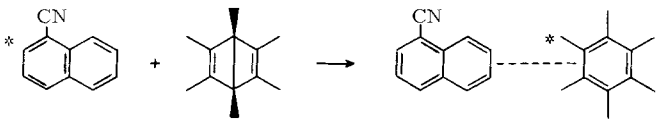
In contrast to photochemical electrocyclic ring openings, photochemical electrocyclic ring closures are not generally adiabatic. These reactions often are constrained to be diabatic because reaction endothermicity makes the adiabatic pathway energetically forbidden. There is, however, one case for which the photochemical generation of an excited state product has been suggested[18,19]. Excitation of triphenylamine (or *N*-methyl-*N*,*N*-diphenylamine) in hydrocarbon solvents at room temperature yields corresponding carbazoles under oxidative conditions from their excited triplet state[20-22]. The suggested intermediate for this reaction is ylide *(6)*, possibly resulting from "6e" cyclization. Evidence for this ylide comes from the detection of an absorption due to *(6)* during flash



R = C_6H_5, CH_3 *(6)*

photolysis. The results of these flash spectroscopic studies suggested that the triplet of diphenylamine converts adiabatically into the triplet of *(6)*.

Photoexcitation of 1-naphthalenecarbonitrile *(7)* in the presence of hexamethyldewarbenzene *(1a)* (hexane solution, room temperature) results in generation of a singlet exciplex of hexamethylbenzene-1-naphthalenecarbonitrile *(8)*[23]. It is proposed that the reaction is adiabatic, *i.e.*, excited 1-naph-



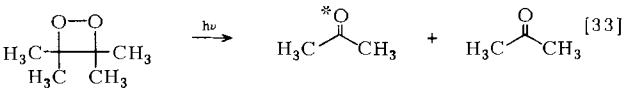
(7) *(1a)* *(8)*

thalenecarbonitrile *(7)* interacts with the Dewar compound *(1a)* to cause isomerization and formation of the singlet exciplex, all on the S_1 energy surface.

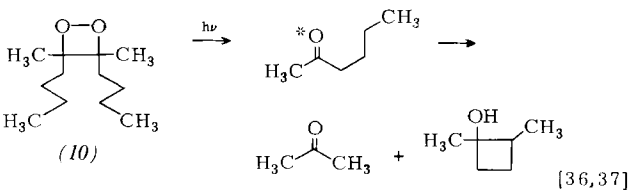
4.2. Cycloeliminations

Cycloelimination reactions provide a second general type of process that, in a few special cases, exhibits adiabatic photochemistry. As in the case of valence isomerization, the general feature of the close approach in coordinate space and energy of the excited electronic surface to that of the ground state surface along the reaction coordinate is expected to favor a diabatic photochemical process yielding ground state products[24,25]. Product luminescence has, however, been observed in several reaction systems in which an adiabatic process successfully competes with surface jumps to S_0.

One remarkable example is that of the adiabatic photodissociation of 1,2-dioxetanes. Dioxetanes ("dimers" of corresponding carbonyl compounds) undergo quantitative dissociation to carbonyl products both upon thermolysis and upon photolysis[26-41]. Dioxetanes possess a high energy content with respect to carbonyl products ($\approx$63 kcal/mol), require low energy of activation for thermal decomposition ($\approx$24 kcal/mol) and exhibit efficient thermal generation of triplet carbonyl products[27]. Direct or sensitized excitation of dioxetanes, *e.g. (9)* and *(10)*, has been shown to produce electronically excited carbonyl products.



(9) [33]



(10) [36,37]

The generation of electronically excited products was identified in these cases either directly by their emission or indirectly through consideration of the photochemical products. One of the important observations was the dependence of the ratio of singlet to triplet excited acetone on the wavelength of excitation in the case of tetramethyldioxetane *(9)* as given in Table 1[33]. Similarly, in the case of *(10)* the yield of triplet 2-hexanone was dependent on the triplet energy of the sensitizers used, but the mechanism of decomposition by these sensitizers is not clear[36,37].

Table 1. Production of electronically excited acetone in the photochemical decomposition of tetramethyl dioxetane *(9)* [33].

Irradiation conditions	$(CH_3)_2CO$ S_1 [%]	$(CH_3)_2CO$ T_1 [%]	Comments
Direct, 366 nm	10	43	[a]
Direct, 320 nm	25		[b]
Direct, 297 nm	30		[b]
Direct, 240 nm	35		[b]

[a] At 6 °C in benzene solution by the method of *P. Lechtken* and *N. J. Turro*, J. Am. Chem. Soc. *94*, 2886 (1972). The exciting light was absorbed solely by *(9)*. [b] Determined by comparison of dioxetane luminescence with that of equally absorbing acetone solutions.

The photolysis of *(9)* has been studied by picosecond spectroscopy[39] in order to determine the rate of formation of acetone singlet from *(9)**. Remarkably, the "rise time" of acetone fluorescence was found to be $<10\times10^{-12}$ s, *i.e.*, the conversion of *(9)** into acetone (S_1) occurs in just a few vibrations.

The observation of electronically excited products allows one to categorize the photodecomposition of dioxetanes as an adiabatic process. A model[41] for the adiabatic photoreactions of dioxetanes bearing a topological similarity to the general picture presented for photocycloreversions of valence isomers of aromatic compounds is available (Fig. 6)[6,11,12]. A feature that may allow the decomposition of dioxetanes to be adiabatic as opposed to most other fragmentation reactions is once again the large tilt in the excited state surface of the correlation diagram brought about by the thermal content of dioxetanes. This may result in a *shallow* minimum on the excited surface and allows the molecules to "spill over" this shallow minimum on the excited surface to excited carbonyl products. We do not wish to rule out "dynamic" effects as

the source of the high efficiency of adiabatic photochemistry, *i.e.*, the nuclear motion on the T_1 surface may be so fast that intersystem crossing at S-T crossings cannot compete with motion on the T_1 surface. Shallow minima on the excited singlet surface may facilitate conversion to the lower surface (triplet). This leakage to the T_1 surface would occur in competition with crossing the barrier on the excited surface. The wavelength dependence of the ratio of singlet to triplet excited acetone production may then be indicative of the competition between crossing the barrier on the same excited surface and jumping to the lower surface. Molecules with higher energy content (short wavelength excitation) cross the barrier more efficiently (to produce singlet excited acetone) than those of lower energy (longer wavelength excitation) which jump to the lower surface to produce triplet acetone.

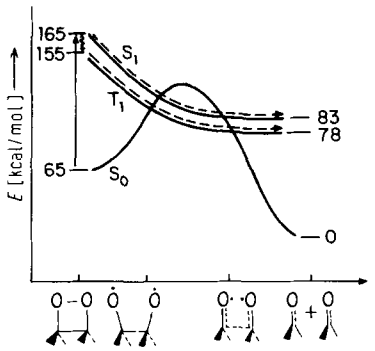
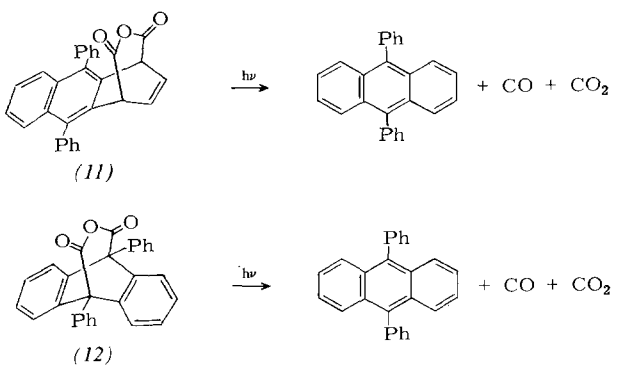
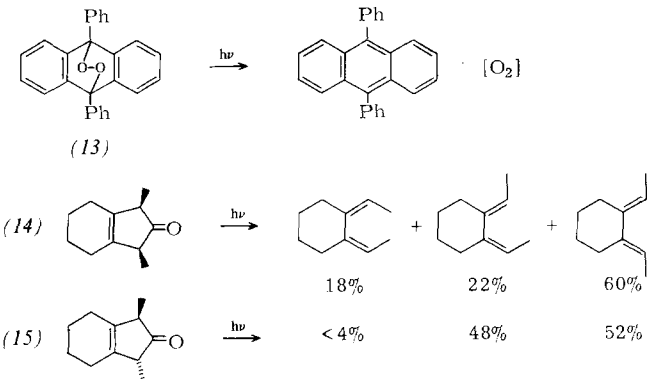


Fig. 6. Schematic representation of the S_0, T_1, and S_1 surfaces of tetramethyl-1,2-dioxetane *(9)* for the decomposition into two acetone molecules.

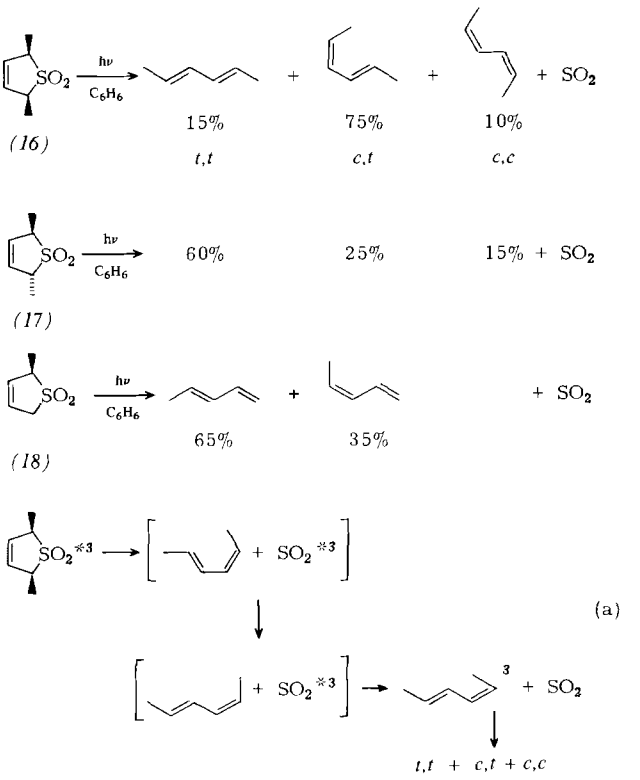
Although the cycloreversion of "Dewar arenes" and the photodecomposition of dioxetanes are different in kind, their adiabatic character may be due to the same tilting of the excited state surface due to the large relative energy content of the reactants (Fig. 6). This results in an effective decrease in the energy barrier between the "funnel minimum"[42] and the product excited state on the excited hypersurface allowing for adiabatic passage to excited state products. Although the large imbalance between reactant and product states exists in many other exothermic reactions, the diabatic processes are present in competition and often prevent the observation of product state luminescence. An example of this is found in the direct singlet state excitation of 1,4- and 9,10-dicarboxylic anhydrides *(11)* and *(12)* which results in the formation of 9,10-diphenylanthracene[43, 44]. An extensive search for excited state products was not successful. This illustrates that there are many factors controlling the nature of photoreactions and points out the need for further study in this area.



Short wavelength excitation of 9,10-diphenylanthracene endoperoxide *(13)* gives 9,10-diphenylanthracene and oxygen[45]. In analogy with the behavior of dioxetanes this photodecomposition might possibly generate singlet oxygen, but results of such an adiabatic channel have not been reported. This reaction may be adiabatic for the additional reason that generation of ground state oxygen (triplet) is a spin forbidden process. It should, however, be cautioned that if the molecular motion and spin motion are coupled (availability of a spin flip mechanism)[46] the conversion of singlet excited reactants into ground state triplet products (or triplet excited state reactants into ground state singlet products) would be allowed and an adiabatic path may not be important. This is illustrated by the excited triplet decarbonylation of cyclopentenone *(14)* and *(15)* where no excited triplet product was observed[47].

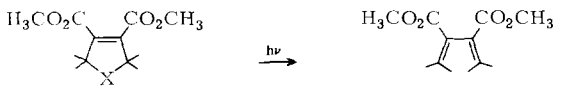


Another triplet photofragmentation reaction in which an adiabatic channel has been suggested is in the elimination of sulfur dioxide from sulfolenes *(16)—(18)*[48]. Benzene sensi-



tized photolysis of *(16)—(18)* resulted in the extrusion of sulfur dioxide to give the diene. Based on the known photochemistry of dienes[49], the formation of the diene triplet is ruled out. Formation of *cis-cis* hexadiene prompts the authors to suggest an adiabatic generation of triplet excited sulfur dioxide ($E_T \approx 72$ kcal/mol) which is expected to transfer energy to the cage pair diene [eq. (a)].

These arguments, however, are based on the assumption of the concerted nature of the reaction process. Recently, evidence has been provided for the biradical nature of similar photoextrusion reactions [eq. (b)][50]. Similar involvement of biradicals in reactions of *(16)—(18)* could, however, explain



(b)

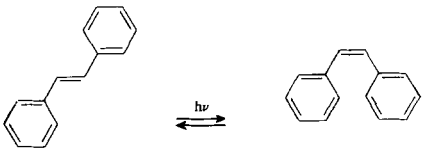
X = S, SO, SO_2

the result without involving the excited states of sulfur dioxide.

4.3. Geometric Isomerization

Some interesting examples of adiabatic photochemistry are provided by the geometric isomerization of certain polyenes. Alkenes, including polyenes in general, upon direct or triplet sensitized excitation undergo geometric *(cis-trans)* isomerization about the double bond(s)[49]. All theoretical studies directed toward understanding the energy surfaces for this reaction suggest a preference for twisting about the double bond on the singlet and triplet excited surfaces of monoenes and dienes (*i.e.*, the surface topology of Fig. 4). Although the calculations do not all agree with respect to the stabilization of the twisted geometries in higher polyenes, they all favor a lower stabilization of the twisted geometries in higher polyenes, and they all favor a lower stabilization as compared to monoenes and dienes. The above model suggests the general occurrence of a maximum on the ground surface and minimum on the excited surface near the twisted geometry. This would facilitate a jump of the representative point from an excited surface to the ground surface near the twisted geometry. In spite of the availability of this diabatic geometric isomerization several olefins appear to undergo adiabatic geometric isomerization.

Triplet sensitized and direct $S_0 \rightarrow T_1$ excitation of stilbene results in geometric isomerization[49,51-64]. The photostationary state ratio of *cis* product to *trans* product as well as the quantum yield of isomerization is found to be dependent on the concentration of low energy triplet sensitizers as well as on the concentration of *trans*-stilbene. Furthermore, during benzophenone sensitized geometric isomerization of stilbene, quenching with azulene [$E_T \approx 38$ kcal/mol] favors the formation of *trans*-stilbene. Thus, both azulene and low energy triplet sensitizers are able to deactivate the excited stilbene triplet selectively to the *trans* isomer. This is consistent with the postulate that the *trans* triplet and a twisted triplet are in thermal equilibrium on the triplet surface and that the *trans*-stilbene triplet is selectively quenched by the above-mentioned quenchers. This model, due to *Hammond* and coworkers[61], involves the adiabatic conversion of *cis*-stilbene triplet to *trans*-stilbene triplet *via* the twisted triplet. A recent flash photolysis study of *p*-nitrostilbene is consistent with the model[65]. Both *cis*- and *trans-p*-nitrostilbene give rise to a common transient with the same absorption and decay constant upon flash excitation. Furthermore, this transient is quenched by oxygen and azulene in a manner similar to that found in the studies of stilbene. If the common transient is in fact due to the triplet of *trans-p*-nitrostilbene, it represents an adiabatic conversion from *cis* triplet to *trans* triplet.



Since the *cis* and *trans* isomers of stilbenes do not possess a large energy difference either in the ground (S_0) or excited triplet (T_1) states, the structural feature responsible for the adiabatic channel is probably different than in the cases of Dewar arenes and dioxetanes. It appears that a small energy difference in the triplet state between the isomers is sufficient to tilt the surface toward the *trans* isomer[61]; this is pictured in Figure 7. This tilt permits an equilibration between the twisted and *trans* triplet configurations such that the *trans* shape is favored for deactivation to the ground state surface. The closeness of approach of the S_0 and T_1 surfaces at the twisted geometry does not lead to a "funnel" through which the representative point can jump efficiently, since spin-orbit coupling is required as a mechanism for intersystem crossing and since spin-orbit coupling is very weak in hydrocarbon systems, the $T_1 \rightarrow S_0$ interconversion is slow at all geometries. It is interesting to speculate that the twisted geometry may, in fact, be the best geometry for effective spin-orbit coupling since the *p*-orbitals of the central carbon-carbon bond are roughly orthogonal to one another in this structure[46].

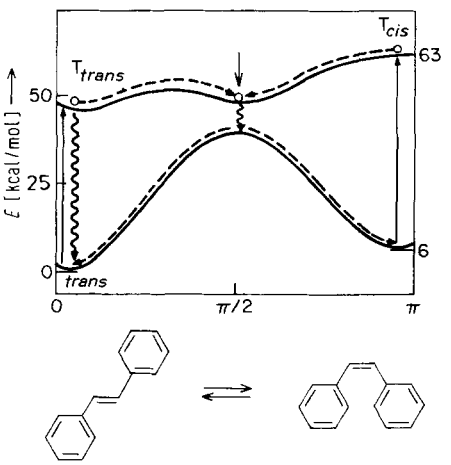
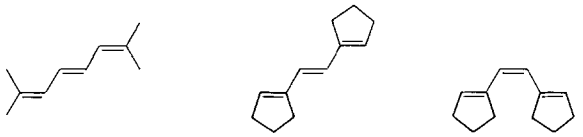


Fig. 7. Qualitative surface description of the geometric isomerization of *trans*- and *cis*-stilbene. π = angle of twist around the central bond. Arrow indicates "phantom triplet".

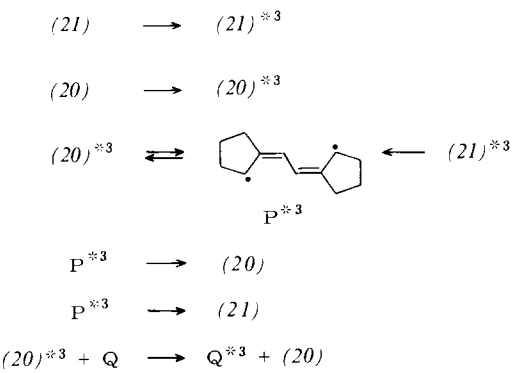
Photochemically-induced geometric isomerization of 2,4-hexadienes and 1,3-pentadienes have been studied in considerable detail. One early report[66] proposed an adiabatic interconversion among geometric isomers of 2,4-hexadiene in the triplet manifold. The system was later shown to be complicated due to impurities[67]. There have been several reports

on the concentration-dependent geometric isomerization of dienes in the triplet excited state[68-71]. Both 2,4-hexadienes and 1,3-pentadiene undergo concentration dependent isomerization from *cis* to *trans* isomers only at high concentrations (≈ 1 M)[70]. No definitive experiments have been carried out to delineate the reasons for the above observation. Studies of isomerization in several trienes [*(19)* and *(20)*] have



(19) *(20)* *(21)*

also demonstrated a concentration dependence in their geometric isomerization reactions[72-76]. Also, azulene is found to have a profound influence on the photostationary state. As with the stilbenes, these observations suggest the presence of a quantum chain process and the data are presented in Table 2. These experimental results are explained by the postulate that the planar *trans* triene triplet must be energetically close to, and hence exist in equilibrium with twisted and quenchable triene triplet, as in the case of stilbene[61]. Then these triplets must be the ones quenched by azulene and by ground state cisoid trienes as shown below for *(20)*. Apparently, a small difference in triplet energy be-



tween *cis* and *trans* isomers is able to tilt the triplet surface toward the *trans* isomer and thus allow an adiabatic conversion of *cis* to *trans*-triplet.

Table 2. Ratio of *trans- (20)* to *cis*-1,2-bis(1-cyclopentenyl)ethylene *(21)* at photostationary state. Sensitizer: 2-naphthylphenyl ketone [a].

Triene conc. [M × 10³]	Quencher conc. [b] [M × 10³]	*(20)*:*(21)*
2.76	—	0.73 ± 0.01 : 1
8.27	—	0.80 ± 0.02 : 1
13.80	0.50	1.53 ± 0.03 : 1
13.80	1.00	2.18 ± 0.08 : 1
13.80	2.00	3.52 ± 0.07 : 1
13.80	3.00	4.23 ± 0.08 : 1
13.80	4.00	4.50 ± 0.10 : 1
13.80	5.00	6.30 ± 0.40 : 1
16.60	—	0.86 ± 0.01 : 1
23.50	—	0.95 ± 0.06 : 1
55.30	—	1.28 ± 0.04 : 1

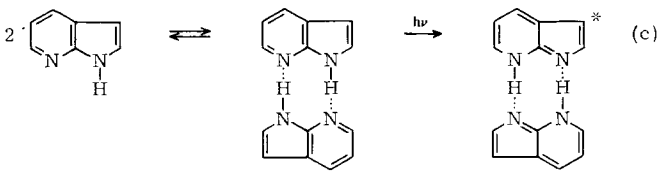
[a] 2-Naphthylphenyl ketone: 2.5×10^{-2} M; solvent: benzene. [b] Quencher: guaiazulene.

As in the studies of stilbene, the adiabatic channel in the photochemistry of *(19)* and *(20)* probably represents a special case since most other trienes appear to isomerize by diabatic processes[76].

4.4. Proton Transfer and Electron Transfer

As we have seen in the previous examples, the occurrence of a minimum in the excited state surface near a maximum in the ground state surface may predispose a system to undergo diabatic conversion of excited state reactants to ground state products. There are several cases for which the two surfaces are well separated throughout, a favorable condition for adiabatic reaction. One of the most striking cases involves that of proton transfer. Numerous studies of the acidity of electronically excited species have demonstrated that proton transfer processes, being very rapid, often establish a dynamic equilibrium during the lifetime of an excited state[4a]. The pK_a^* and pK_a, the acidity constant for the excited state and ground state species respectively, are often very different due to the difference in electronic configurations[4, 77, 78]. The transfer of electric charge from a donor to an acceptor (one of which is electronically excited) may lead to an electronically excited charge transfer complex or an electronically excited radical ion pair. Several excellent reviews on excited state acid and base reactions and electron transfer reactions are available[79-82]. In this section, we shall discuss only a few prototypical examples.

Interesting excited state prototropic behavior is shown by 1,7-diazaindene. In non-hydrogen bonding solvents, it exhibits two fluorescence bands[83, 84]. Studies of methylated derivatives and of the effect of temperature and concentration on these bands indicate that the second fluorescence band originates from an electronically excited tautomer formed by double proton transfer on the excited singlet surface of a hydrogen bonded dimer [eq. (c)].



Dimer formation, which is concentration dependent, is not necessary for proton transfer since the solvent can also serve

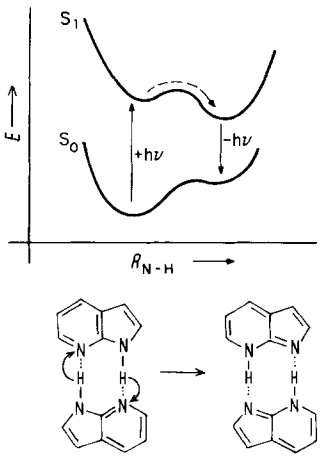
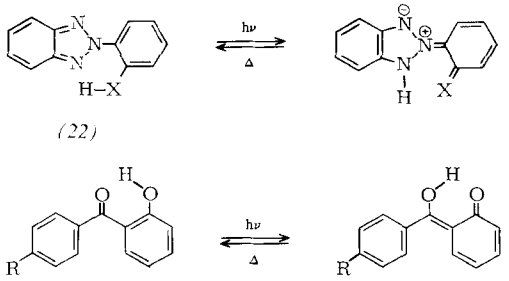


Fig. 8. Schematic representation of the adiabatic proton transfer on the excited singlet surface of the 1,7-diazaindene dimer.

as a proton donor. For example, in ethanol solution similar fluorescence bands which are not concentration dependent are attributed to double proton transfer between ethanol and excited singlet 1,7-diazaindene[84]. The double proton transfer can be visualized using the surface diagram shown in Figure 8.

Reversible intramolecular proton transfer is probably the basis of the effectiveness of certain photostabilizers that have a great commercial importance because of their ability to protect polymers from photodegradation[85]. These photostabilizers [*e.g., (22)* and *(23)*] absorb light and form an unstable tautomer, possibly *via* an adiabatic proton transfer. The tautomer thermally reverts to the starting material and, in the cycle, photon energy, potentially capable of causing rupture and crosslinking of polymer chains, is degraded harmlessly into heat.



(22)

(23)

The production and study of radical ion pairs *via* flash spectroscopy has revealed that the ions may be produced in electronically excited states[86]. For example, following an initial flash, a triplet radical ion pair may be monitored spectroscopically. In the case of [pyrene]* and 3,5-dimethoxy-*N,N*-dimethylaniline, the decay of the triplet radical ion pair is due to intersystem crossing to a singlet radical ion pair followed by an electron transfer that regenerates pyrene and 3,5-dimethoxy-*N,N*-dimethylaniline in their ground states[86]. Both a "fast" and a "slow" decay of the radical ion pair have been observed and ascribed to "geminate" or cage electron transfer and to "homogeneous" or diffusion-reencounter electron transfer, respectively.

4.5. Excimers/Exciplexes; Excited State Complexes

The formation and reactions of weakly bound molecular complexes involving electronically excited molecules may also be considered as an adiabatic photochemical process. An excimer is a short-lived excited state complex formed from two molecules that are identical in their ground state[87]. Aromatic hydrocarbons, such as pyrene, readily form such associations in the excited state and are not complexed in the ground state[87]. The excimer is often luminescent and its spectrally broad and red-shifted emission is characteristic of a bound state to repulsive surface transition (Fig. 9).

Similarly, exciplexes[86, 88, 89] are complexes of excited state and ground state molecules of dissimilar nature. For example, exciplexes are readily formed between excited aromatic hydrocarbons and 1,3-conjugated dienes[90-93] or amines[89, 94]. The approach of the excited and ground state species to form the excited state complexes, $^*A + B \rightarrow {}^*(AB)$ is an adiabatic process. Many excellent review articles are available on the nature of the bonding in these complexes[95], the kinetics of excimers[86] and exciplexes[96] and the possible role of such complexes in photodimerization[97, 98] and photo-

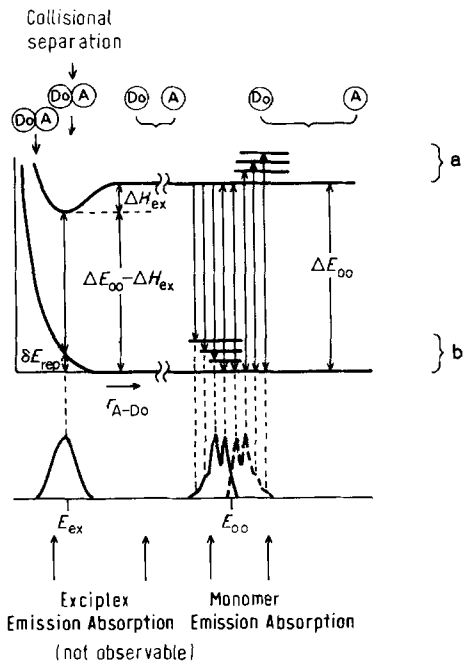


Fig. 9. Schematic description of excimer (Do = A) or exciplex (Do ≠ A) emission. The abscissa represents approach of the two partners. At the left, Do (donor) and A (acceptor) are colliding; at the right, Do and A are separated in space. a) Discrete vibrational states of the electronically excited monomer; b) discrete vibrational states of the monomer in the electronic ground state.

cycloaddition[99]. One such case, involving formation of an excimer, will be considered in more detail.

In the case of anthracene[5] and 9-methylanthracene[100, 101] a stable dimer exists in the ground state. The dianthracene species, when excited to its singlet state, produces luminescent products and displays both an excimer (*(AA), $\Phi_f = 4 \times 10^{-3}$) and monomer (*A, $\Phi_f = 3.7 \times 10^{-3}$) anthracene emission through adiabatic channels. In Figure 10 a surface diagram as suggested by *Förster* is presented to show the details of these processes. As might be expected, the close approach of the excited and ground state surfaces at intermediate values of r the intermolecular separation would favor a diabatic relaxation from the upper to lower surfaces and this appears to be the dominant reaction channel. This decomposition is similar to the photodecomposition of dioxetanes (see Section 4.2), but the presence of an additional minimum due to the excimer in the excited surface allows adiabatic conversion of excited anthracene dimers to both excimer and excited anthracenes. A recent investigation of the solvent viscosity and temperature dependence of the photodissociation of dianthracene and di-9-methylanthracene and related compounds suggests a benzyl-like radical precursor to the excimer state[101].

Charge transfer luminescence[95] may also be envisioned as the result of a more subtle adiabatic process. Charge transfer complexes have a bound ground state surface, and excitation to an electronically excited and bound surface is often possible. This excited state complex, the result of a vertical transition, has the geometry of the ground state complex and is subsequently collisionally relaxed to a new configuration of

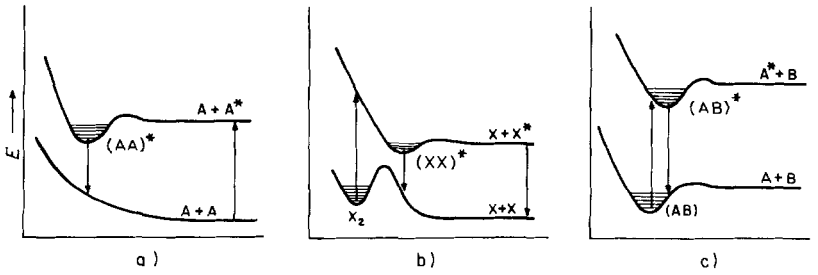


Fig. 10. Schematic representation of excimer (or exciplex) emission: (a) excimer formation with large separation of ground and excited surfaces at all geometries; (b) excimer formation with dimer formation providing a maximum on the ground surface; (c) exciplex or charge transfer complexation with large separation of ground and excited states for all geometries.

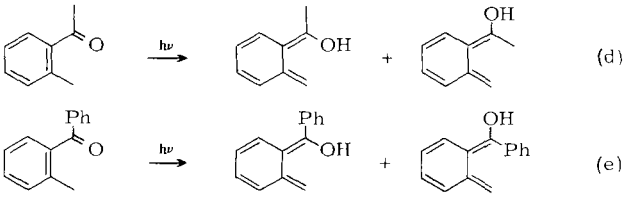
the preferred excited state geometry. Luminescence from this bound state to the ground state shows a large Stokes shift, and the adiabatic process is that of the change in geometry and bonding in the excited state relaxation process as portrayed in Figure 10c. Salts of methylpyridinium cations with anions such as Br^- or N_3^- form strongly bound ground state complexes (ionic) and weakly bound excited state complexes (radical pair)[102]. Following direct excitation of the ionic species an adiabatic transformation to the excited radical pair geometry occurs with subsequent emission and relaxation to the ground state. The Stokes shift between the frequency of absorption and of fluorescence is 33600 cm^{-1} ($\approx$96 kcal/mol) for the methylpyridinium-bromide system, reflecting the large stabilization energy of the process.

Similarly, the observation of spectral shifts between absorption and emission frequencies due to interactions between a molecule and its solvent sphere[103] is indicative of an adiabatic process. Excitation of a molecule to an excited state by a vertical transition results in an excited species with ground state geometry and a ground state orientation of the solvent molecules. A rapid adiabatic relaxation leads to an excited state geometry of the molecule and a different solvent environment. The fact that the solvent geometry and stoichiometry have been altered may be considered as a photochemical transformation in a supermolecule. Analysis of spectral shifts as a function of temperature, solvent type, and solvent viscosity are very helpful in the elucidation of such excited state adiabatic transformations[104].

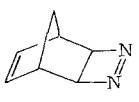
4.6. Pseudo-Adiabatic Process

In the previous examples of adiabatic photochemistry, the identification of products in excited electronic states is facilitated by their luminescence or by chemical inference from quenching studies; however, there exist several types of photochemical reactions for which this straight-forward identification is not possible. The problem lies in defining the "chemical step": *if an excited state reactant converts to an excited state intermediate species generally differing in nuclear configuration and electronic charge density distribution from that of the reactant, this step may be viewed as an adiabatic chemical process even if a subsequent diabatic process leads to ground state products.* For example, if photochemical *trans-cis* isomerization occurs (Fig. 4) *via* the pathway *trans* (S_1)$\rightarrow$Z$\rightarrow$*cis* (S_0) or *trans* (T_1)$\rightarrow{}^3$D$\rightarrow$*cis* (S_0), the classification of these reactions as adiabatic or diabatic depends on whether Z and ^{3}D are considered as primary products. We will term overall reactions for which diradical primary products or minima are produced in an adiabatic fashion as pseudo-adiabatic; some discussion of several examples of this behavior may prove illuminating.

One example of a pseudo-adiabatic reaction is provided by the photoenolization of *o*-alkylacetophenones and -benzophenones[105-107]. Excitation of *o*-methylacetophenone and *o*-methylbenzophenone gives rise to two geometric isomers of the enol in the excited triplet state [eq. (d) and (e)]. At the outset, it appears that an adiabatic process occurs in which an enol is produced directly in its triplet state, which isomerizes to either of two different isomeric ground state enols. A more recent study[108, 111] suggests the generation of an excited triplet intermediate of twisted geometry rather than the



vertically excited enol triplet. A quenchable intermediate of lifetime $\approx 10^{-7}$ s is observed upon flash excitation of *o*-methylacetophenone. The diradical character of this intermediate is evidenced by its reaction with the paraquat ion[112], an efficient electron transfer radical trap. Quenching by oxygen causes a concomitant increase in enol yield. This result leads to the conclusion that the excited enol intermediate is probably present on the excited surface common to the two geometric isomers of the enol. No evidence is currently available to favor the formation of the vertically excited enol triplet. On the other hand, based on the known mechanistic details of photohydrogen abstraction[113, 114], one would expect the formation of the *twisted* enol as the primary intermediate because the favored approach for hydrogen abstraction would generate this geometry. The feature which makes this reaction "pseudo-adiabatic" is the availability of another ground state surface (due to rotation of the double bond in the enol), into which the intermediate can leak, in addition to the surface due to hydrogen abstraction. At this stage, it is debatable whether the minima on the excited surface corre-



(24)



(25)

sponding to hydrogen abstraction and adiabatic isomerization are the same or different.

Further examples of "pseudo-adiabatic" photoreactions are provided by the photodissociation of the cyclic azoalkanes *(24)*, *(25)*, and *(28)*[115,116]. Results of sensitized and direct photolysis of *(24)* and *(25)* are presented in Figure 11.

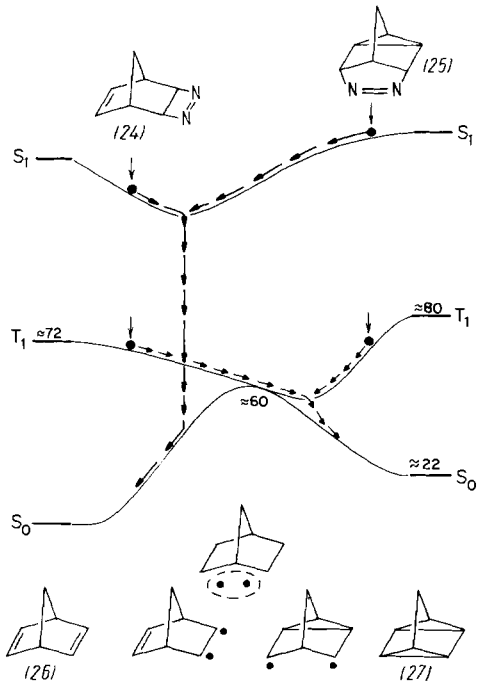
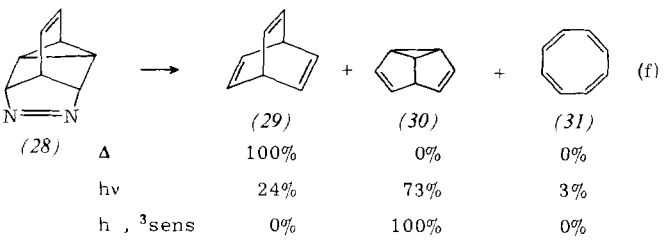


Fig. 11. Schematic representation of the potential surfaces for the conversion of norbornadiene *(26)* into quadricyclane *(27)*. Results of direct and sensitized photolysis of *(24)* and *(25)* (arrows). Energy given in kcal/mol.

Triplets of *(24)* and *(25)* prefer to give quadricyclane, whereas singlets proceed to give norbornadiene *(26)* preferentially. The triplet state of *(28)* shows a preference for formation of semibullvalene *(30)* while the singlet S_1 shows a preference for formation of barrelene *(29)* [eq. (f)]. Results of sensitization studies of *(26)* are reminiscent of the triplet photochemistry of the corresponding barrelenes[117]; but, the generation of triplet excited barrelene in the decomposition of *(26)* is inconsistent with known barrelene photochemistry[13]. The results are actually compatible with the generation of a triplet intermediate on the excited surface connecting barrelene and semibullvalene. Thus, what appears to be an adiabatic process is in fact a "pseudo-adiabatic" process. The excited triplet intermediate formed by the decomposition of cyclic azoalkanes has access to another ground surface connecting semibullvalene and barrelene.



(f)

Similarly, preferential formation of quadricyclane upon sensitized irradiation of *(24)*, *(25)*, and norbornadiene *(26)* is consistent with the formation of a common intermediate, most probably on the excited triplet surface[118]. This can be visualized using the model presented in Figure 11. It should be mentioned, however, that the excited hypersurface correlating the molecular rearrangements of the corresponding hydrocarbons can be reached from azoalkanes *(24)*, *(25)*, and *(28)* either directly or through additional minima on the excited surface.

Further examples of "pseudo-adiabatic" photoprocesses may be found in the geometric isomerization of polyenes[75]. Direct excitation of dienes and trienes in general results in geometric isomerization of one of the many possible double bonds. On the other hand, triplet sensitization induces isomerization of more than one bond per excitation[66,67]. Similar multibond isomerization per excitation process has been observed in 2,6-dimethyl-2,4,6-octatriene (alloocimene)[73,74] and 3,5-heptadien-2-one[119]. This multibond isomerization, in the case of hexadiene, can be imagined to proceed through a diabatic process involving "1,4-diradical-type"[66,67] twisted geometry.

This would involve simultaneous rotation of both bonds on the excited surface followed by leakage onto the lower surface at an intermediate geometry as shown in Figure 4. The other possibility would be an adiabatic process involving direct conversion of the triplet TT isomer to that of TC and CC through successive one bond rotations, but consideration of the concentrations and quencher dependence chemistry of hexadiene rules out this possibility. A final possibility, which is favored by temperature and viscosity dependent triplet isomerization of 2,4-hexadiene, is the pseudo-adiabatic process[120]. This involves the relaxation of the excited triplet diene through one bond rotation to the "allylmethylene" type diradicaloid geometry. This twisted triplet which exists on the excited surface can undergo rapid equilibration with other possible twisted "allylmethylene" geometries and leakage to all three isomers occurs from these minima. Similar arguments also tend to explain the observed multibond rotation of trienes[72-75]. Thus, this multibond isomerization like photoenolization and photodissociation of azo compounds becomes "pseudo-adiabatic" due to the presence of several minima on the excited surface which can attain thermal equilibrium during the lifetime of the triplet state.

4.7. Adiabatic Photoreactions Leading to Primary Diradical Products. Ditopic and Polytopic Reactions

Correlation diagrams and the postulate that a plane of symmetry serves as a good zero order model have been used to elucidate the mechanism of n,π^* states[3a,6]. Such diagrams are termed Salem diagrams. This approach emphasizes the behavior and electronic symmetries of the diradical (D) and zwitterionic (Z) states that are characteristic of systems in which a sigma or pi bond is broken or made. A discriminating feature of these reactions is the reaction *topicity* or *the total number and nature of radical sites generated in the primary photoproduct.* For example, the diradical-forming photochemical reactions which occur when a n,π^* state of acetone (S_1 or T_1) reacts with methane [eq. (g)] or with ethylene [eq. (h), R = H] are *ditopic* because the primary products [a radical pair in eq. (g) and a diradical in eq. (h)] contain only *two* low-lying electronic states. On the other hand, the hydrogen abstraction and addition reactions [eqs. (i) and (j)]

$$(CH_3)_2C{=}O + CH_4 \xrightarrow{h\nu} (CH_3)_2\dot{C}OH + \dot{C}H_3 \quad (g)$$

$$(CH_3)_2C{=}O + RCH{=}CHR \xrightarrow{h\nu} \text{oxetane} \quad (h)$$

are *tritopic:* three low lying radical sites are formed due to the degeneracy at the oxygen radical site.

$$(CH_3)_2C{=}O + HO{-}R \longrightarrow (CH_3)_2\dot{C}OH + \dot{O}R \quad (i)$$

$$(CH_3)_2C{=}O + RCH{=}CHR \longrightarrow \text{oxetane} \quad (j)$$

Surfaces for reactions of n,π* states to form diradical primary products commonly involve a surface crossing near the primary product geometry or a surface touching near the primary product geometry (Fig. 12). The crossing between the S_0 and S_1 surfaces is weakly avoided, but the S_0 and T_1 surface crossing persists for realistic situations which do not involve the strictly planar symmetry. Whether the weakly avoided crossing (AC) of the singlet surfaces is a true minimum (from which jumps to S_0 or to ^1D may occur) or is a funnel (leading predominantly to ^1D) will depend on the system under study. In some favorable cases, the minimum (an exciplex!) may be detected by kinetic, spectroscopic or chemical means.

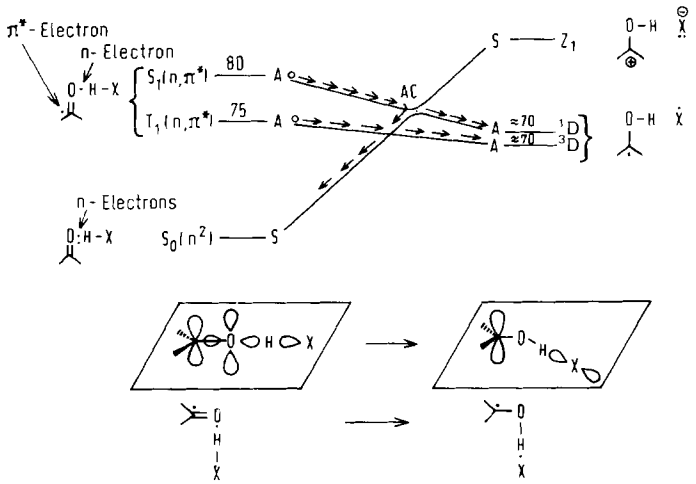


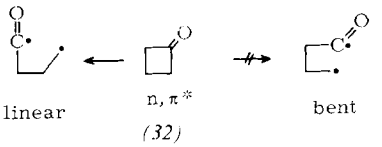
Fig. 12. First order correlation diagram for coplanar hydrogen abstraction. The energies of S_1, T_1, ^1D, and ^3D (in kcal/mol) are typical for hydrogen abstraction by an alkanone. AC = weakly avoided crossing.

The difference between an adiabatic and diabatic photoreaction is subtle in cases corresponding to Figure 12. If the representative point travels directly from $S_1(n,\pi^*)$ to ^1D without pausing in the minimum due to the avoided crossing, the reaction would be termed as adiabatic. If the representative point pauses in the exciplex minimum and then jumps to the lower singlet surface and travels to ^1D, the reaction is formally diabatic. The chemical consequences of these two situations are manifest in reaction efficiency from S_1. In the adiabatic passage to ^1D, the reaction efficiency is higher than in the diabatic passage since in the latter case transitions to S_0 occur in competition with transition to ^1D.

In contrast to the $S_1(n,\pi^*)\rightarrow{}^1D$ pathway, the $T_1(n,\pi^*)\rightarrow{}^3D$ pathway does not have a leakage point back to S_0. As a result the adiabatic $T_1(n,\pi^*)\rightarrow{}^3D$ process is expected to be more efficient than the diabatic $S_1(n,\pi^*)\rightarrow{}^1D$ process.

Experimental support for the occurrence of a diabatic pathway from S_1 and an adiabatic pathway from T_1 is found in the Type II reactions[121] and cycloaddition reactions[122] of alkanones: reaction efficiency from S_1 is much less efficient than from T_1.

In the case of the photochemical α-cleavage of alkanones both ditopic and tritopic pathways are possible. The ditopic (or bent acyl) pathway is often thermochemically allowed from S_1 or T_1, but is electronically forbidden, while the tritopic (or linear acyl) pathway is often thermochemically forbidden but electronically allowed. The photochemical α-cleavage of cyclobutanones *(32)* (Fig. 13) probably proceeds *via* the electronically allowed tritopic pathway. The adiabatic photoreaction $S_1(n,\pi^*)\rightarrow{}^1D$ (linear acyl) produces an *electronically excited* radial center since the linear acyl fragment is an excited electronic state of the bent acyl fragment.



(32)

The difference between the linear (electronically excited state) and bent (electronic ground state) acyl moieties is manifested in their chemistries[123]. The loss of CO from a bent acyl radical of the type $RCH_2\dot{C}O$ requires an activation energy of ≈14 kcal/mol, but the loss of CO from a linear acyl radical has a much lower activation energy. Indeed, cyclobutanone undergoes photodecarbonylation even at 77 K, consistent with the idea that loss of CO is essentially unactivated.

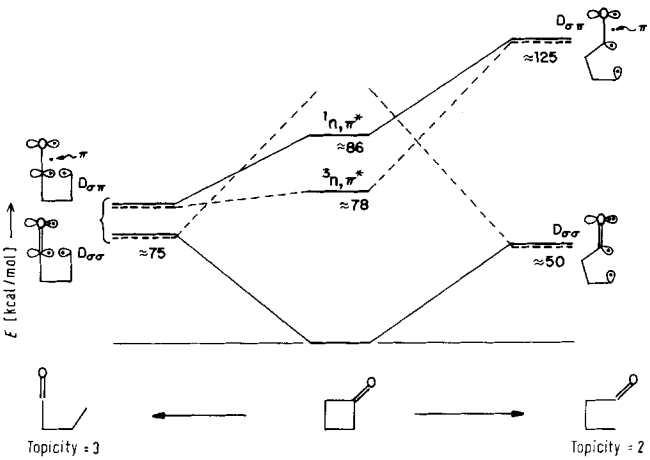


Fig. 13. Comparison of the planar α-cleavage of cyclobutanone *(32) via* bent (right) and linear (left) reaction pathways. The diradical states are labeled σ if an odd electron is contained in the molecular plane and π if an odd electron exists above and below the molecular plane.

5. Conclusion

Only a few adiabatic photoreactions have been substantiated by convincing experimental support. It is possible,

however, that many photoreactions are pseudo-adiabatic and that the experimental distinction between these and adiabatic photoreactions may be difficult. Pseudo-adiabatic reactions, in turn, may be difficult to distinguish from photophysical radiationless processes. Despite their scarcity in number, adiabatic photoreactions provide an insight into the nature of electronically excited surfaces and help to define the structural features that allow a representative point on an excited surface to make it "all the way" from the reactant geometry to the product geometry before it makes its inevitable jump to the ground state.

The "rules of the game" for predicting adiabatic photoreactions are still developing. However, excited state reactions involving small changes in covalent bonding (proton and electron transfer, excimer and exciplex formation) are commonly found to occur adiabatically. Photoreactions involving more extensive changes in covalent bonding may occur as a result of reaction exothermicity which causes tilting in surfaces leading from R* to P* and causes the representative point to sweep past geometries that "get close" to S_0 without making a jump to the lower surface. Triplet reactions should generally be adiabatic if the R*→P* conversion is exothermic and if no large energy barrier occurs between these structures (*i.e.*, even if S_0 "comes close" to T_1). Unless strong spin-orbit coupling occurs a surface jump is unlikely. Finally, reactions for which the excited singlet (S_1) and S_0 surfaces are far apart for all geometries ("allowed" pericyclic ground state reactions) are candidates for efficient adiabatic photoreactions.

In conclusion, the notion of adiabatic organic photoreactions completes a troika of related surface processes (Fig. 14):

(1) adiabatic photochemistry;
(2) diabatic photochemistry;
(3) chemiluminescence.

In process (1) the energy of an absorbed photon puts the representative point on an excited surface. Nuclear motion commences and continues on the excited surface until "chemistry" has occurred (the nuclear shape becomes sufficiently different from that of the reactant so that a "primary product" can be said to be formed).

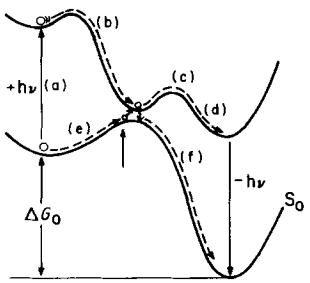


Fig. 14. Schematic representation of an adiabatic photoreaction: (a)→(b)→(c)→(d); a diabatic photoreaction: (a)→(b)→(f), and a chemiluminescent reaction: (e)→(c)→(d). Radiationless jumps occur at place indicated by arrow.

In process (2), the representative point jumps to S_0 before "chemistry" has occurred. Ambiguous cases will arise for this process. The notion of pseudoadiabatic photoreactions provides some insight into the problem but does not clarify it.

Finally, in process (3) the representative point of a high energy reactant commences motion on a ground surface and then "jumps" to an electronically excited surface at a geometry which brings S_0 and an excited (usually a T) surface "close together." In this regard, the observed chemiluminescence of the high energy content reactants—dioxetanes and Dewar benzenes—is easy to understand.

The authors at Columbia University thank the National Science Foundation, The Air Force Office of Scientific Research, and the National Institutes of Health for their generous support of this research.

Received: September 11, 1978 [A 281 IE]
German version: Angew. Chem. *91*, 597 (1979)

[1] *Th. Förster*, Pure Appl. Chem. *24*, 433 (1970); *34*, 225 (1973).
[2] *M. Kasha*, Discuss. Faraday Soc. *9*, 14 (1950).
[3] a) *N. J. Turro*, Modern Molecular Photochemistry, Benjamin-Cummings, Menlo Park, California 1978, p. 52ff.; b) *L. Salem*, J. Am. Chem. Soc. *96*, 3486 (1974); c) *R. C. Dougherty, ibid. 93*, 7187 (1971); d) *W. G. Dauben, L. Salem, N. J. Turro*, Acc. Chem. Res. *8*, 41 (1975); e) *A. Devaquet*, Pure Appl. Chem. *41*, 455 (1975); *J. Michl*, Topics Curr. Chem. *96*, 1 (1974).
[4] a) *J. F. Ireland, P. A. H. Wyatt*, Adv. Phys. Org. Chem. *12*, 131 (1976); b) *Th. Förster*, Angew. Chem. *81*, 364 (1969); Angew. Chem. Int. Ed. Engl. *8*, 333 (1969).
[5] In contrast to the situation for polyatomic organic molecules, adiabatic photoreactions of diatomic or triatomic molecules are well-known: *J. Calvert, J. Pitts, Photochemistry*, Wildy, New York, NY, 1965.
[6] *E. E. Van Tamelen*, Acc. Chem. Res. *5*, 186 (1972).
[7] *N. J. Turro, V. Ramamurthy, T. J. Katz*, Nouv. J. Chim. *1*, 363 (1977).
[8] *R. V. Carr, B. Kim, J. K. McVey, N. C. Yang, W. Gerhartz, J. Michl*, Chem. Phys. Lett. *39*, 57 (1976).
[9] *N. C. Yang, R. V. Carr, E. Li, J. K. McVey, S. A. Rice*, J. Am. Chem. Soc. *96*, 2297 (1974).
[10] *P. Lechtken, R. Breslow, A. H. Schmidt, N. J. Turro*, J. Am. Chem. Soc. *95*, 3025 (1973).
[11] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[12] *W. Th. A. M. van der Luft, L. J. Osterhoff*, J. Am. Chem. Soc. *91*, 6042 (1969).
[13] *D. Grimbert, G. Segal, A. Devaquet*, J. Am. Chem. Soc. *97*, 6629 (1975).
[14] *J. Michl*, Mol. Photochem. *4*, 278 (1972).
[15] *J. Michl*, Mol. Photochem. *4*, 257, 287 (1972).
[16] *C. A. Renner, T. J. Katz, J. Pouliquen, N. J. Turro, W. H. Waddell*, J. Am. Chem. Soc. *97*, 2570 (1975).
[17] *N. J. Turro, P. Lechtken, A. Lyons, R. R. Hautala, E. Carnahan, T. J. Katz*, J. Am. Chem. Soc. *95*, 2035 (1973).
[18] *E. W. Forster, K.-H. Grellmann*, J. Am. Chem. Soc. *94*, 634 (1972); *ibid.*, Chem. Phys. Lett. *14*, 536 (1972).
[19] *E. W. Forster, E. Rischer*, Chem. Commun. *1972*, 1315.
[20] *E. J. Bowen, J. H. D. Eland*, Proc. Chem. Soc. London *1963*, 202.
[21] *K.-H. Grellmann, G. M. Sherman, H. Linschitz*, J. Am. Chem. Soc. *85*, 1881 (1963).
[22] *H. Linschitz, K.-H. Grellmann*, J. Am. Chem. Soc. *86*, 303 (1964).
[23] *G. N. Taylor*, Z. Phys. Chem. N. F. *101*, 237 (1976).
[24] *J. Michl*, Pure Appl. Chem. *41*, 507 (1975).
[25] *J. Michl*, J. Am. Chem. Soc. *98*, 6427 (1976).
[26] For a review of dioxetane decomposition, see: *N. J. Turro, P. Lechtken, N. E. Schore, G. Schuster, H. C. Steinmetzer, A. Yekta*, Acc. Chem. Res. *7*, 97 (1974).
[27] *K. R. Kopecky, J. E. Filby, C. Mumford, P. A. Lockwood, J.-Y. Ding*, Can. J. Chem. *53*, 1103 (1975).
[28] *T. Wilson, A. P. Schaap*, J. Am. Chem. Soc. *53*, 1103 (1975).
[29] *P. Lechtken, A. Yekta, N. J. Turro*, J. Am. Chem. Soc. *95*, 3027 (1973).
[30] *N. J. Turro, P. Lechtken*, Tetrahedron Lett. *1973*, 565.
[31] *W. J. Baron, N. J. Turro*, Tetrahedron Lett. *1974*, 3515.
[32] *N. J. Turro, W. H. Waddell*, Tetrahedron Lett. *1975*, 2069.
[33] *P. Lechtken, H.-C. Steinmetzer*, Chem. Ber. *108*, 3159 (1975).
[34] *P. Lechtken, A. Yekta, N. E. Schore, H. C. Steinmetzer, W. H. Waddell, N. J. Turro*, Z. Phys. Chem. N. F. *101*, 79 (1976).
[35] *N. J. Turro, D. Brewer, W. Farneth, V. Ramamurthy*, Nouv. J. Chim. *2*, 85 (1978).
[36] *C. S. Foote, T. R. Darling*, Pure Appl. Chem. *41*, 495 (1975).
[37] *C. S. Foote, T. R. Darling*, J. Am. Chem. Soc. *96*, 1625 (1974).
[38] *G. B. Schuster, N. J. Turro, H. C. Steinmetzer, A. P. Schaap, G. Faler, W. Adam, J. C. Liu*, J. Am. Chem. Soc. *97*, 7110 (1975).

[39] *K. K. Smith, J.-Y. Koo, G. B. Schuster, K. J. Kaufmann*, Chem. Phys. Lett. *48*, 267 (1977).
[40] For example, see: *E. M. Evleth*, J. Am. Chem. Soc. *98*, 1638 (1976) and references therein.
[41] *N. J. Turro, A. Devaquet*, J. Am. Chem. Soc. *97*, 3859 (1975).
[42] *J. Michl*, Top. in Curr. Chem. *46*, 1 (1974).
[43] *A. Zweig, K. R. Huffmann, J. B. Gallivan, M. K. Orloff, F. Halverson*, J. Am. Chem. Soc. *96*, 1449 (1974).
[44] *A. Zweig*, Pure Appl. Chem. *33*, 389 (1973).
[45] *J. Rigaudy, C. Brelieve, P. Scribe*, Tetrahedron Lett. *1978*, 687.
[46] *L. Salem, C. Rowland*, Angew. Chem. *84*, 86 (1972); Angew. Chem. Int. Ed. Engl. *11*, 92 (1972).
[47] *T. R. Darling, J. Pouliquen, N. J. Turro*, J. Am. Chem. Soc. *96*, 1247 (1974).
[48] *J. Saltiel, L. Metts*, J. Am. Chem. Soc. *89*, 2233 (1967).
[49] *J. Saltiel, J. D'Agostino, E. D. Megarily, L. Metts, M. Wrighton, O. C. Zafiriou*, Org. Photochem. *3*, 1 (1973).
[50] *R. M. Kellogg, W. L. Prins*, J. Org. Chem. *39*, 2366 (1974).
[51] a) *R. S. Mulliker, C. Roothann*, Chem. Rev. *41*, 219 (1947); b) *H. E. Simmons*, Prog. Phys. Org. Chem. *7*, 1 (1970).
[52] *B. Hudson, B. Kohler*, Annu. Rev. Phys. Chem. *25*, 437 (1974).
[53] *I. Baraldi, M. C. Bruni, F. Momicchioli, J. Langletand, J. P. Malrieu*, Chem. Phys. Lett. *51*, 493 (1977).
[54] *G. Orlandi, W. Siebrand*, Chem. Phys. Lett. *30*, 352 (1975).
[55] *J. B. Birks*, Chem. Phys. Lett. *38*, 437 (1976); *54*, 430 (1978).
[56] *G. Orlandi, G. C. Marconi*, Chem. Phys. *8*, 458 (1975).
[57] *J. N. Kushick, S. A. Rice*, J. Chem. Phys. *64*, 1612 (1976).
[58] *V. Bonacic-Koutecky, S. Ishimaru*, J. Am. Chem. Soc. *99*, 8134 (1977).
[59] *A. Warshel, M. Karplus*, J. Am. Chem. Soc. *96*, 5677 (1974).
[60] *K. Schulten, I. Ohmine, M. Karplus*, J. Chem. Phys. *64*, 4422 (1976).
[61] *G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowarn, R. C. Counsel, V. Vogt, C. Dalton, J. Am. Chem. Soc. 86*, 3197 (1964).
[62] *J. Saltiel, D. W. L. Chang, E. D. Megarity, A. D. Rousseau, P. T. Shannon, B. Thomas, A. K. Uriarte*, Pure and Appl. Chem. *41*, 559 (1975), and references therein.
[63] *D. Valentine, Jr., G. S. Hammond*, J. Am. Chem. Soc. *94*, 3449 (1972).
[64] *R. Benson, D. F. Williams*, J. Phys. Chem. *81*, 215 (1977).
[65] *D. V. Bent, D. Schulte-Frohlinde*, J. Phys. Chem. *78*, 446, 451 (1974).
[66] *H. L. Hyndman, B. M. Monroe, G. S. Hammond*, J. Am. Chem. Soc. *91*, 2852 (1969).
[67] *J. Saltiel, L. Metts, M. Wrighton*, J. Am. Chem. Soc. *91*, 5684 (1969).
[68] *R. Hurley, A. C. Testa*, J. Am. Chem. Soc. *92*, 211 (1970).
[69] *G. F. Vesley*, Mol. Photochem. *4*, 519 (1972).
[70] *J. Saltiel, D. W. Townsend, Alan Sykes*, J. Am. Chem. Soc. *95*, 5968 (1973).
[71] *M. Bigwood, S. Bove*, Bull. Soc. Chim. Belges *82*, 685 (1973).
[72] *R. S. H. Liu*, Pure Appl. Chem. Suppl. *1*, 335 (1971).
[73] *R. S. H. Liu*, Pure Appl. Chem. Suppl. *1*, 335 (1971).
[74] *R. S. H. Liu, Y. Butt*, J. Am. Chem. Soc. *93*, 1532 (1971).
[75] *M. Denny, R. S. H. Liu*, Nouv. J. Chim., in press.
[76] *V. Ramamurthy, R. S. H. Liu*, J. Am. Chem. Soc. *98*, 2935 (1976).
[77] *A. Weller, W. Urban*, Angew. Chem. *66*, 336 (1954).
[78] *G. Jackson, G. Porter*, Angew. Chem. *66*, 336 (1954).
[79] *A. Weller*, Prog. React. Kinet. *1*, 7 (1961).
[80] *E. Vander Doanckett*, Prog. React. Kinet. *5*, 273 (1970).
[81] *J. F. Ireland, P. A. H. Wyatt*, Adv. Phys. Org. Chem. *12*, 131 (1976).
[82] *W. Klöpffer*, Adv. Photochem. *10*, 311 (1977).
[83] *C. A. Taylor, M. A. El-Bayoumi, M. Kasha*, Proc. Nat. Acad. Sci. USA *63*, 253 (1969).
[84] a) *K. C. Ingham, M. Abu-Elgheit, M. A. El-Bayoumi*, J. Am. Chem. Soc. *95*, 5023 (1971). b) *K. C. Ingham, M. A. El-Bayoumi*, J. Am. Chem. Soc. *96*, 1674 (1972).
[85] *M. Pape*, Pure Appl. Chem. *41*, 535 (1975).
[86] *K. Schulten, H. Staerk, A. Weller, H. J. Werner, B. Nickel*, Z. Phys. Chem. N. F. *101*, 371 (1976).
[87] *J. Birks:* Photophysics of Aromatic Molecules, Wiley, London 1970, p. 200.
[88] *D. A. Labianca, G. N. Taylor, G. S. Hammond*, J. Am. Chem. Soc. *94*, 3679 (1972).
[89] *H. Knibbe, D. Rehm, A. Weller*, Ber. Bunsenges. Phys. Chem. *73*, 839 (1969).
[90] *L. M. Stephenson, D. G. Whitten, G. F. Vesley, G. S. Hammond*, J. Am. Chem. Soc. *88*, 3365 (1966).
[91] *N. C. Yang, D. M. Shold, J. K. McVey*, J. Am. Chem. Soc. *97*, 5004 (1975).
[92] *F. D. Lewis, C. E. Hoyle*, J. Am. Chem. Soc. *97*, 5950 (1975).
[93] *J. Saltiel, D. E. Townsend, B. D. Watson, P. Shannon*, J. Am. Chem. Soc. *97*, 5688 (1975).
[94] *N. C. Yang, D. M. Shold, B. Kim*, J. Am. Chem. Soc. *98*, 6587 (1976).
[95] *S. Nagakura* in *E. C. Lim:* Excited States, Vol. 2, Academic Press, New York 1975, pp. 321–383.
[96] *W. Ware*, Pure Appl. Chem. *41*, 635 (1975).
[97] *J. K. McVey, D. M. Shold, N. C. Yang*, J. Chem. Phys. *65*, 3375 (1976).
[98] *Th. Förster*, Pure Appl. Chem. *34*, 225 (1973).
[99] *N. C. Yang, K. Srinivasachar, B. Kim, J. Libman*, J. Am. Chem. Soc. *97*, 5006 (1975).
[100] *J. Menter, Th. Förster*, Photochem. Photobiol. *15*, 289 (1972).
[101] *J. Ferguson, M. Puza*, Chem. Phys. Lett. *53*, 215 (1978).
[102] *G. Briegleb, J. Trensceni, W. Herre*, Chem. Phys. Lett. *3*, 146 (1969).
[103] *A. T. Amos, B. L. Burrows*, Adv. Quant. Chem. *7*, 313 (1973).
[104] *L. A. Halliday, M. R. Topp*, Chem. Phys. Lett. *48*, 40 (1977).
[105] *N. C. Yang, C. Rivas*, J. Am. Chem. Soc. *83*, 2213 (1961).
[106] *E. F. Zwicker, L. I. Grossweiner, N. C. Yang*, J. Am. Chem. Soc. *85*, 2672 (1963).
[107] *E. F. Ullman, K. R. Huffman*, Tetrahedron Lett. *1965*, 1863.
[108] *G. Porter, M. F. Tchir*, Chem. Commun. *1970*, 1372.
[109] *G. Porter, M. F. Tchir*, J. Chem. Soc. *A 1971*, 3772.
[110] *E. Migirdicyan, A. Despres, V. Lejeune, S. Leach*, J. Photochem. *3*, 383 (1975).
[111] *D. M. Findlay, M. F. Tchir*, Trans. Faraday Soc. I *1976*, 1096.
[112] *R. D. Small, Jr., J. C. Scaiano*, J. Am. Chem. Soc. *99*, 7713 (1977).
[113] *J. C. Scaiano*, J. Photochem. *2*, 81 (1973/74).
[114] *P. J. Wagner*, Top. in Curr. Chem. *66*, 1 (1976).
[115] *H. E. Zimmerman, N. E. Buehler, G. E. Keck, M. G. Steinmetz*, J. Am. Chem. Soc. *98*, 7680 (1976).
[116] *N. J. Turro, W. R. Cherry, M. F. Mirbach, M. J. Mirbach*, J. Am. Chem. Soc. *99*, 7388 (1977).
[117] *H. E. Zimmerman, R. W. Binkley, R. S. Givenas, M. A. Sherwin*, J. Am. Chem. Soc. *89*, 3932 (1967).
[118] *S. Murov, G. S. Hammond*, J. Phys. Chem. *72*, 3797 (1968).
[119] *A. F. Kluge, C. P. Lilly*, J. Am. Chem. Soc. *93*, 4458 (1971).
[120] *J. Saltiel, A. D. Rousseau, A. Sykes*, J. Am. Chem. Soc. *94*, 903 (1972).
[121] *N. C. Yang, S. P. Elliot*, J. Am. Chem. Soc. *91*, 7550, 7551 (1969).
[122] *M. Niemcyzk*, Ph. D. Dissertation, Columbia University 1972.
[123] *N. J. Turro, W. E. Farneth, A. Devaquet*, J. Am. Chem. Soc. *98*, 7425 (1976).

Compounds of Alkali Metal Anions

By James L. Dye[*]

Anions of sodium, potassium, rubidium, and cesium are stable both in suitable solvents and in crystalline solids. The latter can be prepared either by cooling a saturated solution or by rapid solvent evaporation. Thermodynamic arguments show that alkali metal anions can probably exist in saturated solutions of the alkali metals in any compatible solvent, but that below saturation, dissociation into the cation and solvated electrons is favored in highly polar solvents such as ammonia. The key to solvent-free salts of the alkali metal anions is stabilization of the *cation* by incorporation into a suitable crown or cryptand complex. By using such complexes it also appears possible to produce "electride" salts in which the charge of the complexed cation is balanced by a trapped electron. The chemical, electrical, and optical properties of salts of the alkali metal anions and "electrides" could provide useful applications.

1. Introduction

Alkali metals are exceptionally good electron donors, tending to form monopositive ions by donation of one electron to an acceptor atom or molecule. The resultant cation has a stable inert gas electron configuration with a filled outer p-shell. Because of this, the history of compounds of the alkali metals has been that of the cations and it was long thought that, except in metals and alloys, only the +1 oxidation state could exist. Yet the existence of alkali metal anions *in the gas phase* has been recognized for 30 years[1,2]. These anions were proposed as major species in metal-ammonia solutions in 1965[3,4] and in metal-amine solutions in 1969[5]. The isolation and characterization of a crystalline Na^- salt[6,7] in 1974 firmly established that the −1 oxidation state of alkali metals could exist in condensed phases. This has opened a new field of research on the properties of these highly-reducing species both in solutions and in solids. It is the purpose of this article to describe the current status of research in this field and to speculate on possible future developments.

2. Properties of Alkali Metals in Solution

The preparation of salts of the alkali metal anions has its origins in the study of metal-ammonia solutions and solvated electrons[8-11]. However, the discovery of alkali metal anions may have actually been delayed by the fact that ammonia is "too good" a solvent so that the dissociation reaction

$$M^- \rightleftharpoons M^+ + 2e^-_{solv} \qquad (1)$$

lies far to the right in dilute solutions and most properties are only mildly influenced by the cation. This does not mean that metal-ammonia solutions are simple: quite the contrary; ion-pair formation, electron spin-pairing and the onset of metallic behavior occur as the solutions are concentrated[8]. Because of these complications, alkali metal anions could be present in concentrated metal-ammonia solutions, but there is no specific evidence of such species in this solvent.

2.1. Solutions in Amines and Ethers

When any alkali metal except lithium is dissolved in an aliphatic amine, poly-ether or hexamethyl phosphoric triamide (HMPA), two prominent optical absorption bands are observed. One, in the infrared region at 1200—2000 nm, is the relatively metal-independent band of the solvated electron. The other band, whose position depends upon the metal, solvent and temperature, can be assigned to the alkali metal anion[5]. The proof of this assignment has been discussed in detail elsewhere[6,7,12-17] and will be included here only as needed for the description of specific systems or properties.

Progress in identifying the species in metal-amine and metal-ether solutions was hampered by low solubility, rapid decomposition, and the ease of extraction of sodium from borosilicate glass[18]. The problem of low solubility was overcome by the use of crown ether[19] and cryptand[20] complexing agents. Extraction of sodium from glass presents a major problem only at low concentrations and can be completely eliminated by using a fused silica apparatus. Unfortunately, problems arising from solution decomposition are still with us but can be minimized by working with rigorously clean vessels[21] and at reduced temperatures.

2.2. Optical Spectra

Each alkali metal anion is characterized by a broad, intense, structureless absorption band which depends upon metal, solvent and temperature and is strongly asymmetric on the high-energy side. These features are characteristic[5] of the so-called charge-transfer-to-solvent (ctts) bands[22,23] of other anions such as the halides, hydroxide, amide, *etc.* The spectra are also similar in shape and in solvent-[12] and temperature-dependence to those of the solvated electron in various solvents[12] but the absorption maxima occur at higher energies. Figure 1 shows the spectra of Na^-, K^-, Rb^-, Cs^- and e^-_{solv} in ethylenediamine[24]. The spectrum of e^-_{solv} obtained by pulse-radiolysis[25] (solid circles) compares well with that obtained by dissolving lithium (solid line) in ethy-

[*] Prof. Dr. J. L. Dye
Department of Chemistry, Michigan State University
East Lansing, Michigan 48824 (USA)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0587 $ 02.50/0

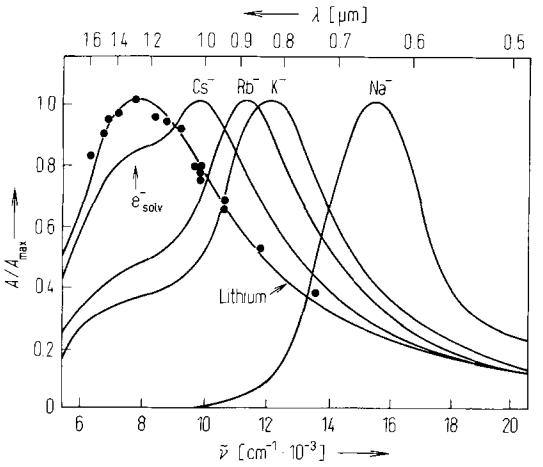


Fig. 1. Optical spectra of Li, Na, K, Rb, and Cs in ethylenediamine [24] with identification of absorption peaks of Na^-, K^-, Rb^-, Cs^- and e^-_{solv}. Solid circles are for e^-_{solv} produced by pulse radiolysis [25].

lenediamine. The infrared shoulders obtained for solutions of K, Rb and Cs are attributed to the solvated electron and the ratio of this absorbance to that of the anions depends strongly on concentration (see Eq. 1). The solvent-dependence of the peak positions is illustrated by Figure 2, which compares the peak positions of Na^-, K^- and e^-_{solv} in various solvents. The solvent-dependence of the absorption maximum of e^-_{solv} correlates in turn with that of I^- [23].

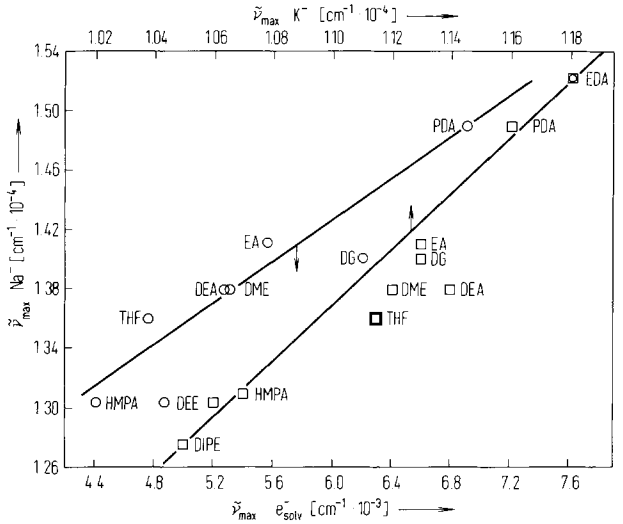


Fig. 2. Wavenumbers of the absorption maxima of Na^-, K^- and e^-_{solv} at 25 °C in various solvents. Open squares are for K^-, open circles are for e^-_{solv}. Solvent identification: DEA = diethylamine; DEE = diethyl ether; DG = diglyme; DIPE = di-isopropyl ether; DME = dimethoxyethane; EA = ethylamine; EDA = ethylenediamine; HMPA = hexamethyl phosphoric triamide; PDA = 1,2-propanediamine; THF = tetrahydrofuran.

Matalon, Golden and *Ottolenghi*[5] showed that the wavenumber of maximum absorbance of the alkali metal anions varies inversely with the estimated anion radius, in accord with the predictions of ctts theory. The observed temperature-dependence of the peak position is also predicted by this theory[5, 12]. We conclude that the absorption spectra of M^- in solution are similar to those of other anions.

An examination of ctts theory might lead one to conclude that the excited state bears no relation to excited states of the isolated anion. This does not necessarily follow, however. Excited states of the anion might lie above the ionization limit in the gas phase, yet be observable in solution or in crystals, either because of a strong perturbation of the continuum level or because of low probability for direct excitation to the continuum level of the solvent. In fact, auto-ionization apparently occurs from excited states of the alkali metal anions and other anions in solution[26-28] suggesting that the continuum level lies at lower energies than does the first excited state. It is probably appropriate to consider the intense absorption band of M^- in solution and in crystals as originating from an s to p transition, modified by the presence of solvent molecules or neighboring ions and including a contribution from direct bound-continuum transitions[28].

2.3. Conductivity

The conductivities of sodium and cesium solutions in ethylenediamine[29] and methylamine[30] have been measured. The optical spectra show that sodium solutions in these two solvents consist primarily of Na^+ and Na^- while dilute cesium solutions contain mainly Cs^+ and e^-_{solv}. The differences in conductivity of these solutions are striking—as shown in Figure 3. The rapid drop in conductivity with increasing concentration for solutions containing Cs^+ and e^-_{solv} in the amines resembles the behavior in ammonia and can be readily accounted for in terms of ion-pairing between Cs^+ and e^-. The high limiting conductance of e^-_{solv} in both ethylenediamine and methylamine is also similar to the behavior in ammonia especially when the appropriate viscosity corrections are made as in Figure 3. The conductivities and the similarity in optical spectra thus provide strong evidence that metal solutions in methylamine and in ethylenediamine which do *not* contain alkali metal anions are similar to metal-ammonia solutions. By contrast, the conductivities of sodium solutions in methylamine and ethylenediamine show that the mobility of Na^- is "normal" and that the extent of

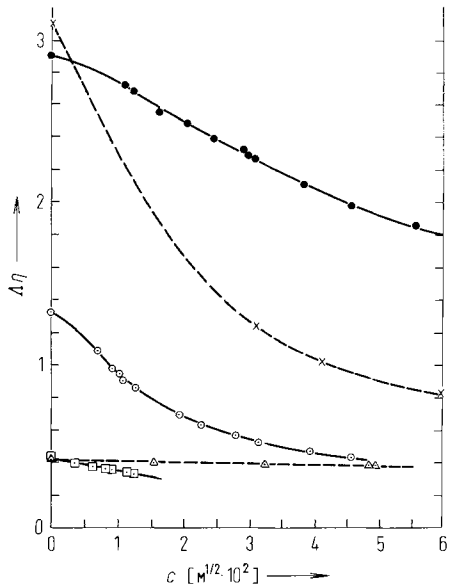
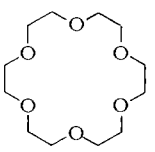


Fig. 3. Product of equivalent conductance (Λ) and solvent viscosity (η) for solutions of Na in methylamine ⊡ [30], and ethylenediamine △ [29], and of Cs in methylamine ⊙ [30], ethylenediamine × [29], and ammonia ● [83].

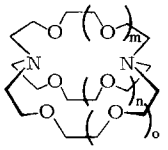
ion pairing between Na^+ and Na^- is small, as expected for a large interionic contact distance.

2.4. The Effect of Crown Ethers and Cryptands

One of the major barriers to experimental studies of alkali metal solutions in amines and ethers is the generally low solubility. Combined with the ever-present tendency towards decomposition, this low solubility has made reproducible measurements difficult. By using crown-ether and cryptand complexes such as those of [18]crown-6 *(1)*, and C222, we



[18] crown-6



Cryptands
C222, $m = n = o = 1$

were able to dramatically increase metal solubilities in a number of solvents[12, 19, 20, 31]. For a cation complexing agent (Cry = cryptand) the equilibrium (2) shifts the equilibrium (3) to the right, thus increasing the concentration of M^- in

$$M^+ + Cry \rightleftharpoons M^+Cry \quad (2)$$

$$2M_{(s)} \rightleftharpoons M^+ + M^- \quad (3)$$

the saturated solution. (This also applies for crown ethers as complexing agent.) When excess metal is present, equilibrium (4) determines the relative concentrations of M^- and

$$M^- \rightleftharpoons M_{(s)} + e^-_{solv} \quad (4)$$

e^-_{solv}. In the absence of excess metal, equilibrium (1) governs the relative concentrations of M^- and e^-_{solv}. The addition of a cation-complexing agent shifts reaction (1) to the right by reducing the concentration of M^+. Equilibrium (3) requires that the product of the activities of M^- and *free* cation cannot exceed the limit imposed by the solubility of metal. These reactions permit a measure of control over the composition tion of the solutions. The maximum value of the ratio $[M^-]/[e^-_{solv}]$ for a given metal is determined by the solvent and the temperature according to reaction (4). If this ratio is large, solutions consisting of primarily complexed M^+ and M^- can be prepared by maintaining an excess of metal in the preparation vessel. Alternatively, if K_1[*] is not too small and K_2 is large, the addition of equimolar amounts of complexing agent and metal can yield solutions whose composition is mainly complexed M^+ and e^-_{solv}. Section 3 considers the thermodynamics of these reactions in more detail.

2.5. Nuclear Magnetic Resonance

The ability to prepare concentrated metal-amine solutions (up to 0.2 M and higher) by using crown ethers and cryptands opened the door to NMR studies of alkali metal anions[32, 33]. It was known[34, 35] from NMR studies with salts that the release of Na^+ from a Na^+C222 complex is slow on the NMR time scale, so that separate ^{23}Na-NMR signals were expected and found for Na^+Cry and for Na^-. Figure 4 shows the spectra obtained in three solvents[33]. The calculated diamagnetic shift of $\delta = -2.6$ for Na^- compared with Na(g)[33, 36] is

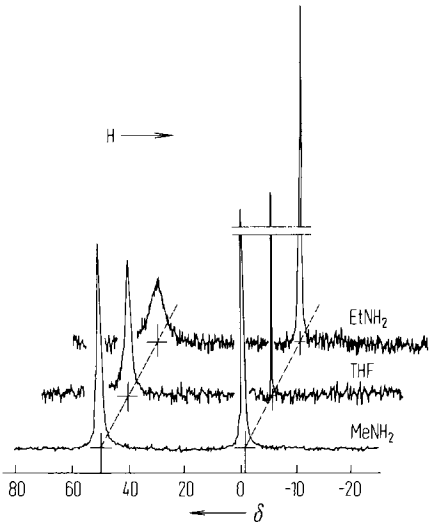


Fig. 4. ^{23}Na-NMR spectra of Na ' C222, Na solutions ($\approx$0.1 M) in three solvents [33]. All shifts are referred to $Na_{(g)}$. Positive shifts are paramagnetic. The peaks of Na ' C222 at the left are at $\delta = +49.5$. The peaks of Na at the right are at $\delta = -2$.

very close to the measured shifts[33] of $\delta = -1.4$, -1.6, and -2.3 for Na^- in methylamine, ethylamine and tetrahydrofuran respectively. This is to be compared with *paramagnetic* shifts of 60.5, 72.2 and 50.4 for Na^+ in water, methylamine and the cryptate complex respectively. The absence of an appreciable paramagnetic shift for Na^- in solution proves that the solvent is prevented from interacting appreciably with the 2p electrons by the presence of the outer 2s electrons. This, in fact, provides the strongest evidence that Na^- in solution is truly an alkali metal anion rather than, say, a solvated cation with two solvated electrons in the vicinity or a solvated cation attached to a solvated electron pair.

The NMR spectra[33] of Rb^- in ethylamine and in tetrahydrofuran (THF) show single lines at $\delta = +26.2$ and $+14.4$ ppm respectively relative to Rb(g) while the peak for Cs^- in THF occurs at $\delta = +52.3$ ppm relative to Cs(g). These are to be compared with values of $\delta = +213$ and $+348$ for aqueous Rb^+ and Cs^+ respectively. Exchange effects[17] sometimes prevent the observation of the NMR signal of M^- and may be the reason that we have not yet been able to observe K^- by NMR even in solutions whose optical spectra show the existence of high concentrations of this species.

2.6. Other Solution Properties of Alkali Metal Anions

The rate of reaction of Na^- with water in ethylenediamine is much slower than that of e^-_{solv} and the reaction order in water is also different[21, 37]. The rate of formation of Na^- from solvated electrons and Na^+ has been studied by pulse radiolysis[14, 38]; the reaction is second order w.r.t. e^-_{solv}. The dependence of the rate on the concentration of Na^+ is complex and suggests[14] that electron-pairing precedes the formation of Na^-. Photolysis of M^- in the wavelength region of the absorption maximum leads to the production of solvated electrons[39-47], sometimes in a spin-polarized state[40, 46, 47] (CIDEP). Photoelectron emission has also been

[*] K_1 is the equilibrium constant for reaction (1).

observed[28] from e^-_{solv} and from Na^- in HMPA. These observations generally support the assumption that alkali metal anions are new species and not just a combination of the solvated cation and two solvated electrons.

2.7. Ion pairs and "Monomers" in Solution

The electron spin resonance (ESR) spectrum of the solvated electron consists of a single narrow line with a g-value near that of the free electron. When the electron interacts strongly with an alkali cation so that appreciable electron density exists at a metal nucleus with spin I, and when this electron-cation pair has a long enough lifetime (generally microseconds or longer) then a hyperfine pattern results with $2I+1$ nearly equally spaced lines[48-51]. Pulse radiolysis[38,52,53] and photolysis[43] studies in the presence of alkali cations have shown that the optical spectrum of e^-_{solv} is blue-shifted by formation of the ion-pair (also referred to as an alkali metal "monomer"). The magnitude of this blue-shift increases as the polarity of the solvent decreases and correlates well with the electron contact density at the alkali nucleus as determined by ESR measurements[53]. Changes in the cation-electron contact density and in the spectrum with solvent and temperature have been attributed to the formation of solvent-shared and contact ion-pairs[51]. Although the sensitivity of the ESR technique permits easy detection of the monomer species, the equilibrium concentration of monomers, M, in amines and ethers is generally small compared with M^- and e^-_{solv}. Crown ethers or cryptands shift the equilibrium

$$M \rightleftharpoons M^+ + e^- \qquad (5)$$

to the right in the absence of excess metal. Although the concentration of monomers is low, they may play important roles in the exchange kinetics of complexed M^+ and M^- and in the rate of decomposition of metal solutions.

3. Thermodynamic Considerations

The proposed existence of alkali metal anions in ammonia[3,4] was based on thermodynamic arguments. Our search for salts of the alkali metal anions (which we refer to as "alkalides") was also based on thermodynamic predictions of their stabilities and we continue to be guided in the search for appropriate metals, solvents and complexing agents by approximate calculations of stability constants. Questions have also arisen about the possible existence of anions of other metals such as the alkaline earths. It is a simple matter to show thermodynamically that the existence of an ion such as Ca^- in solution is thermodynamically impossible while the gold anion, Au^-, may well be thermodynamically stable. In this section some of the pertinent thermodynamic arguments will be given. Some of the predictions can be made with reasonable accuracy; others are far less certain, either because key measurements have not yet been made or because of limitations of the theory of solvation free energies or lattice energies. In either case, it is often possible to make reasonably accurate *relative* calculations which at least permit comparisons among the alkali metals.

3.1. Stability of Metal Anions in Ammonia as Solvent

It is possible to calculate accurate values of ΔH^0 and ΔG^0 for the process

$$e^-_{(g)} + M_{(s)} \rightarrow M^-_{(g)} \qquad (6)$$

from electron affinities[2,54], properties of the solid and gaseous elements[55], and statistical thermodynamics calculations of entropies[56]. The values of ΔH^0_6 and ΔG^0_6 for the alkali metals and some other metallic elements at 25 °C are given in Table 1[*].

Table 1. Thermodynamic estimates [a] used to judge the stability of anions in ammonia to dissociation into metal and solvated electrons.

Metal	Estimated anion radius r (Å)	Electron Affinity	ΔH^0_6	ΔG^0_6	ΔH^0_7	ΔG^0_7	
						298 K	238 K
Li	2.35	59.8	96.7	67.7	− 65.8	1.8	− 11.8
Na	2.72	52.9	53.4	30.6	− 78.1	− 5.6	− 20.2
K	3.27	48.4	39.1	18.2	− 59.3	13.5	− 1.1
Rb	3.39	46.9	36.4	14.4	− 56.3	15.2	0.8
Cs	3.55	45.5	30.7	10.9	− 54.9	18.5	3.8
Au	2.00	222.7	140.9	109.0	− 61.5	5.1	− 8.3
Ag	2.00	125.7	156.4	125.4	− 46.0	21.4	7.9
Cu	1.93	118.3	217.5	185.7	5.5	72.5	59.0
Ba	3.5	− 52.1	225.4	202.3	137.7	207.9	193.7
Pt	3.55	205.3	357.5	320.6	271.9	328.2	316.9
Te	2.3	183.3	11.0	− 20.8	− 156.5	− 91.4	− 104.5
Pb	2.2	101.3	91.2	66.0	− 86.8	− 14.7	− 29.2
Bi	2.2	101.3	103.3	72.3	− 74.7	− 8.4	− 21.8
Tl	2.1	48.2	131.5	104.6	− 58.1	12.8	− 1.4
Sb	2.2	101.3	158.6	126.3	− 19.5	45.6	32.5
Sn	2.2	120.6	179.0	152.2	1.0	71.4	57.3

[a] All values given in kJ mol^{-1}; $\Delta H^0_8 = 247 - 535\,(1/r)$; $\Delta G^0_8 = 334 - 511\,(1/r)$ evaluated by fitting data for the halide ions (see text).

If the solvation free energy of $M^-_{(g)}$ is more negative than that of $e^-_{(g)}$ by an amount equal to or greater than that given in Table 1 then the reaction

$$e^-_{solv} + M_{(s)} \rightarrow M^-_{solv} \qquad (7)$$

[*] Many of the thermodynamic estimates described in this article have not been previously published. Details of the calculations are available from the author on request.

is feasible and we can expect M^- to be stable to dissociation into the (solid) metal and solvated electrons. According to the Born equation[57] both the Gibbs free energy of solvation and the enthalpy of solvation of an ion are inversely proportional to the ionic radius. Since the Born equation is based on a continuum model and fails to account for specific solvation of the ions, it is not appropriate to use it directly. A better procedure is to use the known free energies and enthalpies of formation of Cl^-, Br^- and I^- in ammonia[58] together with the thermodynamics of formation of the corresponding gaseous anions to calibrate the dependence of the solvation enthalpy and Gibbs free energy upon radius. Specifically, ΔG_8^0 and ΔH_8^0 for

$$X^-_{(g)} + e^-_{(Pt)} \rightarrow X^-_{(NH_3)} + e^-_{(g)} \tag{8}$$

are linear functions of the reciprocal of the anion radii of Cl^-, Br^- and I^-. These thermodynamic functions were obtained by combining the reactions

$$\frac{1}{2}X_2 + e^-_{(Pt)} \rightarrow X^-_{(NH_3)} \tag{9}$$

$$\frac{1}{2}X_2 \rightarrow X_{(g)} \tag{10}$$

$$X_{(g)} + e^-_{(g)} \rightarrow X^-_{(g)} \tag{11}$$

The values of ΔG_9^0 and ΔH_9^0 were obtained from the tabulation of *Latimer* and *Jolly*[58] and are based upon $\Delta G_f^0 = 0$ and $\Delta H_f^0 = 0$ for H^+ in ammonia. The values of ΔG^0 for reactions (10) and (11) were obtained from known atomization free energies and enthalpies[55] of the halogens and their electron affinities[54]. By assuming that the solvation free energy and enthalpy of other anions depend upon radius in the same way as those of Cl^-, Br^- and I^-, we can calculate ΔG_8^0 and ΔH_8^0 for any anion if we know its radius. Following the suggestion of *Matalon, Golden* and *Ottolenghi*[5] we can estimate the radius of an alkali metal anion by subtracting its ionic radius from the interatomic distance in the metal. The radius of Au^- (2.0 Å) was obtained by subtracting the radius of Cs^+ from the cesium-gold distance in the ionic compound CsAu[59]. The values[58] $\Delta G_f^0 = -182$ kJ mol^{-1}, $\Delta H_f^0 = -159$ kJ mol^{-1} for Na^+ in NH_3 at 25 °C and $\Delta H_f^0 = -182$ kJ mol^{-1} for $e^-_{(NH_3)}$ combined with $\Delta G_{12}^0 \approx 0.0$ at 25 °C[60] for the process

$$Na_{(s)} \rightarrow Na^+_{(NH_3)} + e^-_{(NH_3)} \tag{12}$$

gives $\Delta H_{13}^0 = \Delta G_{13}^0 = -182$ kJ mol^{-1} for

$$e^-_{(NH_3)} \rightarrow e^-_{(Pt)} \tag{13}$$

at 25 °C based upon the convention that the enthalpy and free energy of formation of $H^+_{(NH_3)}$ are zero. Addition of reactions (6), (8) and (13) gives reaction (7). The values of ΔH_7^0 and ΔG_7^0 at 25 °C and ΔG_7^0 at −35 °C for a number of metallic elements are given in Table 1. The results show that the reaction of solvated electrons with metal to produce ammoniated metal anions with filled outer s-orbitals may be thermodynamically permitted for all of the alkali metals and for gold[*] and silver. It appears that Cu^- would not be stable to dissociation into $Cu_{(s)}$ and e^-_{solv}.

For ions which do not have the added electron in an s-orbital, the calculations predict stability for Te^-, Pb^-, Bi^-, and Tl^-. The first three of these elements do form anions in ammonia[61,62] which have also recently been isolated in crystalline salts[63–68], but in these cases the anions are polymeric rather than monomeric. Salts which contain polymeric anions of antimony and tin have also been isolated[63,65,67]. Our calculations indicate instability of *monomeric* Sb^- and Sn^- in ammonia but the addition of metal-metal bonding would stabilize polymeric anions.

The existence of detectable concentrations of such ions as Ba^- and Pt^- in ammonia is clearly impossible from a thermodynamic viewpoint. In the former case, the negative electron affinity of barium shows that Ba^- is not even stable in the gas phase. On the other hand, while platinum has a large electron affinity the lattice energy is so great that conversion of $Pt_{(s)}$ to Pt^- by the action of solvated electrons is not thermodynamically permitted.

3.2. Dissociation of M^- to M^+ and Solvated Electrons in Solution

The calculations described above were made for ammonia solutions because we have sufficient data to calculate Gibbs free energies and enthalpies of formation of ions in ammonia, but not in amines and ethers. Similar calculations could be made for amine and ether solvents if sufficient solubility and/or e.m.f. data were available. Yet ironically, we have no *specific* evidence for the existence of alkali metal anions in ammonia. Let us examine the predicted concentrations for the most favorable case, that of Na^-. From the data in Table 1 we can calculate that for the reaction

$$e^-_{(NH_3)} + Na_{(s)} \rightleftharpoons Na^-_{(NH_3)} \tag{14}$$

at −35 °C, $K_{14} \approx 3 \times 10^4$. However, in a dilute solution away from metal we must also consider the equilibrium

$$Na^-_{(NH_3)} \rightleftharpoons Na^+_{(NH_3)} + 2e^-_{(NH_3)} \tag{15}$$

for which $K_{15} \approx 4 \times 10^{-6}$ M^2. This predicts that at a sodium concentration of 10^{-3} M (neglecting the effect of activity coefficients) the ratio $[Na^-]/[e^-]$ should be about 0.15. If the optical spectrum of Na^- were appreciably different from that of e^- in ammonia as it is in amine and ether solvents, then the presence of this concentration of Na^- would be easily detectable. Certainly, upon addition of a sodium salt the presence of Na^- should be observable. However, no prominent optical band of Na^- has been observed either in the presence or absence of sodium salts. We must conclude that either the calculation given for Na^- in Table 1 is in error by 15 kJ mol^{-1} or more, or the optical band of Na^- is shifted into the infrared in ammonia as originally suggested by *Golden et al.*[3]. We conclude that, while such calculations as these cannot be used to determine concentrations, they do demonstrate that the existence of alkali metal anions in ammonia, amines, and ethers is not prohibited on thermodynamic grounds.

[*] *W. J. Peer* and *J. J. Lagowski* [J. Am. Chem. Soc. *100*, 6260 (1978)] have recently shown that Au^- can be formed in liquid ammonia.

3.3. Stability of Metal Anions in Amine and Ether Solvents

Alkali metal solubilities[29] and spectra[24,69] have been measured for ethylenediamine solutions at 25 °C. The extinction coefficients of Na^- and e^-_{solv} in ethylenediamine are 8.2×10^4 and 2.0×10^4 M^{-1} cm^{-1} respectively[13,14]. These measurements permit estimation of the equilibrium constants K_1, K_3, and K_7 for ethylenediamine as solvent (see Table 2).

Although (excluding Li^-) Na^- is most stable and K^- is least stable relative to e^-_{solv} in the presence of excess metal, the concentration of M^- in the saturated solution increases regularly from Na^- to Cs^-. The dissociation of M^- to $M^+ + 2e^-_{solv}$ is least likely for Na^- and most likely for K^-. This apparently anomalous position of potassium solutions seems to reflect extra stabilization of the solvated electrons in the presence of K^+, perhaps *via* ion pairing. Such an effect has actually been observed both by the addition of a potassium salt to a solution of sodium in ethylenediamine[13] and by pulse radiolysis studies[14]. The appearance of the spectral peak of the solvated electrons occurs in this case but not when Rb^+ or Cs^+ are added.

Solubility and spectral data in other solvents are too sparse to permit evaluation of equilibrium constants. However, it is clear that the values of K_2 increase while K_1 and K_3 both decrease as the solvent polarity decreases. Thus, all metals except lithium when dissolved in ethylamine show primarily the optical band of M^- with little contribution from e^-_{solv}. Based upon the effect of C222 on the optical spectrum[70] we estimate that $K_1 < 10^{-20}$ for sodium in tetrahydrofuran. Therefore, solutions of sodium in this solvent, even in the presence of excess cryptand consist essentially of $Na^+C222\,Na^-$ with no detectable solvated electron concentration. By contrast, solutions of potassium in tetrahydrofuran with cryptand contain largely $K^+C222\,K^-$ when excess potassium is present, but mainly $K^+C222\,e^-_{solv}$ when an equivalent of cryptand is present[70].

Table 2. Estimation of equilibrium constants K_1, K_3 and K_7 for reactions of alkali metal anions in ethylenediamine at 25 °C from optical spectra and solubilities.

Metal	Solubility (M)	Path lenght (cm)	Absorbance Data Used A_e	A_M	Ref.	K_1 (M^2)	K_3 [a] (M^2)	K_7
Li	0.29	0.1	2	<0.05 [b]	[24]	$>4 \times 10^{-4}$	$<2 \times 10^{-2}$	<7
Na	2.39×10^{-3}	1.0	0.09	0.91	[69]	3×10^{-11}	1.4×10^{-6}	220
K	1.04×10^{-2}	1.0	2.0	0.46 [c]	[69]	1.6×10^{-6}	2.7×10^{-5}	4.1
		0.01	0.2	0.65	[24]	2.3×10^{-6}	2.7×10^{-5}	3.4
Rb	1.31×10^{-2}	1.0	0.84	0.40	[69]	1.7×10^{-8}	4.3×10^{-7}	50
		0.1	0.36	0.68	[24]	1.0×10^{-7}	4.3×10^{-5}	20
Cs	5.4×10^{-2}	0.01	0.6	0.9	[24]	4×10^{-5}	7×10^{-4}	5

[a] $K_3 = K_1 K_7^2$. [b] Estimated conc. of $Li = 3 \times 10^{-3}$ M. [c] In the presence of 1×10^{-3} M added K^+.

3.4. Stability of Metal Anions in Crystals

Attempts to grow crystals containing alkali metal anions were based upon their stability in solution, and the realization that stabilization of the cation by its inclusion in a cryptand cavity might prevent the spontaneous recombination of M^+ and M^- to form the metal. The fact that alkali cations are strongly complexed by the appropriate cryptand, even in as good a solvent as water, means that the gas phase complexation reaction

$$M^+_{(g)} + Cry_{(g)} \rightarrow M^+Cry_{(g)} \quad (16)$$

is strongly exothermic and highly favored. There are no direct data for this reaction, but indirect methods can be used to evaluate ΔH^0_{17} and ΔG^0_{17} for the reaction

$$Cry_{(s)} + M_{x(s)} + M_{y(s)} \rightarrow M^+_x Cry M^-_{y(s)} \quad (17)$$

in which M_x and M_y may be the same or different. If ΔG^0_{17} is negative then the salt $M^+_x Cry M^-_y$ is stable to decomposition into its components Cry, M_x and M_y. By adding all of the ΔH^0 and ΔG^0 values for the reactions listed in Table 3 one obtains ΔH^0_{17} and ΔG^0_{17}. While the *absolute* values of ΔH^0_{17} and ΔG^0_{17} given in Table 4 may be in error by as much as ± 50 kJ because of errors of measurement and the various approximations made, their *relative* values should be much more reliable. Since we can prepare the crystalline salt $Na^+C222\,Na^-$, even in the presence of an excess of sodium and cryptand, it appears to be thermodynamically stable. The calculated value of ΔG^0_{17} for this salt is $+32$ kJ mol^{-1} which is within the estimated absolute error of the value $\Delta G^0_{17} \leq 0$ required for thermodynamic stability. It appears safe to assume that any proposed salt with a value of ΔG^0_{17} equal to or more negative than that of the reference salt $Na^+C222\,Na^-$ is likely to be thermodynamically stable. Of course, these calculations do not preclude decomposition *via* destruction of the cryptand moiety, a process which we have found to be very common.

A critical quantity in these calculations is the interionic distance in the crystalline salt. The sum of the calculated radii r_{Na^+Cry} and r_{Na^-} is larger than the measured distance in the salt $Na^+C222\,Na^-$ by 14%. This could be caused by lack of sphericity of the cryptated cation, an error in the estimate of its size or that of Na^-, and/or compression of these relatively "soft" ions in the crystal. The cation-anion distances in $Na^+C222\,I^-$[76] and $K^+C222\,I^-$[77] are within a few percent of those calculated on the basis of the ionic radius of I^- and the radii of Na^+C222 and K^+C222 calculated from the ligand thickness[73]. Therefore, the most likely source of error in the estimate of the interionic distance in $Na^+C222\,Na^-$ is an error in the estimated radius of Na^- or neglect of the compression of this ion and of the cryptated cation in the crystal. In order to compensate for this reduction in interionic distance, all of the calculated anion radii were reduced by 14% in computing the lattice energy and entropy in step (h) of Table 3.

Table 3. Steps in thermodynamic cycle used to evaluate ΔH^0_{17} and ΔS^0_{17}.

	Reaction step	Origin of data or estimate	Typical data source
a)	$M^+_{(aq)} + Cry_{(aq)} \rightarrow M^+Cry_{(aq)}$	Enthalpies of complexation and equilibrium constants	[71]
b)	$Cry_{(s)} \rightarrow Cry_{(aq)}$	Solubility of cryptand as a function of temperature, enthalpies of solution of pure cryptand in water	[b]
c)	$M_{(s)} \rightarrow M^+_{(g)} + e_{(g)}$	ΔH^0 and ΔG^0 of atomization plus ionization potentials of $M_{(g)}$. Use Sackur-Tetrode equation for entropies of gaseous species.	[55, 56]
d)	$M^+_{(g)} \rightarrow M^+_{(aq)}$	Tabulated hydration enthalpies and free energies	[72]
e)	$M^+Cry_{(aq)} \rightarrow M^+Cry_{(g)}$	Born equation plus estimate of size of M^+Cry from ligand thickness	[57, 73, 74]
f)	$M_{(s)} + Cry_{(s)} \rightarrow M^+Cry_{(g)} + e_{(g)}$	Sum of a—e	
g)	$M_{(s)} + e_{(g)} \rightarrow M_{(g)}$	ΔH^0 and ΔG^0 of atomization plus electron affinity of $M_{(g)}$ and calculation of entropy as in (c) above	[54, 55]
h)	$M^+_x Cry_{(g)} + M_{x(g)} \rightarrow M^+_x Cry M^-_{y(s)}$	Kapustinskii equation for lattice energy; ΔS^0 from size and comparison with alkali metal halides [a]	[74, 75]
i)	$Cry_{(s)} + M_{x(s)} + M_{y(s)} \rightarrow M^+_x Cry M^-_{y(s)}$	Sum of f, g, and h	

[a] A plot of ΔS^0_h for formation of alkali halide lattices from the gaseous ions *vs.* $(r_{M^+} + r_{X^-})^{-1}$ is linear, following the equation $\Delta S^0_h = -47.8 - 29.2\,(r_{M^+} + r_{X^-})^{-1}$, while for the alkaline earths the equation is $\Delta S^0_h = -72.2 - 53.6\,(r_{M^{2+}} + r_{X^-})^{-1}$ (S in JK^{-1} mol^{-1}, r in Å).
[b] Data not available so $\Delta H^0_h = \Delta G^0_h = 0.0$ was used in preparing Tables 4 and 5. Recent calorimetric measurements give $\Delta H^0_h = -24.5$ kJ mol^{-1}; *M. H. Abraham*, University of Surrey (England), private communication, (1979).

Calculated values of ΔH^0 and ΔG^0 for steps (f), (h) and (i) of Table 3 are given in Table 4 for a few selected salts. Calculations involving the cryptated alkaline earth cations included the necessary valence corrections but are probably less certain than those for the alkali metals. Nevertheless, they indicate that salts such as $Ba^{2+}C222(Na^-)_2$ should be thermodynamically stable.

These calculations also provide estimates of the thermodynamic stability of "electrides"[78]. To calculate ΔH^0_{18} and ΔG^0_{18} for the process

$$Cry_{(s)} + M_{(s)} \rightarrow M^+Cry e^-_{(s)} \qquad (18)$$

we assume that the electron occupies the octahedral holes in a closest-packed lattice of cryptated cations. Therefore the effective "radius" of the trapped electron is $0.414\,r_{M^+Cry}$ and the lattice energy is assumed to be the same as that of a salt in which a hard monovalent anion just fits into the octahedral hole. Compression of the packed cations or delocalization of the electrons would be expected to predict even greater stabilities. The conservative estimates given in Table 4 suggest that "electrides" should be stable. The values of ΔH^0_{16}, ΔG^0_{16}, ΔH^0_{18}, and ΔG^0_{18} for a number of other possible compounds are given in Table 5.

At the very least, the results given in Tables 4 and 5 for a variety of crystalline salts of "alkalides" and "electrides" suggest that this field is potentially a very rich one for the synthesis of a variety of new compounds. The predicted thermodynamic stabilities of salts of the alkaline earth cryptates are particularly striking. In the following sections we will describe our progress in the preparation of "alkalide" and "electride" salts and speculate about possible future developments.

Table 4. Estimated thermodynamic data [a] for assessment of the stability of some crystalline salts of the type $M^+_x Cry M^-_y$ ($M_x = M_y$, $M_x \neq M_y$) and $M^+Cry e^-$ at 25 °C. The subscripts f, h, and i refer to the corresponding reactions in Table 3.

$M^+_x Cry M^-_y$ $M^+Cry e^-$	ΔH^0_f	ΔG^0_f	ΔH^0_h	ΔG^0_h	ΔH^0_i	ΔG^0_i
$Na^+C222Na^-$	259	255	−323	−258	− 10	28
$Li^+C211Li^-$	245	226	−356	−291	− 14	2
K^+C222K^-	231	227	−303	−238	− 33	6
$K^+C222Na^-$	231	227	−322	−257	− 38	0
$Ba^{2+}C222(Na^-)_2$	715	721	−966	−866	−197	−114
K^+C222e^-	231	227	−294	−229	− 63	− 3
$Li^+C211Au^-$	245	226	−373	−307	13	27
$Ba^{2+}C222(e^-)_2$	715	721	−880	−782	−165	− 61

[a] All values in kJ mol^{-1}. ΔH^0_h and ΔG^0_h not included (see however footnote [b] of Table 3).

Table 5. Selected estimated values of the enthalpy and Gibbs function (in kJ mol^{-1}) at 25 °C for the formation of crystalline salts of type $M^+_x Cry M^-_y$ or $MCry e^-$ from the metal and the cryptand [a].

$M^+_x Cry M^-_y$ $M^+Cry e^-$	ΔH^0 [b]	ΔG^0 [b]
$Li^+C211Na^-$	− 41	− 19
Li^+C211K^-	− 35	− 10
$Li^+C211Cs^-$	− 33	− 8
Li^+C211e^-	− 74	− 29
Li^+C211H^-	19	58
$Li^+C211Ag^-$	26	41
$Li^+C211Cu^-$	85	99
$Na^+C222Li^-$	19	51
Na^+C222e^-	− 35	26
$Na^+C221Na^-$	− 5	17
Na^+C221e^-	− 33	11
$Ba^{2+}C222(Li^-)_2$	−197	−120
$Ba^{2+}C222(Cs^-)_2$	−136	− 51
$Ba^{2+}C222(Au^-)_2$	−197	−123
$Ba^{2+}C222(Ag^-)_2$	−188	−113
$Ba^{2+}C222(Cu^-)_2$	−134	− 59
$Ca^{2+}C221(Na^-)_2$	−177	−115
$Ca^{2+}C221(e^-)_2$	−154	− 70
$Cs^+C322Cs^-$	− 2	30
$Rb^+C222Rb^-$	− 28	12

[a] Values of ΔH^0_h and ΔG^0_h not included (however, see footnote [b] in Table 3).
[b] Reaction: $Cry_{(s)} + M_{x(s)} + M_{y(s)} \rightarrow M^+_x Cry M^-_y$ or $Cry_{(s)} + M_{(s)} \rightarrow M^+Cry e^-_{(s)}$.

4. Solid Compounds Containing Alkali Metal Anions

By late 1973 the evidence for alkali metal anions in solution was very strong, and thermodynamic estimates indicated potential stability of crystalline ionic salts of the type M^+CryM^-. Rapid evaporation of methylamine or ethylamine from concentrated solutions of sodium or potassium in these solvents in the presence of cryptand C222 left deposits of metallic-looking gold-colored films on the glass walls. Upon cooling a solution of Na^+C222, Na^- in ethylamine (≈ 0.1 M) from +5 °C to dry-ice temperatures, a gold-colored powder precipitated from solution. Slow cooling resulted in the growth of hexagonal crystals of the salt $Na^+C222\,Na^-$. Analysis[6] and a crystal structure determination[7] confirmed the existence of this first solid compound containing an alkali metal anion. The isolation and characterization of other members of this class of compounds has been hampered by difficulties with stabilities and with finding the proper solvents for crystallization, but recently we have made considerable progress in this area.

4.1. Preparation and Characterization of $Na^+C222\,Na^-$

4.1.1. Preparation of Powdered and Crystalline Forms

The preparation of this salt is relatively simple provided one pays close attention to solvent purity and cleanliness of the glassware. The type of vessel used is shown in Figure 5.

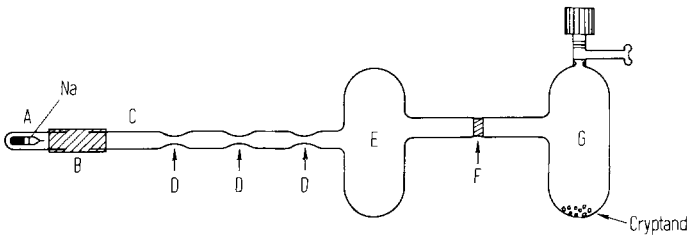


Fig. 5. Apparatus for the preparation of the crystalline salt $Na^+C222\,Na^-$ [74]. A to G see text.

The sodium, previously transferred under vacuum into small diameter glass tubing is inserted into glass tube A after scoring the metal-containing tube with a glass knife. Heat-shrinkable Teflon tubing B is used to connect tube A to side-arm C. Cryptand is then introduced into vessel G and the entire apparatus is evacuated. Then the tube containing sodium is shaken into the flexible connection B between A and C, broken under vacuum and moved to the constriction. A vacuum seal-off is made behind the metal sample and with the vessel re-attached to the vacuum manifold, metal is successively distilled into vessel E through two or three constrictions while pumping ($\approx 10^{-5}$ torr). (With volatile cryptands vessel G must be cooled during this operation.) Solvent sufficient to produce about 0.05 M cryptand is condensed in G, the cryptand is dissolved and the solution is transferred into E and allowed to contact the metal mirror at 0 °C for a few hours. The solution is then poured through the frit F into G and cooled to −78 °C, resulting in the precipitation of finely-divided crystals of $Na^+C222\,Na^-$. To improve the yield, the supernatant blue solution is poured from the crystals at −78 °C back through the frit F into E for further agitation on the metal at 0 °C. After pouring the supernatant liquid into E for the last time it is distilled into a waste flask and either diethyl ether or *n*-pentane is condensed on the salt in order to remove any unreacted cryptand or other organic-soluble impurities. Provision is usually made on vessel G for transfer of the washed salt into a number of tubes which can be individually sealed-off under vacuum. Crystals of $Na^+C222\,Na^-$ up to ≈ 1 mm in diameter can be grown by slowly cooling a solution which is formed by redissolving the salt in ethylamine.

4.1.2. Crystal Structure of $Na^+C222\,Na^-$

In its gross features, the crystal structure[7] of this salt may be viewed as hexagonal closest-packing of the large cryptated cations with the smaller Na^- ions occupying the octahedral holes. The cryptand forms a cage for Na^+ with three-fold symmetry and an anti-prismatic arrangement of the ether oxygens. Views down the three-fold axis and side-on are shown in Figure 6. The shape of the cryptate moiety and relative positions of Na^+ and Na^- are similar to those in

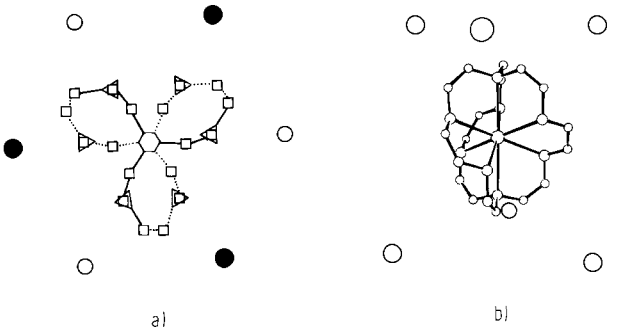


Fig. 6. Views of the structure of $Na^+C222\,Na^-$ [7]. (a) Looking down the three-fold axis; filled-in circles represent the "top" Na^- ions; open circles the bottom ones. Triangles represent O atoms, squares represent CH_2 groups. The two N atoms and Na^+ are co-linear at the center. Solid lines connect atoms above the center; dotted lines below the center. (b) Perspective side-view of the structure.

$Na^+C222\,I^-$ [76]. The closest Na^- to Na^- distances are 8.83 Å in the packing planes perpendicular to the three-fold axis while the closest distance between Na^- ions in different planes is 11.0 Å. This could result in considerable anisotropy of those properties which depend upon the distance between anions such as the electrical conductivity.

4.1.3. Properties of $Na^+C222\,Na^-$

Crystals of this salt frequently grow as thin hexagonal plates with shiny metallic-looking faces. Their color at liquid nitrogen temperature is bright yellow-gold, which darkens reversibly to a yellow-bronze appearance at room temperatures. The crystals melt with decomposition at 83 °C to yield gray particles suspended in a clear fluid. Analysis after cooling shows that most of the cryptand remains intact and apparently sodium metal is released upon melting. By contrast, crystals left in evacuated tubes for several days at room temperature and under ambient light conditions darken irreversibly, apparently with decomposition of the cryptand. When a sample was kept in the dark at room temperature for three weeks, no apparent decomposition occurred, but the apparent photosensitivity has not yet been investigated further.

Packed powders of $Na^+C222Na^-$ have the temperature-dependent electrical conductivity expected for a semiconductor. As shown in Figure 7, $\log\rho$ *vs* $1/T$ gives a straight line over six decades of resistance where ρ is the specific resistance. The magnitude of the resistance depends upon the packing pressure and decreases with time as the sample anneals. Considering this salt as a semiconductor gives a band

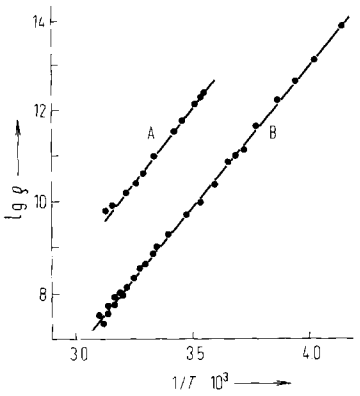


Fig. 7. Semi-log plot of specific resistance of powdered samples of $Na^+C222Na^-$ *versus* the reciprocal of the temperature. Sample A was relatively loosely-packed. The data shown for the tightly-packed sample B were measured at both increasing and decreasing temperatures [82].

gap of 2.4 eV. This salt is diamagnetic, as indicated both by ESR studies and by static susceptibility measurements. No magnetic anomalies have been found between 300 and 4.2 K. The ESR spectrum shows only an extremely weak signal probably caused by trapped electrons.

4.1.4. The Optical Spectrum of Thin Films of $Na^+C222Na^-$

Powdered or crystalline samples of this compound can be dissolved in a number of amines and ethers to give deep blue solutions. Upon cooling such solutions (except in methylamine and ammonia) the salt precipitates. When solutions in methylamine, ethylamine or THF are rapidly evaporated, the walls are covered with a thin film which appears gold by reflected light and blue by transmitted light. The absorption spectrum of such a film is shown in Figure 8. In all cases with this compound the three distinctive features shown in Figure 8 were observed[78]. The major peak at 15400 cm^{-1} (650 nm) is characteristic of Na^- in solution[12] and probably arises from a 3s to 3p transition, modified by crystal-field effects. The origins of the pronounced shoulder at 18900 cm^{-1} and the small but distinct peak at 24500 cm^{-1} are unknown although the latter could arise from a bound-free transition corresponding to the band-gap of 2.4 eV shown by conductivity. Figure 8 also shows that the gold-colored film formed by using [18]crown-6 in the presence of solvent vapor has the major absorption band at 15400 cm^{-1} but shows neither the extra peak at 24500 cm^{-1} nor the shoulder at 18900 cm^{-1}.

The spectrum shows clearly why crystals of $Na^+C222Na^-$ appear metallic by reflected light. The high absorption in the near-infrared and sharp cutoff in the visible mimic the plasma absorption of metals. This can lead to a striking metallic appearance even for nonconducting crystals[79].

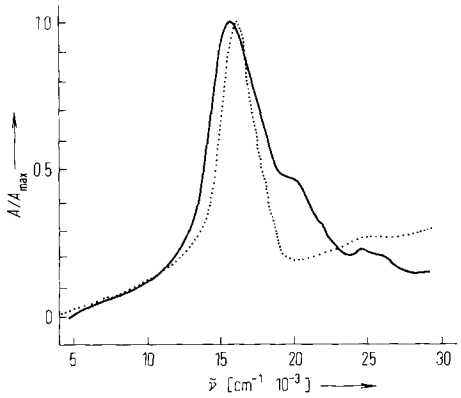


Fig. 8. Absorption spectra of a thin, solid solvent-free film of $Na^+C222Na^-$ (solid line) [78] and of a film of Na^+ 18C-6 Na^- containing some methylamine (dotted line) [81].

4.1.5. Summary of the Properties of $Na^+C222Na^-$

The structure and properties of the salt $Na^+C222Na^-$ in the crystalline state and in solution, confirm that Na^- is a "genuine" spherical anion with two electrons in the 3s orbital. Were it not for the tendency of Na^- to donate electrons to any available acceptor, a variety of salts could probably be prepared. However, stability requires that the counterion be extremely reluctant to pick up an electron. Any bare metal cation would probably be reduced by Na^- and we will probably be forced to continue to use complexed metal cations or perhaps such species as tetraalkylammonium cations. While the latter will probably not pick up the electron by simple attachment, it is known that solvated electrons can react with small tetraalkylammonium ions, breaking the C N bond. Therefore, salts such as $R_4N^+Na^-$ may not be stable.

4.2. Other Salts of Alkali Metal Anions

The crystalline compound described in the previous section can be prepared either by crystallization from a solution containing largely Na^+C222 and Na^- or by rapid evaporation of solvent from such a solution. By controlling the complexing agent, metal, and solvent, one can prepare a wide variety of concentrated solutions containing M^+Cry (or M^+ crown ether), M_y^- and/or e^-_{solv}. The metals M_x and M_y may be the same or different. In this section we describe some (as yet incompletely characterized) solids prepared either by crystallization from such solutions or by rapid solvent evaporation.

4.2.1. Solids Prepared by Crystallization

The only crystalline solids which we have prepared to date contain the cryptand C222 with various alkali metals—no crystals have been made with other cryptands or with crown ethers, nor have any "electrides" been crystallized. However, there seems to be no fundamental restriction on the preparation of such compounds if one can find the appropriate solvent and conditions for crystallization.

In addition to the salt of Na^-, we have prepared other crystalline solids which appear to be K^+C222K^-, $K^+C222Na^-$, $Rb^+C222Rb^-$ and $Cs^+C222Cs^-$. The methods of preparation are similar to those used for $Na^+C222Na^-$(s) except that isopropylamine was used rather than ethylamine for salts of K^-, Rb^- and Cs^-. All of the

crystals have a metallic appearance which ranges in color from light gold for $Na^+C222Na^-$ to greenish-gold for $K^+C222Na^-$ to dark copper-bronze for $Cs^+C222Cs^-$. Solutions containing K^-, Rb^-, Cs^- and e^-_{solv} are much more subject to irreversible decomposition than are those containing Na^-. This makes it difficult to prepare crystalline salts of these anions since all solution manipulations must be done at low temperatures. Once the solvent has been removed, however, all of the crystalline solids prepared so far seem to be reasonably stable and it is likely that we will be able to handle them and characterize them in much the same way as for $Na^+C222Na^-$.

4.2.2. Preparation of Thin Films by Solvent Evaporation

By adjusting the solution stoichiometry and flash-evaporating the solvent (practical only with highly volatile solvents) it is relatively easy to prepare solvent-free transparent films or powders whose spectral properties[78] indicate the presence of M^- and/or e^-. Such films have been prepared from solutions of all of the alkali metals in methylamine in the presence of both crown ethers and cryptands. Films which show optical bands of M^- appear blue by transmitted light and vary in color from gold to dark-bronze by reflected light, depending on the metal, while films which have only an infrared band (presumably the absorption band of trapped electrons) appear blue by transmitted light and very dark blue-black by reflected light.

Attempts to prepare crystals or powders by slow solvent evaporation have been generally unsuccessful, with irreversible decomposition usually occurring instead of precipitation of the desired compound. Solutions and solids that contain [18]crown-6 tend to be more stable to irreversible decomposition than those that contain C222. However, in the former case[74], solid films of $Na^+18C\text{-}6Na^-$ also require the presence of some solvent. Removal of solvent leads to the formation of solid sodium and [18]crown-6, without apparent decomposition of the crown ether. Evidently the axial position(s) in the $Na^+18C\text{-}6Na^-$ salt must be occupied by solvent in order for the salt to be stable. It is interesting that films prepared by evaporating solutions containing [18]crown-6 and either K, Rb or Cs give spectra which do *not* change when all of the solvent is removed.

4.2.3. Absorption Spectra of Films

Films prepared by evaporation of methylamine from solutions with stoichiometric amounts of M^+, C222 and M^- (M^+C222M^-) show strong absorption bands which are characteristic of the anion. The shoulder and extra peak seen with films of $Na^+C222Na^-$ are not observed for any of the other metals. Indeed, when films are prepared from solutions of $K^+C222Na^-$ the peak of Na^- is a single narrow band. The origin of this change in spectrum and that obtained with [18]crown-6 (see Fig. 8) remains a mystery although we expect a change in crystal structure from $Na^+C222Na^-$ to $K^+C222Na^-$ or to $Na^+18C\text{-}6Na^-$. Since we are now able to prepare crystalline samples of $K^+C222Na^-$, it may be possible to determine the origin of these spectral differences.

Even before the isolation and characterization of $Na^+C222Na^-$, we had prepared dark blue solid powders and films by solvent evaporation from solutions which contained largely M^+ cryptand (or M^+ crown ether) and solvated electrons[7]. The ESR spectra of such powders consists of a very intense narrow line at the free-electron g-value, suggesting the presence of trapped electrons and extensive motional narrowing of the ESR signal. Recently *Harris* and *Lagowski*[80] observed narrow ESR lines from solids produced by freezing metal-ammonia solutions which contained [18]crown-6. They attribute the signal to an ammoniated electron in the vicinity of a complexed cation. In our case, *solvent-free* blue solids are obtained so that the electrons can no longer be solvated but may simply occupy the anion sites in the crystal lattice. We refer to these solids as "electrides" although the disposition of the electrons with respect to the complexed cations is unknown.

We have measured the absorption spectra of "electride" films with both cryptand C222 and [18]crown-6 as complexing agents (cf. Fig. 9)[81]. Often the infrared band which we attribute to trapped electrons is accompanied by an M^- absorption. In some cases the relative intensities of the two bands shifts in favor of M^- as the solution is allowed to contact excess metal[78] (cf. Fig. 10). In addition to the "electride" band at 7400 cm^{-1} and the band of M^-, intermediate absorption peaks of unknown origin are often observed (cf. Fig. 9).

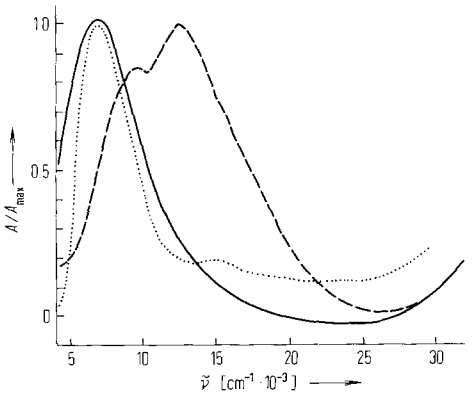


Fig. 9. Spectra of solvent-free thin "electride" films produced by rapid evaporation of methylamine from solutions of $K^+C222e^-_{solv}$ (solid line), $Cs^+18C\text{-}6e^-_{solv}$ (dotted line) and $K^+18C\text{-}6K^-$ (with e^-_{solv}?) (dashed line) [81].

5. Speculation about Properties and Future Potential

Since we have only limited information about the structure and properties of "alkalide" salts, and even less information about "electrides", it is difficult to predict in what ways these substances might be useful. Certainly, as examples of a new oxidation state of a whole family of elements, alkali metal anions are fundamentally interesting. The strongly reducing nature of these compounds may prove useful in syntheses, and the solid-state properties may provide useful materials in such areas as semiconductor behavior, photoelectron emission, photoconductivity, *etc.* In this section we will speculate about the nature of these compounds and indicate some areas of potential usefulness.

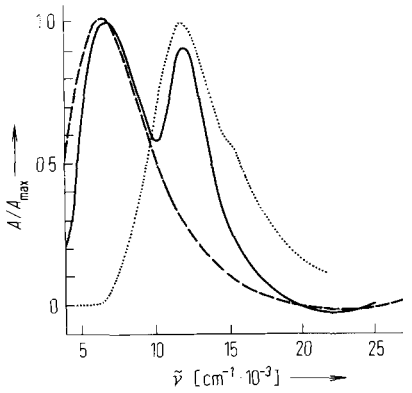


Fig. 10. Spectra of solvent-free thin films produced by evaporation of methylamine from solutions containing cryptand C222 and various relative concentrations of potassium [78]. Spectra for progressively higher concentrations of potassium are in the order, dashed line ("electride"), solid line (mixture), and dotted line K ("potasside").

5.1. Solution Properties

The use of crown-ether and cryptand complexing agents makes it possible to prepare concentrated solutions containing either M^- or e^-_{solv} in a variety of amine and ether solvents. For example, a solution of 0.1 M sodium in THF can be prepared by using the cryptand C222. Since this solution contains mostly Na^+C222 and Na^- and very little e^-_{solv} it might be useful for two-electron reductions. If a one-electron reductant in this aprotic solvent were desired, a solution of potassium with an equivalent quantity of the cryptand C222 would produce K^+C222 and e^-_{solv} with little interference from K .

5.2. Possible New Compounds of "Alkalides" and "Electrides"

The thermodynamic estimates described in Section 3 suggest that compounds such as $Ba^{++}C222(Na^-)_2$ should be thermodynamically stable. Similarly, we predict that solid compounds containing Li^- should be stable. The present challenge is to find appropriate synthetic routes to such substances. In solution, Li^- tends to dissociate into Li^+ and e^-_{solv}. Perhaps a direct vapor-phase reaction or reaction in an inert matrix would avoid some of the problems associated with the use of a polar solvent to dissolve the reacting species. One of the problems which we have encountered in working with lithium and the alkaline earths is the inability to purify these metals by distillation in glass or quartz. As a result, solutions tend to be unstable. Distillation of these metals directly into the apparatus from a metal container might eliminate some of these difficulties.

It should be possible to substitute other cations for cryptated cations provided they are non-reducible. Long chain tetraalkylammonium ions seem attractive at present since they are stable in solution in the presence of Na^-. We are attempting to find suitable conditions for metathesis reactions in solution such as

$$M^+CryM^- + R_4N^+X^- \rightarrow M^+CryX^-_{(s)}\downarrow + R_4N^+M^- \quad (19)$$

If tetraalkylammonium "alkalides" could be prepared, they might eliminate one of the major barriers to practical utilization of alkali metal anions—the complexity and cost of cryptands.

If the solids which we call "electrides" prove to be stoichiometric compounds with one trapped electron for each cation, then it might be possible to prepare a variety of electride salts such as $Ba^{++}C222(e^-)_2$. The increase in electron density in such compounds compared with M^+C222e^- might be enough to give them the properties of "expanded metals", similar to the metallic compound $Ba(NH_3)_6$[8]. The optical and ESR properties of uni-univalent "electrides" such as K^+C222e^- suggest that the electrons are largely localized, perhaps in the traps formed by the octahedral holes between closest-packed cations. As the electron density increases, enough electron-electron overlap may occur to give metallic behavior.

5.3. Possible Uses for the Solid Compounds

Whether the semiconducting properties of $Na^+C222Na^-$ and similar salts of the other alkali metal anions will be useful depends primarily on their stability. It now appears that the parent compound is stable at room temperature *in vacuo* in the dark. Even its reactivity with air is not as great as we first thought. For example, a compressed pellet of powdered $Na^+C222Na^-$ remained gold-colored and shiny in air until reaction with moisture in the air began on the surface. Further surface reaction, as observed under a microscope, occurred at water droplets with little or no general surface corrosion.

Light absorption by Na^- in the solid is very efficient and covers a broad spectral range extending throughout the visible and near infrared (cf. Fig. 8). If solids can be found in which this absorption is followed by auto-ionization as in solution[26, 28], and if the lifetime of the conduction electron so produced is long enough, sodium anions might be efficient for photoelectric energy conversion. Because the electron is only weakly bound to such anions as Cs^- and may be even more weakly bound in "electride" salts the photoelectric properties of these substances would be most interesting. At least in principle, such compounds have the potential to extend the wavelength of photoelectron emission farther into the red than is possible with currently available photoemissive surfaces.

Of course, such speculation about potential uses for "alkalides" and "electrides" is based upon very little fundamental information about their properties. Before more can be done to utilize these compounds, a great deal of study is needed to determine their properties. Measurements are not easy with such reactive materials even when they can be prepared in pure form. However, we hope that the demonstration that the −1 oxidation state of the alkali metals is stable will stimulate others to investigate such systems and find uses for them.

The author is grateful to the National Science Foundation for current support of this research under Grant No. DMR77-22975 and to the U. S. Department of Energy for prior support under Contract No. EY-76-S-02-0958. Thanks are due to the many graduate students and post-doctoral research associates who worked on this project, most of whom may be identified as co-authors of papers from this laboratory. Previously unpub-

lished work described in this paper was done by M. DaGue, H. Lewis, P. Smith, B. VanEck and M. Yemen.

Received: August 9, 1978 [A 282 IE]
German version: Angew. Chem. 91, 613 (1979)

[1] *V. M. Dukel'skii, E. Ya. Zandberg, N. I. Ionov*, Dokl. Akad. Nauk SSSR *62*, 232 (1948).
[2] For the most accurate values of the electron affinities of the alkali metal atoms see: *T. A. Patterson, H. Hotop, A. Kasdan, D. W. Norcross, W. C. Lineberger*, Phys. Rev. Lett. *32*, 189 (1974).
[3] *S. Golden, C. Guttman, T. R. Tuttle, Jr.*, J. Am. Chem. Soc. *87*, 135 (1965).
[4] *S. Golden, C. Guttman, T. R. Tuttle, Jr.*, J. Chem. Phys. *44*, 3791 (1966).
[5] *S. Matalon, S. Golden, M. Ottolenghi*, J. Phys. Chem. *73*, 3098 (1969).
[6] *J. L. Dye, J. M. Ceraso, M. T. Lok, B. L. Barnett, F. J. Tehan*, J. Am. Chem. Soc. *96*, 608 (1974).
[7] *F. J. Tehan, B. L. Barnett, J. L. Dye*, J. Am. Chem. Soc. *96*, 7203 (1974).
[8] For a detailed discussion of the properties of metal-ammonia solutions see: *J. C. Thompson:* Electrons in Liquid Ammonia. Oxford University Press, Oxford 1976.
[9] Review articles on metal-ammonia solutions include: a) *C. A. Kraus*, J. Chem. Educ. *30*, 83 (1953); b) *W. L. Jolly*, Prog. Inorg. Chem. *1*, 235 (1959); c) *M. C. R. Symons*, Rev. Chem. Soc. *13*, 99 (1959); d) *U. Schindewolf*, Angew. Chem. *80*, 165 (1968); Angew. Chem. Int. Ed. Engl. *7*, 190 (1968); e) *T. P. Das*, Adv. Chem. Phys. *4*, 303 (1962); f) *J. L. Dye*, Sci. Am. *216*, 77 (Feb. 1967); g) *M. H. Cohen, J. C. Thompson*, Adv. Phys. *17*, 857 (1968).
[10] A collection of "landmark papers" in the metal-ammonia field has been given by *W. L. Jolly:* Metal-Ammonia Solutions. Dowden, Hutchinson & Ross; Stroudsberg, Pennsylvania 1972.
[11] Papers resulting from conferences in the field of metal-ammonia solutions and the broader general area of electrons in fluids are: a) *G. Lepoutre, M. J. Sienko:* Metal-Ammonia Solutions, Colloque Weyl I. Benjamin, New York 1964; b) *R. F. Gould*, Chem. Ser. *50* (1965); c) *J. J. Lagowski, M. J. Sienko:* Metal-Ammonia Solutions. Colloque Weyl II, IUPAC, Butterworths, London 1970; d) *U. Schindewolf*, Ber. Bunsenges. Phys. Chem. *75*, (1971); e) *J. Jortner, N. R. Kestner:* Electrons in Fluids. Colloque Weyl III. Springer, Berlin 1973; f) Colloque Weyl IV, Electrons in Fluids—The Nature of Metal-Ammonia Solutions, J. Phys. Chem. *79*, No. 26 (1975); g) International Conference on Electrons in Fluids. Banff, Alberta, Canada, Sept. 1976: Can. J. Chem. *55*, No. 11, 1796—2277 (1977).
[12] *M. T. Lok, F. J. Tehan, J. L. Dye*, J. Phys. Chem. *76*, 2975 (1972).
[13] *M. G. DeBacker, J. L. Dye*, J. Phys. Chem. *75*, 3092 (1971).
[14] *J. L. Dye, M. G. DeBacker, J. A. Eyre, L. M. Dorfman*, J. Phys. Chem. *76*, 839 (1972).
[15] *J. L. Dye*, J. Chem. Education *54*, 332 (1977).
[16] *J. L. Dye*, Sci. Am. *237*, 92 (July, 1977).
[17] *J. L. Dye* in *J. J. Christensen, R. M. Izatt:* Progress in Macrocyclic Chemistry, Vol. 1, Wiley-Interscience, New York, 1979.
[18] *I. Hurley, T. R. Tuttle, Jr., S. Golden*, J. Chem. Phys. *48*, 2818 (1968).
[19] *J. L. Dye, M. G. DeBacker, V. A. Nicely*, J. Am. Chem. Soc. *92*, 5226 (1970).
[20] *J. L. Dye, M. T. Lok, F. J. Tehan, R. B. Coolen, N. Papadakis, J. M. Ceraso, M. DeBacker* in Ref. [11d], p. 659.
[21] *L. H. Feldman, R. R. Dewald, J. L. Dye* in Ref. [11b], p. 163.
[22] *G. Stein, A. Treinin*, Trans. Faraday Soc. *55*, 1086, 1091 (1959).
[23] *M. F. Fox, E. Hayon*, J. Chem. Soc. Faraday Trans. I *72*, 1990 (1976).
[24] *R. R. Dewald, J. L. Dye*, J. Phys. Chem. *68*, 121 (1964).
[25] *J. L. Dye, M. G. DeBacker, L. M. Dorfman*, J. Chem. Phys. *52*, 6251 (1970).
[26] *H. Aulich, B. Baron, P. Delahay*, J. Chem. Phys. *58*, 603 (1973).
[27] *H. Aulich, P. Delahay, L. Nemec*, J. Chem. Phys. *59*, 2354 (1973).
[28] *H. Aulich, L. Nemec, P. Delahay*, J. Chem. Phys. *61*, 4235 (1974).
[29] *R. R. Dewald, J. L. Dye*, J. Phys. Chem. *68*, 128 (1964).
[30] *R. R. Dewald, K. W. Browall*, J. Phys. Chem. *74*, 129 (1970).
[31] *J. L. Dye* in Ref. [11e], p. 77.
[32] *J. M. Ceraso, J. L. Dye*, J. Chem. Phys. *61*, 1585 (1974).
[33] *J. L. Dye, C. W. Andrews, J. M. Ceraso*, J. Phys. Chem. *79*, 3076 (1975).
[34] *J. P. Kintzinger, J.-M. Lehn*, J. Am. Chem. Soc. *96*, 3313 (1974).
[35] *J. M. Ceraso, J. L. Dye*, J. Am. Chem. Soc. *95*, 4432 (1973).
[36] *G. Malli, S. Fraga*, Theor. Chim. Acta *5*, 275 (1966).
[37] *J. L. Dye*, Acc. Chem. Res. *1*, 306 (1968).
[38] *J. W. Fletcher, W. A. Seddon*, J. Phys. Chem. *79*, 3055 (1975).
[39] *H. Linschitz, J. Eloranta*, J. Chem. Phys. *38*, 2214 (1963).
[40] *S. H. Glarum, J. H. Marshall*, J. Chem. Phys. *52*, 5555 (1970).
[41] *A. Gaathon, M. Ottolenghi*, Isr. J. Chem. *8*, 165 (1970).
[42] *D. Huppert, K. H. Bar-Eli*, J. Phys. Chem. *74*, 3285 (1970).
[43] *L. J. Gilling, J. G. Kloosterboer, R. P. H. Rettschnick, J. D. W. van Voorst*, Chem. Phys. Lett. *8*, 457, 462 (1971).
[44] *G. Gabor, K. H. Bar-Eli*, J. Phys. Chem. *75*, 286 (1971).
[45] *M. Fisher, G. Ramme, S. Claesson, M. Szwarc*, Chem. Phys. Lett. *9*, 309 (1971).
[46] *A. Friedenberg, H. Levanon*, Chem. Phys. Lett. *41*, 84 (1976).
[47] *A. Friedenberg, H. Levanon*, J. Phys. Chem. *81*, 766 (1977).
[48] *K. D. Vos, J. L. Dye*, J. Chem. Phys. *38*, 2033 (1963).
[49] *K. Bar-Eli, T. R. Tuttle*, Jr., J. Chem. Phys. *40*, 2508 (1964).
[50] *V. A. Nicely, J. L. Dye*, J. Chem. Phys. *53*, 119 (1970).
[51] *J. L. Dye*, Pure Appl. Chem. *49*, 3 (1977) gives a review of monomers and ion pairs with references to the extensive literature in this field. See also Ref. [17].
[52] *B. Bockrath, L. M. Dorfman*, J. Phys. Chem. *77*, 1002 (1973).
[53] *W. A. Seddon, J. W. Fletcher, R. Catterall*, Can. J. Chem. *55*, 2017 (1977), and references cited therein.
[54] *E. C. M. Chen, W. E. Wentworth*, J. Chem. Educ. *52*, 486 (1975); *H. Hotop, W. C. Lineberger*, J. Phys. Chem. Ref. Data *4*, 539 (1975).
[55] *J. A. Dean:* Lange's Handbook of Chemistry. 11th Edit. McGraw-Hill, New York 1973.
[56] *S. Glasstone:* Textbook of Physical Chemistry. 2nd Edit. Van Nostrand, New York 1946, p. 874.
[57] *E. A. Moelwyn-Hughes:* Physical Chemistry. 2nd Edit. Pergamon Press, New York 1961, p. 882.
[58] *W. M. Latimer, W. L. Jolly*, J. Am. Chem. Soc. *75*, 4147 (1953).
[59] *W. E. Spicer, A. H. Sommer, J. G. White*, Phys. Rev. *115*, 57 (1959).
[60] *J. L. Dye, G. Lepoutre, P. R. Marshall, P. Pajot* in Ref. [11a], p. 92.
[61] *E. Zintl, J. Goubeau, W. Dullenkopf*, Z. Phys. Chem. Abt. *A 154*, 1 (1931).
[62] *E. Zintl, A. Harder*, Z. Phys. Chem. Abt. *A 154*, 47 (1931).
[63] *J. D. Corbett, D. G. Adolphson, D. J. Merryman, P. A. Edwards, F. J. Armatis*, J. Am. Chem. Soc. *97*, 6267 (1975).
[64] *J. D. Corbett, P. A. Edwards*, J. Chem. Soc. Chem. Commun. *1975*, 984.
[65] *D. G. Adolphson, J. D. Corbett, D. J. Merryman*, J. Am. Chem. Soc. *98*, 7234 (1976).
[66] *A. Cisar, J. D. Corbett*, Inorg. Chem. *16*, 632 (1977).
[67] *J. D. Corbett, P. A. Edwards*, J. Am. Chem. Soc. *99*, 3313 (1977).
[68] *P. A. Edwards, J. D. Corbett*, Inorg. Chem. *16*, 903 (1977).
[69] *I. Hurley, T. R. Tuttle, Jr., S. Golden*, in Ref. [11c], p. 449.
[70] *M. Lacoste*, Dissertation, Université des Sciences et Techniques du Languedoc, Montpellier, France 1976.
[71] *E. Kauffmann, J.-M. Lehn, J. P. Sauvage*, Helv. Chim. Acta *59*, 1099 (1976).
[72] *S. Goldman, R. G. Bates*, J. Am. Chem. Soc. *94*, 1476 (1972).
[73] *J.-M. Lehn*, Struct. Bonding *16*, 1 (1973).
[74] *J. L. Dye, C. W. Andrews, S. E. Mathews*, J. Phys. Chem. *79*, 3065 (1975).
[75] *A. F. Kapustinskii*, Q. Rev. Chem. Soc. *10*, 283 (1956).
[76] *D. Moras, B. Metz, R. Weiss*, Acta Crystallogr. Sect. *B 29*, 388 (1973).
[77] *D. Moras, B. Metz, R. Weiss*, Acta Crystallogr. Sect. *B 29*, 383 (1973).
[78] *J. L. Dye, M. R. Yemen, M. G. DaGue, J.-M. Lehn*, J. Chem. Phys. *68*, 1665 (1978).
[79] *H. J. Hesse, W. Fuhs, G. Weiser, L. von Szentpaly*, Chem. Phys. Lett. *41*, 104 (1976).
[80] *R. L. Harris, J. J. Lagowski*, J. Phys. Chem. *82*, 729 (1978).
[81] *M. R. Yemen, M. G. DaGue, J. L. Dye*, unpublished.
[82] *M. R. Yemen, J. L. Dye*, unpublished.
[83] *R. R. Dewald*, J. Phys. Chem. *73*, 2615 (1969).

Spatial Structure Formation in Protein Gels

By M. G. Bezrukov[*]

The present article is concerned with the practical and theoretical aspects of gelation in protein systems. The processes involved are, *inter alia,* so complicated that several types of protein molecule assemblies and conformational changes during the association have to be considered. The gel network can be stabilized by five types of interaction: covalent crosslinking, polar interactions, hydrogen bonding, salt bridges and hydrophobic interactions. The microstructures of gels formed from fibrillated proteins (collagen) and from globular proteins (*e.g.* α- and β-casein) differ considerably. Of practical interest are methods of controlling the solubility of gels, including *e.g.* the use of cross-linking agents and addition of salts.

1. Introduction

The gelatinous state of biopolymers is the structural basis of all living objects. Whereas the structural functions in plants are, as a rule, performed by polysaccharides, in animal organisms this role is played by proteins. Protein gelation has not only been the subject of numerous investigations in biochemistry and molecular biology, it has also been studied from the point of view of protein processing technology. This latter, technological aspect has recently acquired special importance in connection with the development of large-scale industrial methods for the processing of proteins used in the manufacturing of foodstuffs and animal feeds.

The review on protein gels published by *Ferry*[1] in 1948 reflects the views then held on the gelatinous state. A complete picture of the gelatinous state is still lacking. Numerous new experimental data have, however, appeared and require generalizing. In this review we have concentrated our attention on the organization of the spatial arrangements of protein molecules in gelatinous systems, on the causes of their occurrence, as well as on certain practical aspects of controlling the protein functional properties.

2. The Classification of Gels

"The colloidal state of a system such as a gel is easier to observe than to define"—for more than sixty years this statement has led a nomad's life in various papers on the gelatinous state. We see it also *e.g.* in the well known review of *Lipatov* and *Proshlyakova*[2], published in 1961. Nevertheless, a number of sufficiently acceptable definitions of a gel had already been formulated before 1960. In the following we shall consider some of the currently acceptable definitions.

According to *Flory*[3] a system can be regarded as gelatinous if it is characterized by the following properties:

1) It is a colloidal system containing no less than two components;
2) it manifests certain mechanical properties of a solid;
3) both the dispersed component and the dispersion medium are continuously distributed in the volume of the system.

This the most comprehensive definition is of a purely formal nature and does not reflect the reasons for the appearance and the existence of the gelatinous state of a system.

In the works of *Papkov*[4-7] gels are defined as multicomponent systems characterized by two properties: almost complete absence of fluidity and high reversible deformation.

Rogovina and *Slonimsky*[8] define a gel as "a polymer-solvent system in which there exists a spatial network of fairly stable non-fluctuating bonds (*i.e.* those which are not destroyed by thermal motion)". This definition appears to be the most suitable for the aspects of the problem examined in the present paper. It enables an understanding of many features of gelatinous systems.

In accordance with *Papkov*'s classification it is customary to distinguish two types of systems, with participation of a polymer component.

Type 1: Gels formed on the swelling of cross-linked polymers or on the covalent cross-linkage of macromolecules in solution. These gels are thermally irreversible. The absence of fluidity in such systems is caused by the presence of a three-dimensional molecular skeleton of a polymer, stabilized by chemical bonding.

Type 2: Gels formed on the separation of a single-phase polymer solution into two phases caused by a change in thermodynamic conditions or the composition of a system. The absence of fluidity is caused by the formation of a three-dimensional skeleton made up of supermolecular formations whose properties are close to those of a solid; the reversible deformation is due to the elastic bending of the skeletal components.

It is characteristic for a system in the gelatinous state to have a network of polymer molecules. The structure of this three-dimensional network and the causes of its formation can, however, be highly diverse.

A major role in the build-up of the skeleton of polymer molecules in solution is played by the energy balance of the interaction of polymer chain sections with one another and with the solvent. A limited polymer solubility is considered necessary for the system to acquire the gelatinous state[2,7,8].

In the case of polymers with limited solubility some sections of the polymer molecule adhere to each other forming nodes of interaction, while other sections remain in solution. Such a behaviour is due to the diphility of a polymer molecule, *i.e.* to the presence of both lyophilic and lyophobic sections. The nodes of a three-dimensional network are formed as a result of the lyophobic sections coming into contact with one another, whereas the solvation of lyophilic sections ensures the continuity of the network. The nature of the contact interactions between lyophobic sections has been exam-

[*] Dr. M. G. Bezrukov
Institute of Organoelemental Compounds, USSR Academy of Sciences
SU-117813 Moscow, Vavilova 28 (USSR)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0808-0599 $ 02.50/0*

ined[2]; all the possible types of physical bonds (dispersive, polar, hydrogenous, *etc.*) can be involved.

When the three-dimensional network is formed as a result of covalent interactions, all the sections of the polymer molecule can be solvated sufficiently well by the solvent, *i.e.* it is unnecessary for the molecule to be diphilic. The possibility of the existence of gel networks made up of individual polymer molecules remains, however, purely theoretical and is not confirmed by actual examples. All the gels whose microstructures are known to date are characterized by a network made up of supermolecular structures.

The region of gel stability is limited by the temperature at which either the spatial skeleton forming a gel is destroyed and the system passes into the fluid state, or the system loses the solvent and changes to a xerogel. According to their meltability gels can be subdivided into thermally reversible and thermally irreversible gels.

Rogovina and *Slonimsky*[8], as well as *Papkov*[7] attribute the thermal irreversibility of gels mainly to the chemical (covalent) interactions of polymer molecules in the three-dimensional network. This interaction is the strongest of all those possible ($\Delta G > 80$ kcal/mol) in the gel network.

Thermally reversible gels are characterized by the physical interactions of macromolecules with one another. The energy contributions of hydrogen bonds, polar interactions, and hydrophobic interactions are considerably smaller than those of covalent interactions ($\Delta G < 10$ kcal/mol). These physical interactions can be destroyed by the thermal motion at the temperature at which the liquid phase exists.

It should be noted that gels formed by the interaction of polymer chains with polyvalent cations can also be thermally irreversible. Such interactions, in which segments of different polymer chains function as ligands at one complex nucleus, are energetically intermediate between the chemical and the physical interactions. In synthetic polymers they are quite rare and, as a rule, are not taken into consideration. In protein systems, however, the interaction with cations is a factor which in many respects determines the structure.

It is possible to classify gels by a number of other features, *e.g.* by the peculiarities of microstructure or by the phase state.

The most comprehensive classification of gels according to their microstructure is given by *Flory*[3]. He subdivides them into four types:

1. Highly ordered lamellar structures, including also gelatinous mesophases.
2. Polymer networks formed by physical aggregation, mostly disorganized but with local ordering in some portions.
3. Disordered structures formed by dispersed particles.
4. Absolutely disordered covalently cross-linked molecular networks.

The first type of gels can be exemplified by the systems containing phospholipids or soaps. Lamellar structures are unknown for proteins, but some sections of native collagen fibrillae can, with certain reservations, be regarded as mesophases.

It should be noted that any classification of proteins and their gels will be to a great extent arbitrary, and often will not reflect the significant features of their structure. The spatial network of the molecules of a certain protein differs from the network of the molecules of any other protein. The difference lies, primarily, in the individuality of the primary structure of the polypeptide chain.

The possibility of a certain type of interaction occurring lies in the amino acid composition and sequence (primary structure) of the polypeptide chain. The primary structure determines also all the higher levels of protein organization[9] and, in the final analysis, the capability of forming the spatial network of molecules—the basis of the gelatinous state.

3. Collagen and its Degradation Products

We shall not deal with the gels of fibrillar proteins in great detail here since the potential objects of industrial processing—vegetable and single cell proteins (biomasses)—are, according to current thinking, non-fibrillar. Nevertheless, it would seem to us most justifiable to examine the gels of collagen and its degradation products, called gelatin in conventional terminology. Until very recently gelatin was the only protein isolate produced on an industrial scale, and because of this it has been studied in greatest detail.

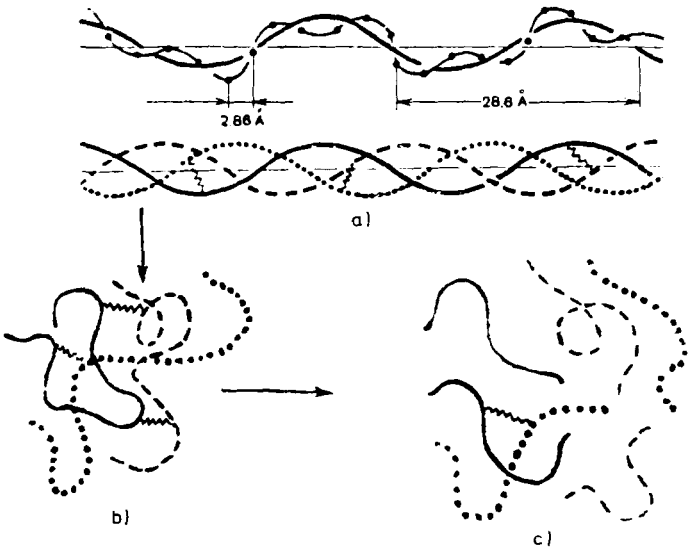


Fig. 1. a) Triple helix of the collagen molecule in the native state, b) its thermal denaturation, and c) hydrolytic cleavage.

The collagen molecule consists of three polypeptide chains: two α_1-chains and one α_2-chain. The three spiral α-chains intertwine with each other and at the same time wind round a common axis, thus forming a triple helix (Fig. 1). Whereas the amino acid sequence in the α_1-chain has already been fully established (Fig. 2), the α_2-chain has not yet been completely deciphered; it is known, however, that the structure of the α_2-chain is very similar to the primary structure of the α_1-chain[10]. Similarity of the primary structure of both these chains, *viz.* the fact that every third amino acid is glycine, is highly important. This highly ordered primary structure ensures the strength of the triple-helix structure of the collagen molecule, as well as the ordering of the arrangement of collagen molecules during fibrillae formation. In the course of fibrillogenesis under natural conditions, collagen molecules are arranged longitudinally and shifted relative to one another by a distance equal to one fourth of the length of the molecule (Fig. 3). This shift is caused by polar interactions between the amino acid side groups; the polar groups

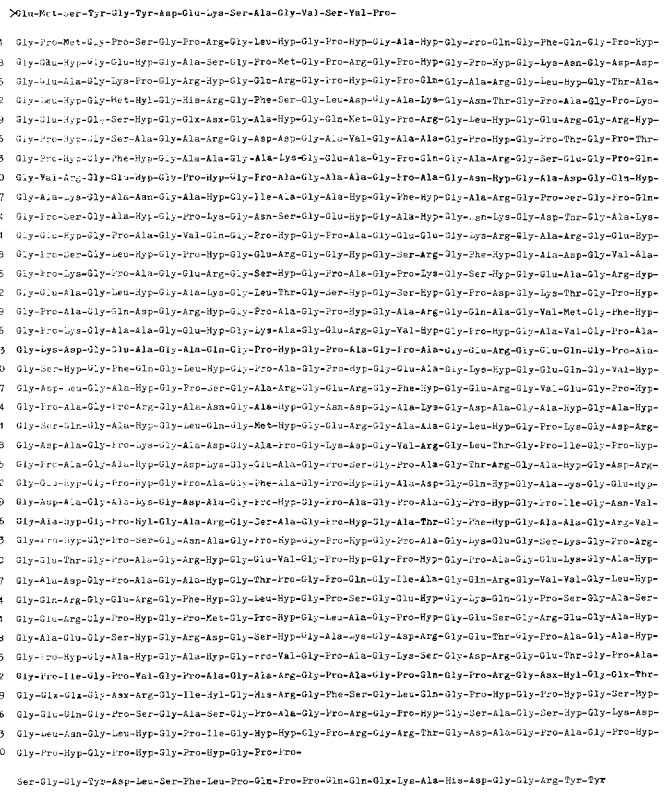


Fig. 2. Primary structure of the α_1-chain of collagen.

are not uniformly distributed along the length of the polypeptide chain, but concentrated in clusters. This spatial concentration of polar groups, together with the shift of a quarter of the length, ensures firm placement of molecules in the fibrilla.

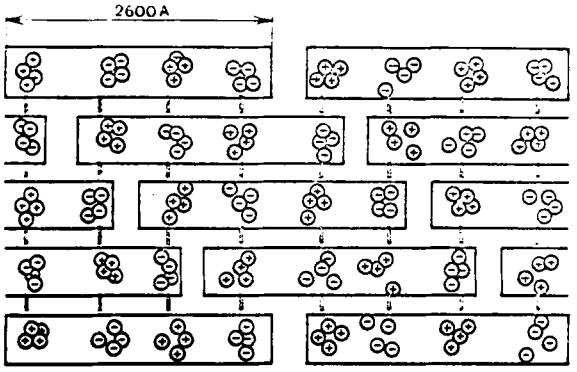
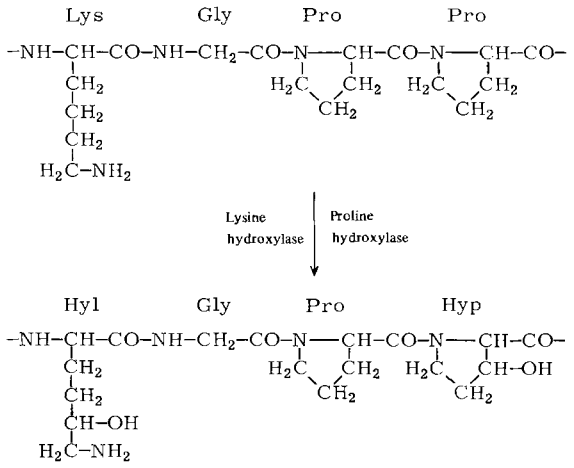


Fig. 3. Arrangement of collagen molecules in the fibrillae.

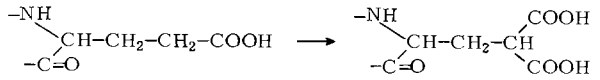
It is as yet impossible to give a comprehensive explanation of the way in which the collagen molecules acquire the limited solubility necessary for fibrillae to be formed and a continuous network to be constructed. It is only known that the collagen molecules are synthesized in the soluble form which at this stage does not contain any typical amino acids, such as, *e.g.* oxylysine, oxyproline, *etc.* The primary molecules (tropocollagen) are transferred by the intercellular liquid to the place where the connective tissue is to be formed and subjected there to enzymic oxidation, first of all by proline and lysine hydroxylases. This formation of hydroxyproline and hydroxylysine leads to the appearance of additional hydrogen bonds (besides the α peptide ones) and an increase in the energy of the interaction of polypeptide chains with one another.



Lysine oxidation does not stop here, and is followed by ε-amino group elimination with the formation of 5-oxonorleucine (see Table 1). The aldehyde group reacts with the free ε-amino groups of lysine with formation of covalent cross-links. More complex bridges (of the desmosine type) are formed if four or more amino acids participate in the cross-linking (Table 1 lists some examples).

In addition to lysine, also glutamic and aspartic acid take part in the formation of cross-links. They form γ-peptide bonds (with lysine) and ester bonds (with serine). The dityrosine cross-linkage should also be mentioned here. It is formed when peroxydases act upon the connective tissue.

Covalent cross-links are formed not only on interaction of the functional groups of the polypeptide chain, but also on bridging of these groups by polyfunctional low-molecular compounds, *e.g.* aldoses (with the formation of a glycoside and an ether bond), aldehydes, and ammonia (yielding amide bridges)[19]. Covalent cross-links also develop inside and between molecules. In this way the supermolecular structure of collagen ceases to be supermolecular and all the spatial protein network becomes a single macromolecule.



During the aging of collagen, which is accompanied by chemical changes in the amino acids of the polypeptide chain, glutamic acid is carboxylated to a γ,γ-dicarboxy derivative[20]. This chelate group of the polypeptide chain captures calcium ions, which results in calcium bridges being formed between the molecules and in the fibrillae losing their flexibility. This process is most characteristic of the collagen of cartilages, tendons and bone tissue.

Thus, if we put aside the participation of other biopolymers in the stabilization of the collagen structure, four types of interaction can be distinguished which determine the rigidity of the spatial arrangement (cf. Fig. 4) of this protein: hydrogen bonds, polar interactions, salt bridges, and covalent cross-linking. For these interactions to take place the initial soluble tropocollagen has to be subjected to three types of changes: 1) oxidation of a number of amino acid groups in

Table 1. Covalent cross-links of protein molecules.

No.	Group 1	Group 2	Type of Crosslinking	Ref.
1	Cys	Cys	Cystine	[11,12]
2	Dehydro-alanine	Lys		[13,14]
3	Glu	Lys		[15]
4	5-Oxonorleucine	Hyl		[16]
5	Lys	Lys	Desmosine	[17]
6	Tyr	Tyr		[18]

the polypeptide chain, 2) covalent cross-linkage by reaction of functional groups of the protein molecule, and 3) covalent cross-linkage by polyfunctional low-molecular reagents.

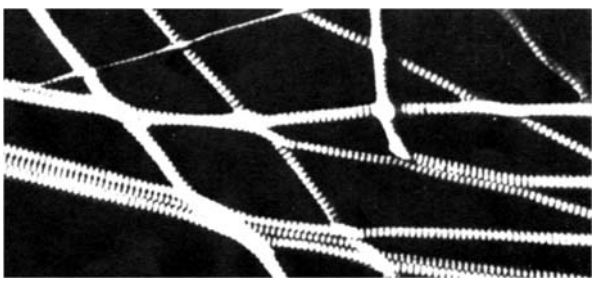


Fig. 4. Photomicrograph of human tendon collagen (× 14000).

Gelatin production processes and the properties of gelatin gels have been examined in sufficient detail by *Veis*[21], *Mikhailov*[19] and *Raikh*[22]. We shall only note here that neither choice of starting material nor of its treatment make it possible to obtain gelatin having a standard composition. This is due to the fact that collagen, even when produced from one and the same type of stock, has a varying degree of hydroxylation (lysine/hydroxylysine and proline/hydroxyproline ratio) and a varying number of cross-links. The procedure for manufacturing gelatin from collagen-containing materials does not make it possible to standardize the extent of chemical degradation of collagen fibers: both the covalent cross-links and the α-peptide bonds in the polypeptide chain are hydrolyzed (Fig. 1). As a result, a mixture of polypeptides having approximately the same amino acid sequence and molecular weights of 30000 to 40000 is obtained. Variations in the gelatin composition naturally affect the properties of gels.

The thermostability of gelatin gels of different origin, however, differ comparatively little and in this respect gelatin may be regarded as a sufficiently standardized substance. As was shown by *Bello et al.*[23,24], α-peptide hydrogen bonds constitute the governing type of interaction during the gelation of gelatin, all other types of interaction are insignificant. It is for this reason that gelatin gels may be considered as uniform with regard to thermostability; for the polypeptide

chains the triple-helix structure remains the most favorable at temperatures below 30 °C. The solubility of gelatin is, however, much higher than that of the initial collagen, and its gel network is thermally less stable. The network of gelatin gels can be fixed, either by coordination coupling (treating the gel with polyvalent cations[25]) or by covalent cross-linking with polyfunctional reagents[26]. In this way one can obtain non-melting gelatin gels.

Electron microscopic studies[27] are in accord with data on the optical rotatory dispersion in gelatin solutions and gels[28] and indicate that the gelatin polypeptide chains pass into solution in the form of a random coil when heated. On cooling, the polypeptide chains once again take on the helical form, with concomitant appearance of spherical aggregates of protein molecules. These spherical particles associate with each other forming unilinear chains with branches (Fig. 5a). This



Fig. 5. Photomicrograph of 2% gelatin gel: a) × 12500 and b) × 50000.

chiefly two-contact type of interaction is observed up to protein concentrations of 12%; above this concentration a random type of aggregation with lateral attachment of spherical particles takes place, resulting in the thickening of fibrillae and in a decrease in the ordering of the system. The structural unit in gelatin gels is thus formed, not by the rod-shaped triple-helix molecules, but by their spherical aggregates. When the unilinear fibrillae are being formed these spherical particles come into contact not only on their surfaces, rather the polypeptide chains of associated protein particles become intertwined. In the fibrillae observed in gelatin gels at a concentration of 1—12% the structural units lose their individuality (Fig. 5b). The only reminder of gelatin fibrillae having originated from the spherical particles is that they have constrictions which create an impression of transversal striation similar to that of the native collagen fibrillae. The periodicity in gelatin fibrillae is much less regular than in collagen, due to a much lower degree of ordering in the arrangement of molecules. In the first place, not all initial spherical particles contain the same amount of protein, as is manifested in their differing size (600—900 Å) and, as a result, in the varying thickness of fibrillae along their length. The ordering of the molecular arrangement in gelatin is disturbed by the differences in molecular weight and, naturally, one cannot expect the shift of a quarter of the length of the molecule observed in the native collagen (Fig. 3). In addition to this, a rapid association of gelatin polypeptide chains on cooling prevents their complete spiralization and decreases the system ordering[29].

The cross-linkage of gelatin molecules in hot solutions (60 °C) fixes the polypeptide chains in the random coil state, resulting in the formation of a non-melting gel. Future investigations on such gels could perhaps give us an indication of how such a gel network is built up of individual polypeptide chains.

Hydrophobic interactions are known to play a substantial role in the stabilization of protein structures, and to predominate in the formation of globules[30].

The hydrophobic interactions differ from the other lyophobic interactions in their energetics, determined by two factors: 1) dispersive forces between the contacting non-polar molecules and 2) changes in the structure of the solvent (water) when it interacts with non-polar molecules.

Contacts of non-polar molecules with water lower the system entropy by increasing the fraction of ordered elements in the water. The minimization of such contacts (transition of molecules to the non-polar environment or their association) is accompanied by an increase in entropy; the system shifts into an energetically more favorable state[31].

The hydrophobic and hydrophilic properties of the amino acids in the polypeptide chain have been studied in great detail by *Tanford*[32]. According to *Tanford* the side groups of serine, histidine, aspartic and glutamic acids are hydrophilic, while all the other amino acids are to a varying degree hydrophobic (from 0 cal/mol for glycine to 3000 cal/mol for tryptophan) and must avoid contact with water.

The polypeptide chain is arranged in space in such a way that the hydrophobic amino acids form the globule nucleus and the hydrophilic amino acids are located on its surface. *Bigelow*[33] showed that the spatial structure of a protein is associated with its averaged hydrophobicity, which characterizes the ratio between the hydrophobic and the hydrophilic groups in the polypeptide chain. When calculating the averaged hydrophobicity, only the quantitative ratios between the hydrophobicities of amino acid radicals and their volumes are used; the position of the amino acids in the polypeptide chain is not taken into account. Such an approach is incapable of reflecting fully all the features of the protein tertiary structure, but nevertheless serves as a first approximation. From *Bigelow*'s calculations it follows that a protein must have a certain averaged hydrophobicity for its globular tertiary structure to be stable. For an equal volume, the geometric figure with the smallest surface is the sphere; when a protein molecule is present in this form it requires only a minimum number of hydrophilic groups to screen the hydrophobic nucleus. This calculated "limiting value" of hydrophobicity is seen to agree with the actual shape of protein molecules in solution. With a larger excess of hydrophobic groups (averaged hydrophobicity higher than the limiting value) the number of hydrophilic groups is not sufficient to screen the nucleus, and the molecules associate; the protein particle in solution then consists of several subunits. With an excess of hydrophilic groups (averaged hydrophobicity lower than the limiting value) the shape of a protein particle in solution can be other than spherical; it will be the more elongated the greater the surface area which can be occupied by hydrophilic groups.

From the above mentioned facts it follows that the increasing hydrophilicity of a collagen molecule in the course of oxidation must facilitate the formation of linear structures and

of a spatial molecular network due to non-hydrophobic interactions. At the same time, the possibility of hydrophobic interactions occurring must decrease. A number of authors, however, point out that hydrophobic contacts contribute to the formation of the gelatin gel network. The bonding of hydrocarbons by gelation can be regarded as proof of the existence of hydrophobic regions within it. Randomly coiled gelatin molecules manifest maximum solubility in benzene[34]. Benzene solubilization decreases with increasing formation of the gel network[35,36], and gel rigidity decreases as a result of interactions with benzene. These findings are in accord with the view of *Mikhailov*[19] that an ordered alternation of hydrophobic and hydrophilic groups in the gelatin polypeptide chain facilitates the occurrence of hydrophobic contacts between molecules in the course of the gel network formation. The role of hydrophobic interactions in the formation of the gelatin structure is, however, much smaller than in the formation of the spatial structures of globular proteins.

4. Spatial Structures of Globular Proteins

Globular proteins, like fibrillated ones, are capable of forming gels in aqueous medium, though only under special conditions and at higher concentrations. As distinct from gelatin, whose gelling is accompanied by the process of protein renaturation, the gelling of non-fibrillated proteins is accompanied in most cases by denaturation. As a rule, denaturation precedes the aggregation of protein particles into linear structures and the formation of a three-dimensional gel network. Specific features of the aggregation of spherical protein particles, particularly the effect of the type of aggregation and the extent of the unfolding of polypeptide chains on the structure of the gel network (cf. Table 2) have been studied by *Tombs*[37].

Proceeding from purely geometric considerations *Tombs* calculated that the protein concentration necessary for formation of a three-dimensional network with fixed pore size is five times greater for a randomly coiled protein molecule than for an unfolded polypeptide chain; for the formation of a compact sphere it is 40 times greater. *Tombs* then considered two extreme types of protein particle aggregation in gelling, the statistical and the ordered (into unilinear chains) types, and calculated that for a three-dimensional gel network to be formed, all other things being equal, the required concentration is 10—12 times greater when the aggregation is random than when it is ordered.

The information available on the microstructure of protein gels is most inadequate. As can be seen from Table 2, a certain agreement can be traced between the sequence of experimental data and the calculations, even though the quantitative ratio of protein concentrations in real systems does not accord with *Tombs'* calculations. This is primarily due to a considerable arbitrariness in the assigning of a gel network to a certain type, since such correlations are carried out "by inspection". Besides, the data on the extent of protein polypeptide chain unfolding are semiquantitative, whereas one can only make a qualitative appraisal of the degree of system ordering. It would seem expedient in future to take into account the number of contacts of network sites with each other (*i.e.* the coordination number). The ordered type of aggregation would be characterized by a coordination number of slightly more than 2. Raising the coordination number corresponds to a decrease in system ordering.

A more definite formulation can be arrived at for gels whose network element is the compact spherical particle. The gels of some lactoprotein fractions can serve as example for such systems. Casein, the chief protein component of milk, is a phosphoprotein and consists of at least 25 fractions[38]. The major part is composed of the α-fraction (up to 60%) and the β-fraction (up to 35%). The two fractions differ only slightly in their molecular weight (23600 and 24000, respectively) and amino acid composition. The main differences between these fractions are their amino acid sequence and degree of phosphorylation[39,40]. A spherical aggregate of

Table 2. Relationship between the structure of the gel network and protein concentration (BSA = bovine serum albumin).

Type of aggregation / Conformational state of protein	Statistical			Ordered		
	Type of network [a]	Protein concentration necessary for gelling. calc. [b]	obs. [c]	Type of network [a]	Protein concentration necessary for gelling. calc. [b]	obs. [c]
Compact sphere	3	400	18% α casein in acid medium	2	40	4% β casein in acid medium
			15% α casein in alkaline medium			3% BSA after heating to 70 °C
Random coil		50	—		5	—
			8% BSA after heating to 100 °C			1% gelatin 0.5% collagen
Unfolded chain	4	10	—	1	1	—

[a] Network type according to *Flory* (cf. Section 2). [b] Relative values calculated after *Tombs* (cf. Section 4). [c] Values found for a real system (in wt.-%).

molecules (micelle) has been shown to be a structural unit of casein and its fractions in solutions, gels and films.

Optical rotatory dispersion and electron microscopy data[41] show that the aggregation of α- and β-casein spherical particles in acid medium occurs without any conformational changes, which in itself is a fairly rare phenomenon. There exists only one other example of such a kind of aggregation without any change in the native structure of protein: β_A-lactoglobulin gels[42]. However, the structure of such gels is not known. At concentrations of >4% casein forms gels in acid media and aggregates into a network in a very ordered way (Fig. 6a). When the concentration increases to 8% the morphology of the gels does not change: unilinear, branched chains of micelles are observed, and the concentration of network nodes increases with increasing protein concentration. During aggregation the spherical particles do not undergo any conformational changes, they preserve their individuality and have only surface contacts (Fig. 6b). Such an ordered aggregation is only possible with the sites of interaction being localized on the surface of spherical particles in a few (probably two polar) zones.

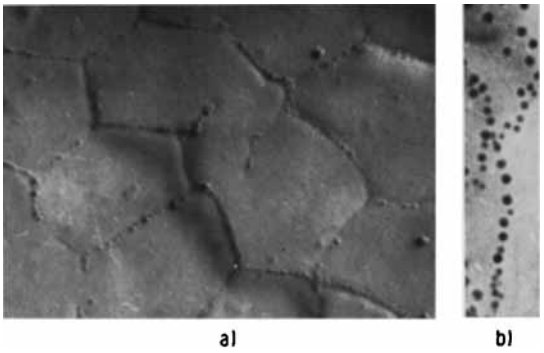


Fig. 6. Photomicrograph of 4% β-casein gel in acid medium: a) × 12500 (freezing-staining) and b) × 50000 (contrasting with phosphotungstic acid).

In contrast to β-casein, α-casein shows no clearly defined localization of the interaction sites, or they occur much more frequently. The aggregation of α-casein globules is thus of a statistical nature. The minimum concentration of α-casein for gelling in acid medium is equal to 18% (Table 2), and

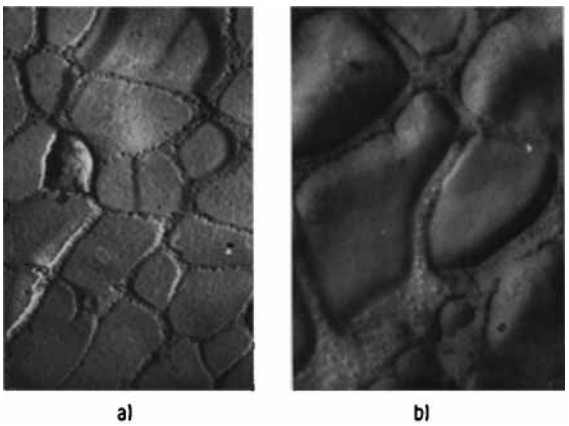


Fig. 7. Photomicrograph of α-casein gel: a) 18% in acid medium (× 12500) and b) 15% in alkaline medium (× 25000).

even at this concentration the gel network is made up of distended globular aggregates (Fig. 7a). With increasing protein concentration the thickness of the fibrillae increases owing to the lateral attachment of globules, while the concentration of network nodes decreases.

In alkaline media the aggregation of α-casein globules is also of a statistical nature (Fig. 7b), but the conformation of the protein molecules changes considerably and approaches that of the random coil. Spherical α-casein particles remain the structural units of the network, but their boundaries are no longer clearly defined. Particle deformation is observed, and mass exchange is possible, as well as the intertwining of polypeptide chains when the network is being formed. With the unfolding of micelles the concentration necessary for gelation decreases and amounts to 15%. The change in concentration is much smaller than one would expect (according to *Tombs*), probably because α-casein particles under gelation conditions are still far removed from the state of a random coil.

Bovine serum albumin (BSA) aggregates on heating owing to the formation of disulfide cross-links[43,44]. On varying the conditions, absolutely different types of aggregation and, consequently, different systems can be obtained— from gels with controlled mechanical properties to amorphous coagulates. The BSA molecule contains a considerable number of disulfide and mercapto groups. On heating to 69 °C the conformation changes only slightly. Only some of the SH groups become accessible to intermolecular cross-linking, and, as assumed by *Tombs*[44], BSA aggregates in a more or less orderly manner, forming a gel network. Heating up to 100 °C causes a more complete unfolding of the polypeptide chain, the number of interaction centers increases and aggregation is of a random nature. Since with such an aggregation the protein concentration required for the gel network to be formed is higher than BSA solubility (7%), flocculation and phase segregation occur.

There are no reliable enough data available on the existence of protein gels having a random coil conformation. We can cite examples of protein gelation where conformational changes from a sphere to a coil or from a coil to an unfolded polypeptide chain occur. Thus, it is well known that gelatin gelation is accompanied by a coil/helix transition[28]. In the collagen gel there are practically no disordered sections of polypeptide chains, whereas in the gelatin gel it is highly probable that some sections are in such a state. Therefore, in Table 2 we have placed gelatin below the level corresponding to the random coil. Collagen is placed above the "unfolded chain" because, as has already been mentioned, the network of its gels is not made up of individual polypeptide chains, but of elongated triple-helix molecular aggregates.

We are thus convinced that real gelatinous systems are much richer in microstructure than would follow from presently existing classifications. These classifications are, however, very useful for making predictions, which albeit are still very far from being quantitative.

Of great interest is the question concerning the reasons for the formation of a continuous gel network in the course of spherical particle aggregation. In 1970 *Tombs*[44] stated that "statistical aggregation must lead to more or less spherical particles, and so gelation is only possible with oriented aggregation". He thought it possible to explain the appearance

of fibrillae by the autocatalytic effect during aggregation of globules, *i.e.* the growth rate of fibrillae is proportional to their length and the growth centers are located at the ends of asymmetric aggregates. *Tombs* refers to the calculations of *Joly et al.*[45], who showed that such an effect can constitute a general phenomenon in the aggregation of globular proteins and can be widely used to explain fibrillae formation.

In 1974, however, *Tombs*[37] pointed out that the most probable shape of the aggregate formed as a result of random interaction between spherical particles must be a non-spherical associate (ellipsoid), serving as the nucleus for linear structures and for the three-dimensional network.

In a real system, complete statistical aggregation seems to be unlikely, since for this to occur the aggregating particles must have absolutely the same properties at any point on their surface. Protein globules, as a rule, have a surface of mosaic structure, *i.e.* there are sites differing in charge density and sign, degree of hydrophobicity, presence of mercapto groups, etc. This leads to a definite orientation, resulting from the interaction of globules. Any increase in orientation of aggregation, however, facilitates the creation of fibrilla-like structures and, hence, of a three-dimensional network.

The types of interactions taking place on aggregation of globular proteins in the gel network are the same as those we have noted for collagen (covalent cross-linkage, polar interactions, hydrogen bonds, salt bridges, hydrophobic contacts). The role of hydrophobic contacts, however, is much greater than in the case of collagen. The contribution of these types of interaction to the formation of a gel network is examined in the following section.

5. Formation of Globular Protein Gels. Interactions in the Gel Network

When examining the interaction of protein molecules in the gel network we should not overlook any one of the five types of interaction enumerated above. The build-up of the three-dimensional network involves the cooperative effect of all these types of interaction. One can, however, distinguish systems where certain forces play a prevailing role.

Gelation of globular proteins by physical aggregation takes place, as a rule, under specific conditions ensuring the denaturation of globules and a limited protein solubility in the system. Thermally reversible gels are, therefore, obtained only at specific values of pH, ionic strength, dielectric constant of the medium, *etc.* Thermally irreversible gels, on the other hand, can be obtained under a much broader range of conditions.

A glycinine solution[37], for instance, gelates at room temperature after addition of urea and alcohol (glycinine is a soya bean protein). This gel, formed as a result of physical interactions, melts reversibly at a temperature of about 60 °C. If the melt is heated to 80 °C a thermally irreversible gel is formed as a result of covalent cross-linking. This gel can be obtained even without adding any urea or alcohol.

Covalent interactions are primarily significant for the proteins which contain a considerable amount of cystine and cysteine and thus form disulfide bonds. Cross-links are, however, possible in other proteins (Table 1)[46,47].

5.1. Covalently Cross-linked Gels

A characteristic property of soya bean proteins is their capability of selfstructurizing and forming gel-like systems on denaturation. This property is widely exploited in the manufacturing of artificial products based on soya protein solutions or dispersions. According to *Aoki* and *Sakurai*[48], and *Wolf*[49], this phenomenon is mainly associated with the formation of intermolecular disulfide bonds, although it cannot be ruled out that other, non-covalent types of interaction also participate in the gelling process. As proof of the validity of this concept the authors refer to the thermal irreversibility of the gels and the influence of various additives. Oxidants accelerate gelation, while reductants (*e.g.* cysteine, sulfites) hinder structurizing and decrease the mechanical strength of gels. According to *Saio et al.*[50] soya bean fractions containing large amounts of sulfur-containing amino acids form gels with a higher strength.

Soya protein denaturation, accompanied by gelling due to covalent disulfide cross-linking, is usually achieved by heating dispersions or solutions[51,52]. The same result is obtained on freezing soya protein solutions[53]. In the latter case denaturation is due to the growth of ice crystals causing the deformation of protein molecules and the appearance of protein concentrated regions (unfrozen solution) and protein diluted regions (ice crystals).

Covalent disulfide cross-linkage, resulting from protein denaturation, plays a major role in the gelation of most proteins which contain mercapto groups.

In the previously mentioned BSA association, disulfide cross-links play the leading role. Data are available on the intermolecular cross-linking capacity by means of the disulfide bonds of $\varkappa$-casein[54]. *Jones et al.*[55], assume an important role to be played by disulfide bonds in the rheological properties of the gels of wheat proteins.

Control of the number of disulfide bonds is widely used in alimentary gels. Addition of disulfide-group reducing agents (cysteine, glutathione, sulfites and their mixtures) to durum wheat-flour decreases the viscosity of dough as a consequence of the decrease in the number of disulfide cross-links. This enables a reduction in consumption of energy necessary for the kneading, extruding and drying of macaroni food products[56,57], and also a control on the quality of bakery products[58,59].

Adding oxidants (KIO_3) to water before cooking rice decreases the protein extraction from grains in the course of boiling and the consistency of the rice remains more compact. *Shintaro* and *Katsuharu*[60] attribute this phenomenon to the transformation of mercapto groups into intermolecular disulfide groups. An unequivocal interpretation is, however, difficult because of the possible oxidation of rice polysaccharides to dialdehydes and their subsequent interaction with the protein.

During the heat treatment of proteins, in addition to the formation of disulfide intermolecular bonds, all other types of covalently bonded cross-linkages can occur (cf. Table 1). For proteins containing large amounts of lysine it is especially characteristic for the formation of cross-links of the desmosine and lysinoalanine types to occur[61].

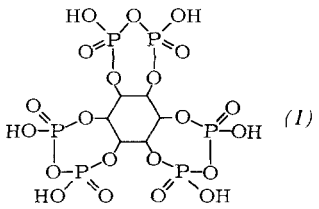
The above mentioned processes can be referred to as the autovulcanization or selfstructurizing of protein systems.

Several authors[62,63] believe that the formation of disulfide bonds does not significantly decrease the protein nutritive value; the other types of cross-linkage mentioned above, however, result not only in substantial changes of rheological properties, but also in a noticeable deterioration of the nutritive properties of foodstuffs.

Many proteins are capable of selfstructurizing, but not always under the conditions convenient from the technological point of view. Therefore, cross-linking agents are added to structurize proteins and control the thermomechanical properties of protein gels.

Sulfur has been used for the structurizing of vegetable proteins[64]; for carrying out the process it is necessary to add 0.1—3% of sulfur with respect to protein. The paste-like system containing 25—30% of protein is treated with the finely dispersed sulfur and then heated under pressure up to a temperature of 170 °C during two minutes. After release of pressure, on cooling a texturized product is obtained which is suitable for use as imitation meat. The nature of the processes taking place is still unclear; it is possible, however, to draw an analogy with the vulcanization of synthetic polymers by sulfur.

Saio et al.[50] have shown that phytic acid *(1)*, and its salts, which are always present in legumes, take part in the structurizing of soya proteins. It has been suggested that phytic acid should be used for the gelation of milk[65]. Skimmed milk containing 3—4% of proteins is treated with 8—15 mmol of an alkaline metal salt of phytic acid at pH 6.1—7.5 and then heated to 85 °C.



(1)

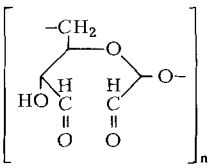
The flour of soft wheats contains proteins having a smaller number of sulfur-containing amino acids than in the flour of durum wheats. When this flour is used in manufacturing macaroni food products, cross-linking agents are necessary to impart the desired rheological properties to the finished product. For this purpose, it has been proposed to add oxidized polysaccharides, in particular dialdehyde starch[66], to the kneaded dough.

Dialdehyde polysaccharides are polyfunctional cross-linking agents capable of forming cross-links with cysteine, lysine and arginine groups of the polypeptide chain. Dialdehyde saccharides are used to fix the fibrous structure of protein solutions in the course of spinning[67].

It has also been suggested that dialdehyde starch be used for the production of various protein gels with controlled mechanical properties[68]. The gels are formed when 0.5—5% of dialdehyde starch is added to protein solutions or dispersions over a broad range of pH and concentrations.

For the same purpose, attempts are known to have been made to use the simplest aldehydes and dialdehydes. *Dürr* and *Neukom*[69] have studied the effect of nine different aldehydes (formaldehyde, propanal, hexanal, glyoxal, glutaraldehyde, α-hydroxyadipaldehyde, *etc.*) on the properties of macaroni food products. All the aldehydes studied imparted a higher rigidity to macaroni and prevented protein extraction during boiling. Dialdehydes gave the finished products a reddish brown color. Aldoses are also used as a cross-linking agent for the production of protein gels[70].

The cross-linking of proteins with the aid of lower aldehydes is used in the production of edible films for the packing of sausagemeat, and of mixtures enriched with fish protein[71]. These films, through which water and hot oil can



pass, are produced by extruding the protein solution through a circular extruder into a coagulation bath with a 0.01—0.1% solution of aldehyde (formaldehyde, acetaldehyde, glutaraldehyde, *etc.*) at a pH of about 6.5. The film stays in this solution for about ten minutes. It is then washed with a 5% sodium chloride solution at pH 8—11 to fix the cross-links and remove the unreacted aldehyde, and finally dried.

Aldehydes are also known to be used for obtaining and stabilizing technical protein gels and films in tanning and in the treatment of furs[72-74]. Many of the cross-linking agents employed are potentially toxic, and while for technical purposes their use is quite justified, their harmlessness in foodstuffs is doubtful. Proteins treated with formaldehyde[75] find application in animal feeding. There are, however, no comprehensive data on the toxicity and nutritive value of protein products containing aldehydes when used as food for human consumption. For a maximum preservation of the nutritive value the protein molecule should undergo the smallest chemical changes during the course of treatment. From this point of view the gels formed as a result of the physical association of proteins are more promising as foodstuffs, although they necessitate media having specific physico-chemical properties and they are more difficult to handle technologically.

5.2. Gelation with Salt Bridges

Until recently only alkaline gels of casein were known; concentrated alkaline casein solutions have been intensively studied in connection with the investigation of glue compositions (based on such solutions). *Fidney*[76] was the first to show that one can obtain casein gels at pH > 11.5. At lower pH values the systems formed are highly viscous but not rigid. Adding the ions of divalent metals results in a reversible gelation of these viscous systems[77]. Casein gels obtained in the presence of $Ca(OH)_2$ have been shown to be thermal reversible in the pH range 11.5—12.5[78]. Of interest from the point of view of being used in foodstuffs are casein gels formed in a neutral medium. *Anson* and *Pader*[79] have proposed a method for obtaining thermally irreversible calcium caseinate gels at pH 6.0. The method involves precipitation of casein from solution with any soluble calcium salt at pH 6.5, followed by heating a 25% aqueous suspension of the freshly precipitated calcium caseinate in an autoclave at 120—125 °C.

Of great interest is the question concerning the formation of a three-dimensional lattice made up of casein molecules in concentrated gels. According to *Rose*[80] the main role in the presence of calcium ions must be played by salt bridges: after removal of calcium from the milk, protein aggregation sharply decreases, and milk curdling is delayed. *Payens*[81] also believes that calcium ions, which react with the carboxy and phosphoric groups of the casein, are located on the surface of the casein micelle and cause the interaction of micelles with each other.

Kalab et al.[82,83] have described a method of producing gels from dried milk. Dried milk is suspended in such an amount of distilled water as to make the protein concentration no less than 17%. The suspension is placed in a sausage casing and kept in boiling water for about 10 minutes. In slightly acid or neutral media the calcium ions are firmly bonded with the protein and do not diffuse into the boiling water. Gel formation is mainly caused by salt bridges, but interaction of the lactose with the protein occurs, especially in the outer layer which is in contact with the boiling water. Hence, covalent cross-links characteristic for the reaction of aldoses with proteins also take part in the formation of the gel network. These two types of interaction cause the spontaneous gelling of condensed milk when it is kept at elevated temperatures. *Kirshmeyer*[84] has shown that a similar process can be effected by heating whole milk concentrated to a protein content of more than 15%.

Addition of calcium and magnesium ions allows smooth control of the solubility and gelation, not only of lactoproteins but also of vegetable proteins[85]. In contrast to the ions of group 2 metals, addition of divalent iron ions sharply reduces protein solubility and causes flocculation[86]. This effect can be due to the directivity of calcium and magnesium interactions, mainly with the protein bound carboxy groups. Iron coordinates with a much larger number of ligands: carboxy, mercapto, disulfide, α-peptide groups, *etc.* In the presence of iron, protein particles will, therefore, aggregate in a less oriented way; the aggregation is of a random nature, and the protein precipitates.

5.3. Gelation Resulting from Physical Interactions

Izmailova et al.[87,88] have studied the process of casein gelation in alkaline medium. They have shown that gels are not formed at a protein concentration of less than 15% and pH below 10.5. A spatial structure of maximum rigidity is observed in the pH range 12.9—13.3. At pH 13.3 the structural rigidity decreases with time, apparently because of protein hydrolysis. The authors believe that intermolecular hydrogen and hydrophobic bonds participate in the gelation process, and the role of disulfide cross-links is insignificant. In many cases of globular protein association hydrophobic contacts play a significant role. According to *Payens*[81], the hydrophobic portions of polypeptide chains are located both inside and on the surface of the casein micelle. The intramicellar hydrophobic interactions stabilize the spherical form of the micelle and make it extremely stable to denaturating effects. The hydrophobic sites on the surface cause micellar association even in the absence of calcium ions.

The important role of hydrophobic contacts in the intermolecular interactions of lactoproteins is confirmed by the results of investigations performed by *Thompson et al.*[89]. The main fractions of casein contain hydrophobic amino acids on the C-terminal ends of the peptide chain. When carboxypeptidases act upon α-casein, tryptophan and leucine split off; when they act upon β-casein, valine and leucine are split off. The ability of these proteins to associate, sharply decreases after the action of the enzyme.

The physical parameters of the hydrophobic nucleus of globular proteins are known to resemble those of ethanol[90]. The addition of hydrophilic organic solvents to the protein solution disturbs the hydrophobic interactions, since the structure of the water changes and facilitates unfolding of the compactly arranged protein molecule. Thus, yeast protein gelates when its solutions are heated in the presence of organic solvents[91].

Unfolding of protein molecules also occurs on addition of urea to the solution. It disrupts the hydrogen and the hydrophobic bonds. This also takes place in a highly acid or highly alkaline medium owing to the mutual repulsion of the similarly charged ionogenic groups in the protein molecule.

Denatured ovalbumin gels in mixtures of water and *n*-propyl alcohol have been studied by *Jirgensons*[92]. The alcohol in these systems acts both as a denaturizing agent and as solvent preventing protein precipitation. Gels are only formed if the alcohol concentration is in the range 40—60%. Outside this range protein precipitation is observed. Gelation occurs at an ovalbumin concentration of over 2%; at lower concentrations, only the viscosity of the solutions increases. Gels of 2% ovalbumin in 50% *n*-propyl alcohol melt reversibly at a temperature of about 67 °C.

Myers and *France*[93] have investigated ovalbumin gels in acetic acid solutions. A 5% protein solution was diluted with aqueous acetic acid solution to give a system containing 1% of protein and 3% of acid. Addition of NaCl in concentrations of up to 0.6 M at 25 °C accelerates gelation and increases gel rigidity. Higher concentrations of NaCl cause protein deposition. *Donnely*[94] obtained ovalbumin gels on adding an alkali to the protein solution. These gels liquefy more readily with increasing pH. According to *McKenzel et al.*[95] the addition of urea decreases the quantity of alkali necessary for gelation. *Jaenike*[96] was able to obtain ovalbumin gels by addition of urea in the pH range 4.7—10.8. It is also possible to cause ovalbumin denaturation and obtain a gel in neutral solutions under the effect of high pressures[97].

Bulankin et al.[98] conclude that ovalbumin gels are formed without the participation of disulfide bonds and that gel formation is a purely physical process. The results obtained by *Izmailova*[99,100], who studied the mechanism of ovalbumin gelation at pH <3 and >10, are in accord with this conclusion: the minimum concentration for gelation of the ovalbumin is equal to 2% in acid medium and 3.5% in alkali medium. A study of gels with the addition of substances which selectively disrupt different types of interactions showed the structural strength in ovalbumin gels to be mainly determined by hydrophobic bonds. This is also indicated by the increase in gel rigidity on warming to 55 °C.

The occurrence of hydrophobic interactions is facilitated by an increase in the ionic strength of a system: many proteins gelate in the presence of alkali metal salts. Gelation of lactoglobulin mixtures was observed on addition of potassium phosphate in concentrations of up to 0.1 M to skimmed

milk at pH 6.8[101]. It is of interest to note that apart from phosphate no other anions, glycerophosphate included, cause gelation. β-Lactoglobulin gelates[40] on acidification to pH 4.6 of a solution containing 4—5% of protein and 50% of ammonium sulfate (see Section 4). Removal of ammonium sulfate from the system by dialysis causes gel liquefaction, with the protein that has not undergone any chemical or conformational changes remaining in solution.

Addition of sodium chloride makes it possible to control the gelation time and the rigidity of ovalbumin[93] and arachin[102, 103] gels (arachin is a groundnut protein). An arachin gel is obtained by heating a 15% protein solution at pH 5—6 to 110 °C or by decreasing the pH from 12 to 4 at room temperature.

The equilibrium between hydrophobic and hydrophilic interactions and the solubility of globular proteins are also controlled by chemical modification of the protein macromolecules. Directed partial hydrolysis of the protein macromolecule can result in its unfolding and can be accompanied by aggregation. Thus the treatment of casein solutions with abomasum enzyme (rennin) is accompanied by cleavage of the hydrophilic portion of the casein κ-fraction. The κ-fraction contains a hydrophobic polypeptide and hydrophilic polysaccharide portions and, as a result, manifests surface-active properties. It screens the hydrophobic nucleus of the casein micelle and holds it in solution. The loss of the hydrophilic part of the molecule results in aggregation of the disorganized components of the casein micelle, which in turn results in protein flocculation and phase separation in the system[104, 105]. It should be remembered that the cleavage of hydrophobic amino acids from α- and β-casein fractions, conversely, impedes aggregation and raises the protein solubility[89].

Preliminary partial hydrolysis of soya protein improves its gelating capacity and makes it possible to control the properties of the gel. For this purpose, the protein is treated with acid, alkali[106] or proteolytic enzymes of vegetable origin[107, 108].

Partial hydrolysis of fish protein, on the other hand, decreases its gelating capacity, while acylation of the amino groups improves both the gelating and the emulsifying capacities of this protein[109]. Acylation affects the properties of different proteins in different ways: it impairs the solubility and the functional properties of yeast protein[110] and improves the solubility of soya protein[111] and casein[112, 113]. The acylation of casein with long-chain acyl halides leads to gelation in the vicinity of the isoelectric point of this protein[114].

Phosphorylation and sulfation of proteins facilitates an increase in the hydrophilicity of protein molecules, disturbance of the globular structure, and unfolding of the polypeptide chains. Vegetable proteins modified in this way acquire gelating capacity, phosphorylated proteins forming gels of a smaller rigidity as compared with those formed by sulfated proteins[115, 116].

Changes in the physico-mechanical properties of the medium and chemical modification of the protein molecule have a different effect on the properties of different kinds of protein. Directed control of the functional properties of proteins requires an individual approach for each and every protein or mixture of proteins.

6. Concluding Remarks

The material collected in this review is not claimed to give an exhaustive coverage of all the aspects and methods of producing protein gels. It does, however, enable one to systematize the current views on gelation in protein systems and to draw a number of conclusions which are of practical use.

The gelatinous state of a system is an intermediate quasi-stable state occurring either during protein dissolution or, on the contrary, during the transition from the dissolved state to the precipitate.

For attainment of this intermediate state there are four fundamental principles:

1. Oxidative thermal structurization of proteins owing to the covalent interaction of their functional groups.

2. Cross-linking of proteins by polyfunctional agents (including metal ions) in solutions.

3. Selection of the physico-chemical conditions of limited protein solubility in a system.

4. Chemical modification of the protein molecule, leading to limited protein solubility.

Received: February 13, 1978 [A 283 IE]
German version: Angew. Chem. *91*, 634 (1979)

[1] *J. H. Ferry*, Adv. Prot. Chem. *4*, 1 (1948).
[2] *Yu. S. Lipatov, I. F. Proshlyakova*, Usp. Khim. *30*, 517 (1961).
[3] *P. Flory*, Faraday Disc. Chem. Soc. *57*, 4 (1974).
[4] *S. P. Papkov*, Kolloidn. Zh. *19*, 333 (1957).
[5] *S. G. Yefimova, S. P. Papkov*, Kolloidn. Zh. *29*, 202 (1967).
[6] *S. P. Papkov*, Vysokomol. Soedin. *A 10*, 2691 (1968).
[7] *S. P. Papkov:* The Physico-chemical Fundamentals of the Processing of Polymer Solutions. Khimiya Publ., Moscow 1971.
[8] *L. Z. Rogovina, G. L. Slonimsky*, Usp. Khim. *6*, 1102 (1974).
[9] *R. Jaenicke*, Biophysik *4*, 299 (1973).
[10] *L. I. Slutsky*, Priroda (Moscow) *2*, 78 (1976).
[11] *A. Hiroshi, S. Masako*, Nippon Nogei Kagaku Kaishi *42*, 544 (1966).
[12] *S. Muthukrishnan*, Acta Histochem. *53*, 175 (1975).
[13] *A. Patshornik, M. Sokolowsky*, J. Am. Chem. Soc. *86*, 1860 (1964).
[14] *A. H. Whiting*, Biochem. Biophys. Acta *243*, 332 (1971).
[15] *H. Harding, G. Rogers*, Biochem. Biophys. Acta *427*, 315 (1976).
[16] *A. J. Bailey, T. J. Sims*, Biochem. J. *153*, 211 (1976).
[17] *W. Traub, K. A. Piez*, Adv. Prot. Chem. *25*, 243 (1971).
[18] *R. Aeschbach, R. Amado, H. Neukom*, Biochem. Biophys. Acta *439* (1976).
[19] *A. N. Mikhailov:* Epidermis Collagen and the Principles of its Processing. Lyogkaya Industriya Publ., Moscow 1971.
[20] *P. V. Hauschka, J. B. Lian, P. M. Gallop*, Proc. Nat. Acad. Sci. USA *72*, 3925 (1975).
[21] *A. Veis:* Macromolecular Chemistry of Gelatin. Pishchevaya Promyshlennost' Publ., Moscow 1971.
[22] *G. Raikh:* Collagen. Lyogkaya Industriya Publ., Moscow 1969.
[23] *J. Bello, H. R. Bello, I. R. Vinograd*, Biochem. Biophys. Acta *57*, 214 (1962).
[24] *J. Bello, H. R. Bello, I. R. Vinograd*, Biochem. Biophys. Acta *57*, 222 (1962).
[25] *C. Hafter, H. Hörmann*, Leder *21*, 237 (1970).
[26] *S. S. Nikolayeva, A. N. Mikhailov*, Vysokomol. Soedin. *B4*, 297 (1977).
[27] *E. F. Titova, E. M. Belavtseva, E. E. Braudo, V. B. Tolstogusov*, Colloid Polym. Sci. *252*, 497 (1974).
[28] *V. N. Izmailova, P. A. Rebinder:* Structurization in Protein Systems. Nauka Publ., Moscow 1974.
[29] *C. Cohen*, J. Biophys. Biochem. Cytol. *1*, 203 (1955).
[30] *W. Kauzman*, Adv. Chem. *14*, 1 (1959).
[31] *G. Nemethy, G. Scheraga, W. Kauzman*, J. Phys. Chem. *72*, 184 (1968).
[32] *C. Tanford*, J. Am. Chem. Soc. *84*, 4240 (1962).
[33] *C. C. Bigelow*, J. Theor. Biol. *16*, 187 (1967).
[34] *G. P. Yampol'skaya, V. N. Izmailova, V. A. Pchelin*, Vysokomol. Soedin. *A 12*, 1923 (1970).
[35] *V. A. Pchelin, V. N. Izmailova, K. T. Ochurova*, Dokl. Akad. Nauk SSSR *123*, 505 (1958).
[36] *V. A. Pchelin, V. N. Izmailova, N. I. Seraya*, Vysokomol. Soedin. *1*, 1617 (1959).
[37] *M. P. Tombs*, Faraday Discuss. Chem. Soc. *57*, 158 (1974).

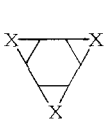
[38] *V. I. Zvyagintsev, A. N. Tolkachov, P. F. Krasheninin*, Prikl. Biokhim. Mikrobiol. *8*, 449 (1972).
[39] *B. Ribadeau-Dumas, G. Brignon, F. Grosclaude, J. C. Mercier*, Eur. J. Biochem. *25*, 505 (1972).
[40] *J. C. Mercier, F. Grosclaude, B. Ribadeau-Dumas*, Eur. J. Biochem. *23*, 41 (1971).
[41] *M. G. Bezrukov, V. M. Belikov, E. M. Belawtseva, E. F. Titova*, Polym. Colloid. Sci., in press.
[42] *M. Sörensen, S. P. Z. Sörensen*, C. R. Trav. Lab. Carlsberg *23*, 55 (1939).
[43] *C. Huggins, D. F. Tapley, E. V. Jensen*, Nature *167*, 592 (1951).
[44] *M. P. Tombs* in *R. A. Laurie:* Proteins as Human Foods. Butterworth, London 1970.
[45] *E. Barbu, M. Joly*, Faraday Discuss. Chem. Soc. *13*, 77 (1953).
[46] *M. Steinberg, C. J. Kim, F. I. Schwende*, Science *190*, 992 (1975).
[47] *A. G. Matoltsy*, J. Invest. Dermatol. *67*, 20 (1976).
[48] *H. Aoki, M. Sakurai*, Nippon Nogei Kagaku Kaishi *42*, 554 (1968).
[49] *N. I. Wolf*, J. Agr. Food Chem. *18*, 969 (1970).
[50] *K. Saiso, M. Kamiya, M. Fujimaki*, Agr. Biol. Chem. *33*, 1301 (1969).
[51] *M. L. Pader*, US-Pat. 2813024 (1957); Chem. Abstr. *52*, 5698i (1958).
[52] *S. F. Loepiktie, R. J. Flier*, US-Pat. 3759715 (1971); Chem. Abstr. *75*, 145078x (1973).
[53] *G. K. Okumura, J. E. Wilkinson*, US-Pat. 3490914 (1970); Chem. Abstr. *72*, 110022c (1970).
[54] *K. Schimasaki, A. Shunrokuro*, J. Biochem. (Tokyo) *75*, 429 (1974).
[55] *J. K. Jones, J. W. Phillips, F. J. R. Hird*, J. Sci. Food Agric. *25*, 1 (1974).
[56] *A. Menger*, Getride Mehl Brot *26*, 307 (1972).
[57] *R. H. Kilborn, K. H. Tipples*, Cereal Chem. *50*, 70 (1973).
[58] *N. A. Chumachenko, L. A. Markianova, A. P. Demchuk, I. M. Roiter*, Khlebopek. Konditer. Promst. *5*, 17 (1974).
[59] *T. W. Craig, R. G. Henika*, US-Pat. 3803326 (1974); R. Zh. Khim. 7P721I (1975).
[60] *M. Shintaro, I. Katsuharu*, J. Jap. Soc. Food Nutr. *25*, 59 (1972).
[61] *K. Deshmukh*, Connect. Tissue Res. *2*, 95 (1974).
[62] *A. P. De Groot, P. Slump*, J. Nutr. *96*, 45 (1969).
[63] *M. M. Hamdy*, J. Am. Oil Chem. Soc. *A 51*, 85 (1974).
[64] *H. D. Waggle*, US-Pat. 3810764 (1974); R. Zh. Khim. 7P61 (1975).
[65] *T. Nagasava, I. Kijosava, J. Tokatsu, K. Kavase*, Jap. Kokai 7340751 (1973); R. Zh. Khim. 16P207II (1974).
[66] *M. A. Andreyeva, M. A. Kalinina, N. I. Nazarov, N. N. Shebershneva*, Khlebopek. Konditer. Promst. *12*, 21 (1973).
[67] *M. Shibuya*, Jap. Kokai 7309452 (1973); Chem. Abstr. *80*, 49541t (1974).
[68] *K. D. Schwenke, L. Prahl, E. Jarmatz, B. Ender, J. Uhlig, A. I. Volnova, S. G. Charatian*, Nahrung *20*, 895 (1976).
[69] *P. Dürr, H. Neukom*, Lebensm. Wiss. Technol. *7*, 89 (1974).
[70] *M. G. Bezrukov, V. M. Belikov, S. V. Rogozhin, N. S. Martinkova, S. V. Vitt*, USSR Auth. Cert. 440012 (1972).
[71] *A. Miyata, M. Takahashi*, Jap. Kokai 7312429 (1973); Chem. Abstr. *80*, 28511t (1974).
[72] *C. Boragine, R. Kitzing*, DOS 2133402 (1970); Chem. Abstr. *76*, 119901d (1972).
[73] *J. Bjorksten*, Adv. Protein Chem. *6*, 343 (1951).
[74] *E. E. Hatfield* in: Effect of Processing Nutritional Value of Feeds. Proc. Symp. 1972, Natl. Acad. Sci., Washington, p. 171.
[75] *T. N. Barry*, N. Z. J. Agric. Res. *15*, 107 (1972).
[76] *M. Fidney, H. Higgins, J. Hayes*, Nature *167*, 224 (1951).
[77] *N. Kopaczewsky*, Lait *16*, 81 (1936).
[78] *S. Nakai, H. K. Wilson, E. O. Harrald*, J. Dairy Sci. *48*, 431 (1965).
[79] *M. L. Anson, M. Pader*, US-Pat. 2813794 (1957); Chem. Abstr. *52*, 5699e (1958).
[80] *D. Rose*, J. Dairy Sci. *45*, 1305 (1962).
[81] *T. A. Payens*, J. Dairy Sci. *49*, 1317 (1966).
[82] *M. Kalab*, J. Dairy Sci. *53*, 711 (1970).
[83] *M. Kalab, P. W. Voisey, D. B. Emmons*, J. Dairy Sci. *54*, 178 (1971).
[84] *O. Kirschmeier*, Milchwissenschaft *24*, 336 (1969).
[85] *S. Sigaehisa, I. Toru*, Jap. Kokai 7622068 (1976); R. Zh. Khim. 12P56 (1977).
[86] *S. Ohtake, J. Kasuga, T. Nakamoto*, Jap. Kokai 75117256 (1975); Chem. Abstr. *84*, 79371 (1976).
[87] *A. S. Zholbosynova, V. N. Izmailova, M. N. Pankratova*, Kolloidn. Zh. *32*, 49 (1970).
[88] *V. N. Izmailova, M. N. Pankratova*, Vysokomol. Soedin. *B 14*, 182 (1972).
[89] *W. P. Thompson, E. B. Kalan, K. Greenberg*, Milchwissenschaft *23*, 227 (1968).
[90] *P. Dunnil*, Sci. Prog. London *53*, 609 (1965).
[91] *K. Kuba, M. Jano, M. Jokoyama, C. Jamashita*, Jap. Kokai 7703896 (1975); Chem. Abstr. *86*, 153968x (1977).
[92] *B. Jirgensons*, Kolloid. J. *74*, 300 (1936).
[93] *N. G. Myers, W. G. France*, J. Phys. Chem. *44*, 1113 (1940).
[94] *J. L. Donnely*, Kolloid. J. *74*, 343 (1936).
[95] *H. McKenzel, M. Smith, R. Wake*, Biochem. *69*, 229 (1963).
[96] *R. Jaenike*, Z. Naturforsch. *B 20*, 21 (1965).
[97] *S. Chiko, S. Keiso*, Arch. Biochem. Biophys. *102*, 367 (1963).
[98] *I. N. Bulankin, Ye. V. Parina, R. I. Agronovich, L. O. Liubartseva, L. S. Kolesnik*, Ukr. Biokhim. Zh. *33*, 307 (1961).
[99] *A. S. Zholbosynova, V. N. Izmailova*, Dokl. Akad. Nauk SSSR *172*, 130 (1967).
[100] *V. N. Izmailova, A. S. Zholbosynova*, Kolloidn. Zh. *29*, 677 (1967).
[101] *I. Liang, T. Nakamura, D. Jonezawa*, Nippon Nogei Kagaku Kaishi *48*, 49 (1974).
[102] *M. P. Tombs*, Biochem. J. *96*, 119 (1965).
[103] *M. P. Tombs, M. Lowe*, Biochem. J. *105*, 181 (1967).
[104] *O. Kirschmeier*, Milchwissenschaft *6*, 396 (1969).
[105] *I. C. Mercier, I. Uro, B. Ribadeau-Dumas, F. Grosclaude*, Eur. J. Biochem. *27*, 535 (1972).
[106] *K. Hashirumo, T. Watanabe*, Nippon Nogei Kagaku Kaishi *49*, 331 (1975).
[107] *A. Pour-El, T. C. Swenson*, Cereal Chem. *53*, 438 (1976).
[108] *A. Pour-El, T. C. Swenson*, US-Pat. 3932672 (1976); R. Zh. Khim. 18P339II (1976).
[109] *R. Miller, H. S. Groninger*, J. Food Sci. *41*, 268 (1976).
[110] *M. D. McElwain, T. Richardson, C. H. Amundson*, J. Milk Food Technol. *38*, 521 (1975).
[111] *K. L. Franzen, J. E. Kinsella*, J. Agr. Food Chem. *24*, 788 (1976).
[112] *L. K. Creamer, E. H. Procher, E. N. Lohrev*, N. Z. Dairy Sci. Technol. *6*, 107 (1971).
[113] *M. T. A. Evans, L. Irons, J. H. P. Petty*, Biochem. Biophys. Acta *243*, 259 (1971).
[114] *M. G. Bezrukov, N. S. Martinkova, S. V. Vitt, V. M. Belikov*, USSR Auth. Cart 440013 (1973); Chem. Abstr. *83*, 204973t (1975).
[115] *R. E. Ferrel, H. S. Olcott, H. Fraenkel-Conrat*, J. Am. Chem. Soc. *70*, 2101 (1948).
[116] *H. S. Olcott, A. Mohammad*, US-Pat. 2513351 (1950); Chem. Abstr. *44*, 10217g (1950).

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.

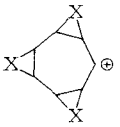
endo-Hydroxytrioxatris-σ-homotropilidenes[**]

By *Horst Prinzbach, Christoph Rücker,* and *Hans Fritz*[*]

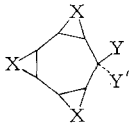
Interesting aspects of the chemistry of trisheterotris-σ-homobenzenes *(1)* include the thermal $[_\sigma 2_s + _\sigma 2_s + _\sigma 2_s]$ cycloreversion to trisheteronins[1a] and the regio- and stereoselective ring cleavage to give biologically important aminohexitols[1b]. Preparation of similar target molecules—such as potentially "trishomobenzenoid" carbenium ions of type *(2)* (X = O, NR), aminoheptitols—requires specifically *endo*-substituted trisheterotris-σ-homotropilidenes *(3)* (X = O, NR; Y = OR, Y′ = H). We have developed preparatively useful syntheses for two (*cis*; α,α,β) of the three isomeric trioxa compounds 1α,2α,4α,5α,7α,9α- and 1α,2α,4α,5β,7β,9α-3,6,10-trioxatetracyclo[7.1.0.0^{2,4}.0^{5,7}]decan-8β-ol [*(8a)* and *(11a)*][2] which comprise the reaction sequences *(4b)*→*(5b)*→*(6c)*→*(7c)*→*(8a)* and *(4b)*→*(5a)*→*(10a)*→*(11a)*[3].



(1)

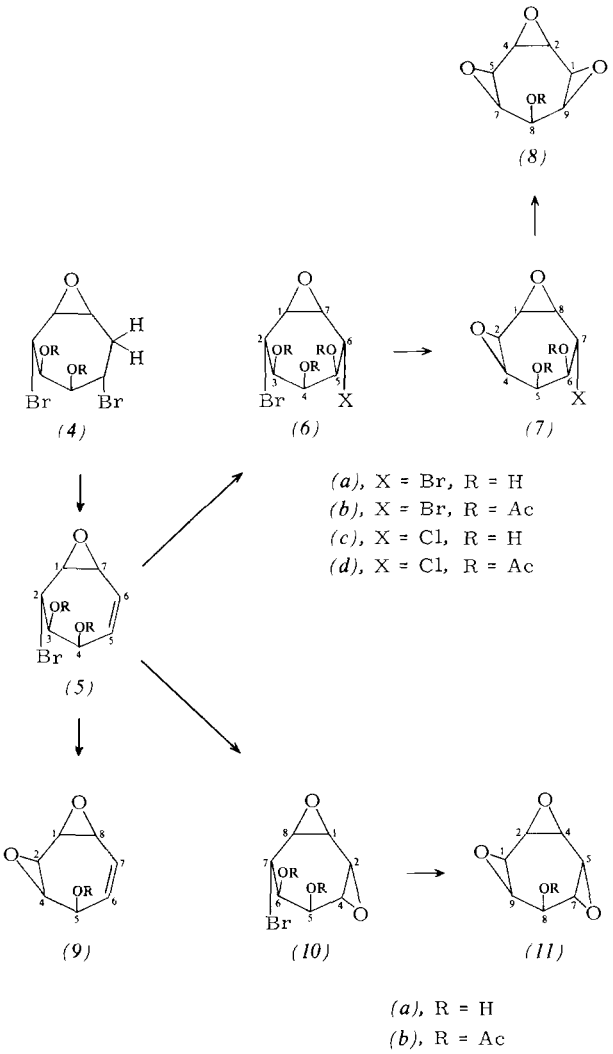


(2)



(3)

The starting material *(4b)*[4] is readily accessible from tropilidene; under controlled conditions in the presence of the weakly nucleophilic base diazabicyclononene (DBN) (THF, 20 °C, 15 h), HBr elimination proceeds without competition, in contrast to the reaction involving, *e.g.*, sodium methoxide/methanol. According to ^{1}H-NMR analysis [($CDCl_3$); $J_{1,2}=6.5$, $J_{2,3}=8.5$, $J_{3,4}=4.5$, $J_{4,5}=5$, $J_{5,6}=10.5$, $J_{6,7}<3$, $J_{1,7}=4.5$ Hz] the diacetate *(5b)* [m.p. 83 °C (CCl_4), isolated quantitatively], as well as the diol *(5a)* [m.p. 113 °C (acetone)], should prefer a twisted conformation[5] (Br, 3-OR quasiequatorial, 4-OR quasiaxial) in which the center of the C C double bond is effectively shielded on the β-side by 2β-H.



The advantage of using *(5b)* as a precursor of *(8a)* is that the site of OH addition on reaction with HOX is immaterial (C-5, C-6) as long as it occurs from the side of the epoxide ring (*i.e.* from the β side); double ring closure always leads exclusively to *(8)*. Since vicinal *trans*-diaxial H/X systems are absent, olefin formation cannot compete. Only unsatisfactory regio- and stereoselectivities are obtained on addition of HOBr [NBS, acetone/water (1:1), 50 °C, 24 h]: never more than 10% of *(6a)* (isolated as *(6b)*; m.p. 173 °C (CCl_4); plane of symmetry evidenced by ^{1}H- and ^{13}C-NMR spectra; $J_{1,2}$ ($J_{6,7}$) ≈ 7, $J_{2,3}$ ($J_{5,6}$) = 11, $J_{3,4}$ ($J_{4,5}$) = 2.5 Hz) together with two epoxide cleavage products (H_2O, HBr). In contrast, addition of HOCl is almost specific [*tert*-butyl hypochlorite, water/acetone (1:1), 50 °C, 8 h]: subsequent hydrolysis affords 90—95% *(6c)* [m.p. 170 °C (subl.); *(6d)*: m.p. 163 °C (acetone/CCl_4); $J_{1,2}=J_{6,7}=7.5$, $J_{2,3}=J_{5,6}=11$, $J_{3,4}=J_{4,5}=2.5$, $J_{1,7}=4.5$ Hz] and 2—5% of the Cl_2 addition product of the same configuration. The price paid for the high yield of *(6c)* is a considerable drawback in the next stage. As expected, only the transformation into *(7c)* proceeds readily in the case

[*] Prof. Dr. H. Prinzbach [†], Dipl.-Chem. Ch. Rücker, Prof. Dr. H. Fritz
Lehrstuhl für Organische Chemie der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. *Ch. Rücker* thanks the Studienstiftung des Deutschen Volkes for a scholarship.

[†] To whom correspondence should be addressed.

of *(6c)* [>90%, m.p. 127 °C (methanol/CCl_4); *(7d)*: m.p. 145 °C (CCl_4/$CHCl_3$); $J_{1,2} \approx 1$, $J_{2,4} = 4$, $J_{4,5} \approx 1$, $J_{5,6} = 4.5$, $J_{6,7} = 8$, $J_{7,8} = 7$, $J_{1,8} = 4.5$ Hz]. During the long time required for elimination of HCl (24 h) the product uniformity is lost; for example, after complete reaction with KOH/methanol (20 °C, 24 h) only 30—35% of *(8a)* is obtained [m.p. 207 °C (subl.); *(8b)*; m.p. 197 °C (subl.); ^{1}H-NMR ($CDCl_3$, 360 MHz): $\delta = 5.65$ (t, 8-H), 3.44 (m, 2-, 4-H), 3.34 (m, 1-, 5-, 7-, 9-H), 2.21 (s, OCH_3); $J_{7,8}$ ($J_{8,9}$) = 1 Hz; ^{13}C-NMR ($CDCl_3$): $\delta = 170.3$ (CO), 67.0 (C-8), 58.7 (C-7, -9), 52.3 (C-1, -5), 48.2 (C-2, -4), 20.9 (CH_3)]; products resulting from substitution at C-2, C-4 and transannular ether formation arise preferentially[6]. The yield rises to the fairly respectable value of 45—50% of *(8a)* [42—48% based on *(4b)*]—with similar by-products—on use of the reagent sodium glycolate/THF which has proved of value in similar cases[7]; only nonspecific decomposition occurs with DBN.

The critical step *en route* from *(5b)* to *(11a)* is epoxidation: the diacetate *(5b)* is resistant to *m*-chloroperbenzoic acid (in $C_2H_4Cl_2$) between 25 and 80 °C. The diol *(5a)* is also oxidized very slowly (3 d, 20 °C) yet with an expectedly high *trans*-selectivity; polymeric material is accompanied by 45% of *(10a)* [m.p. 175 °C (ethyl acetate/benzene); *(10b)*: m.p. 119—120 °C (CCl_4); $J_{2,4} = 4$, $J_{4,5} = 7$, $J_{5,6} = 4.5$, $J_{6,7} = 9$, $J_{7,8} = 8$ Hz] and traces of *(7a)* [m.p. 115 °C (ethyl acetate/benzene); $J_{1,2} = 1.5$, $J_{2,4} = 4$, $J_{4,5} \approx 1$, $J_{6,7} = 8$, $J_{7,8} = 6.5$, $J_{1,8} = 4.5$ Hz]. Nor could the early initiation of decomposition and secondary reactions be delayed by variation of the reaction conditions (peracid, temperature, buffer). No *(10a)* is formed with CF_3CO_3H/Na_2HPO_4 (CH_2Cl_2, 20 °C). Epoxide ring closure *(10a)*→*(11a)* is fast and practically uniform [85—90%; 36—40% based on *(5b)*, m.p. 93—94 °C (acetone/CCl_4); *(11b)*: m.p. 85 °C (CCl_4/pentane); ^{1}H-NMR ($CDCl_3$, 360 MHz): $\delta = 4.90$ (d, 8-H), 3.59 (dd, 1-H), 3.35—3.45 (m, 4-, 5-H), 3.30 (d, 9-H), 3.20 (dt, 2-H), 3.16 (dt, 7-H), 2.21 (s, OCH_3); $J_{1,2} = 3$, $J_{1,9} = 4.5$, $J_{2,4} = 3$, $J_{4,5} = 0$, $J_{5,7} = 5$, $J_{7,8} = 5.5$, $J_{8,9} = 0$ Hz; ^{13}C-NMR ($CDCl_3$): $\delta = 170.4$ (CO), 73.2 (C-8), 57.5, 55.8 (C-7, -9), 51.9, 50.8, 49.2, 48.6 (C-1, -2, -4, -5)].

The alternative of first converting *(5a)* into *(9a)*—the conformation having quasi-*trans*-diaxial OH/Br substituents is readily accessible—and epoxidizing the product is less favorable. Although *(9a)* is formed quantitatively under standard conditions [m.p. 93—94 °C (ethyl acetate/benzene); *(9b)*: m.p. 108—109 °C (CCl_4)], its epoxidation is even slower and more complex than that of *(5a)* and, moreover, non-stereoselective [*ca.* 5—10% of each *(8a)* and *(11a)*][8].

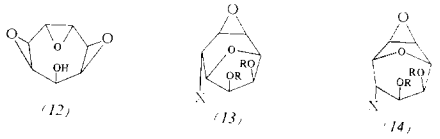
Compounds *(5)*—*(14)* are fully characterized by elemental analysis and spectral data (MS, IR, ^{1}H- and ^{13}C-NMR), and the stereochemistry of the end products *(8)* and *(11)* is chemically confirmed, *e.g.* by oxidation to the tropone trioxides and by comparison with the *exo/endo* alcohols[2] formed from the latter compounds.

Received: June 21, 1978 [Z 39 IE]
German version: Angew. Chem. *91*, 646 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(4b), 59992-03-9; *(5a)*, 67598-52-1; *(5b)*, 67598-53-2; *(6a)*, 67598-54-3; *(6b)*, 67598-55-4; *(6c)*, 67598-56-5; *(6d)*, 67598-57-6; *(7a)*, 67598-58-7; *(7c)*, 67598-59-8; *(7d)*, 67598-60-1; *(8a)*, 67598-61-2; *(8b)*, 67598-62-3; *(9a)*, 67598-63-4; *(9b)*, 67598-64-5; *(10a)*, 67650-77-5; *(10b)*, 67598-65-6; *(11a)*, 67650-78-6; *(11b)*, 67650-79-7

[1] a) *H. Prinzbach, R. Schwesinger, M. Breuninger, B. Gallenkamp, D. Hunkler*, Angew. Chem. *87*, 349 (1975); Angew. Chem. Int. Ed. Engl. *14*, 347 (1975), and references cited therein; b) cf., *e.g.*, the synthesis of streptamine from *cis*-benzene trioxide: *R. Schwesinger, H. Prinzbach, ibid. 87*, 625 (1975) and *14*, 630 (1975), respectively.

[2] The third isomeric alcohol (α,β,α) *(12)* has been obtained from α,β,α-tropone trioxide: *H. Prinzbach, W. Seppelt, H. Fritz*, to be published.



(12) *(13)* *(14)*

[3] Attempted radical halogenation of the CH_2 group in *cis*-tropilidene trioxide [4] led only to substitution in the epoxide rings; *Ch. Rücker*, Dissertation, Universität Freiburg 1979.

[4] *H. Prinzbach, Ch. Rücker*, Angew. Chem. *88*, 611 (1976); Angew. Chem. Int. Ed. Engl. *15*, 559 (1976).

[5] *W. Tochtermann*, Fortschr. Chem. Forsch. *15*, 378 (1970).

[6] Ethers and chlorides of type *(13)* and *(14)*, X = OCH_3, Cl, could be isolated and characterized.

[7] *R. Schwesinger, H. Prinzbach*, Angew. Chem. *84*, 990 (1972); Angew. Chem. Int. Ed. Engl. *11*, 942 (1972).

[8] The hitherto unknown *cis*-2,3:4,5-tropone dioxide (m.p. 88 °C, 44—60%; $J_{1,2} = 3$, $J_{2,4} = 4$, $J_{4,6} = 1.8$, $J_{6,7} = 12$, $J_{7,8} = 3.5$, $J_{1,8} = 4$ Hz) can be obtained *via (9a)*, *e.g.* by oxidation with RuO_4 (RuO_2, 2 equiv. $NaIO_4$, $CHCl_3/H_2O$, 20 °C).

Hexamethyldisilane/Iodine: Convenient *In Situ* Generation of Iodotrimethylsilane[**]

By *George A. Olah, Subhash C. Narang, B. G. Balaram Gupta*, and *Ripudaman Malhotra*[*]

Iodotrimethylsilane[1] has recently found extensive use in organic syntheses. Because of the relative difficulty of preparation and its hydrolytic and photoinstability, emphasis was placed on continued work on the *in situ* generation of the reagent. Work in this area has resulted in the use of phenyltrimethylsilane/iodine[2], allyltrimethylsilane/iodine, and 3,6-bis(trimethylsilyl)-1,4-cyclohexadiene/iodine reagents[3]. These reagents, however, can either produce undesirable by-products or involve tedious syntheses of starting materials. Recently, chlorotrimethylsilane/sodium iodide was also introduced as an iodotrimethylsilane equivalent, but its utility is confined to the essential use of acetonitrile as solvent[4].

We now wish to report the use of hexamethyldisilane/iodine [*(2)*/I_2] as an extremely effective and mild *in situ* iodotrimethylsilane reagent giving no by-products. This reagent can be advantageously used for the mild cleavage of esters *(1)*, carbamates *(5)*, ethers *(3)*, and sulfoxides. Alcohols can be equally well transformed into corresponding alkyl iodides with the reagent.

Esters *(1)* are cleaved to the corresponding acids in very high yield. The reaction was applied with equal ease to methyl, ethyl, and benzyl esters of aliphatic and aromatic carboxylic acids.

$$\underset{(1)}{RCO_2R'} \xrightarrow[2.\ H_2O]{1.\ Me_3SiSiMe_3\ (2)/I_2} RCO_2H + R'I$$

Aliphatic ethers *(3)* can be cleaved to the corresponding alcohols or further transformed into alkyl iodides by varying the reaction conditions. When cyclohexyl methyl ether *(3d)* was reacted with HMDS/I_2 reagent in chloroform solution at

[*] Prof. Dr. G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra
Hydrocarbon Research Institute, Department of Chemistry
University of Southern California
University Park, Los Angeles, California 90007 (USA)

[**] Part 74 in the Series: Synthetic Methods and Reactions. Support for this work by the National Science Foundation and the National Institutes of Health is gratefully acknowledged. Part 73: *G. A. Olah, Y. D. Vankar, M. Arvanaghi*, Tetrahedron Lett., in press.

room temperature, cyclohexanol was obtained in excellent yield. When the reaction mixture was heated under reflux in the absence of chloroform, cyclohexyl iodide was obtained with no alcohol present. Alcohols themselves can be cleanly converted into the corresponding iodides.

$$\underset{(3)}{ROR'} \xrightarrow{(2)/I_2} \underset{(4)}{ROH} + R'I$$

$$\underset{(4)}{ROH} \xrightarrow{(2)/I_2} RI$$

It was observed that cleavage of both esters *(1)* and ethers *(3)* is catalyzed by excess iodine in the system (see Table 1)[5].

General Procedure

To a solution of hexamethyldisilane *(2)*[6] and I_2 (for amounts, see Table 1) in chloroform (15 ml), the substrate [ester *(1)*, ether *(3)*, or carbamate *(5)*] (5 mmol) is added with continuous stirring under a nitrogen atmosphere. The reaction mixture was then heated under reflux and the reaction monitored by TLC and ^{1}H-NMR [cf. ref. [4]]. Usual workup afforded the desired products, which were purified by crystallization or distillation.

A similar procedure was employed in the conversion of alcohols *(4)* into iodides and in the deoxygenation of sulfoxides to sulfides.

Received: May 9, 1979 [Z 252a IE]
German version: Angew. Chem. *91*, 648 (1979)

Table 1. Reactions of esters *(1)*, ethers *(3)*, alcohols *(4)*, and carbamates *(5)* with hexamethyldisilane *(2)*/I_2. The IR, NMR and m.p. or b.p. of the isolated products were in agreement with those of authentic samples.

	Substrate	Substrate:*(2)*:I_2 (molar ratio)	T [°C]	t [h]	Product(s)	Yield [%] [a]
(1a)	Ethyl benzoate	1:0.66:0.66	61	48	Benzoic acid	80
		1:0.6:0.7	25	48		98
(1b)	Benzyl benzoate	1:0.55:0.55	25	3	Benzoic acid	94
					Benzyl iodide	78
(1c)	Methyl 1-adamantanecarboxylate	1:0.55:0.55	61	16	1-Adamantanecarboxylic acid	95
		1:0.9:1.05	25	10		95
(1d)	Methyl cinnamate	1:0.55:0.55	61	16	Cinnamic acid	92
(1e)	Ethyl phenylacetate	1:0.6:0.7	61	24	Phenylacetic acid	95
		1:0.9:1.05	25	10		95
(3a)	Anisole	1:0.66:0.66	61	48	Phenol	95
(3b)	Phenetole	1:0.66:0.66	61	124	Phenol	(30) [b]
		1:1:2	61	16	Phenol	98
(3c)	Benzyl methyl ether	1:1:2	61	2	Benzyl iodide	87
(3d)	Cyclohexyl methyl ether	1:0.66:0.66	25	16	Cyclohexanol	95
		1:1:2	≈100	4	Cyclohexyl iodide	98
(3e)	Cyclohexyl ethyl ether	1:1:2	61	3	Cyclohexyl iodide	98
(4a)	Cyclohexanol	1:1:2	61	5	Cyclohexyl iodide	86
(4b)	1-Nonanol	1:1:2	61	2	Nonanyl iodide	98
(4c)	1-Adamantanol	1:1:2	61	2	Adamantyl iodide	98
(4d)	Benzyl alcohol	1:1:2	61	2	Benzyl iodide	98
(5a)	*N*-Phenyl methylcarbamate	1:0.55:0.55	61	20	Aniline	64
(5b)	Z-Glycine	1:0.55:0.55	50	0.1	Benzyl iodide	100 [b]
					Glycine	100 [b]
(5c)	Boc-Glycine	1:0.55:0.55	50	0.1	*tert*-Butyl iodide	100 [b]
					Glycine	100 [b]
(5d)	Boc-Gly-OBzl	1:1.1:1.1	50	0.1	*tert*-Butyl iodide	100 [b]
		1:1.1:1.1	50	0.5	Benzyl iodide	100 [b]
					Glycine	100 [b]

[a] Isolated yield of the product. [b] Product composition determined by NMR spectroscopy.

The present reagent was also found to be more selective in the cleavage of protective groups frequently employed in peptide chemistry. For example, carbamates *(5)* can be cleaved cleanly in the presence of a benzyl ester.

$$\underset{(5)}{RNHCO_2R'}$$

$$\underset{(5d)}{\text{Boc-Gly-OBz}} \xrightarrow[5\text{ min}]{(2)/I_2} \text{GlyOBzl} \xrightarrow[30\text{ min}]{(2)/I_2} \text{Gly}$$

Sulfoxides, including dibenzyl sulfoxide, diphenyl sulfoxide, dibutyl sulfoxide, and tetramethylene sulfoxide are also rapidly deoxygenated by *(2)*/I_2 to the corresponding sulfides in quantitative yield.

CAS Registry numbers:
(1a), 93-89-0; *(1b)*, 120-51-4; *(1c)*, 711-01-3; *(1d)*, 103-26-4; *(1e)*, 101-97-3; *(2)*, 1450-14-2; *(3a)*, 100-66-3; *(3b)*, 103-73-1; *(3c)*, 538-86-3; *(3d)*, 931-56-6; *(3e)*, 932-92-3; *(4a)*, 108-93-0; *(4b)*, 143-08-8; *(4c)*, 768-95-6; *(4d)*, 100-51-6; *(5a)*, 2603-10-3; *(5b)*, 17136-36-6; *(5c)*, 4530-20-5; *(5d)*, 54244-69-8; benzoic acid, 65-85-0; benzyl iodide, 620-05-3; 1-adamantanecarboxylic acid, 828-51-3; cinnamic acid, 621-82-9; phenylacetic acid, 103-82-2; phenol, 108-95-2; cyclohexanol, 108-93-0; cyclohexyl iodide, 626-62-0; nonyl iodide, 4282-42-2; 1-adamantyl iodide, 768-93-4; aniline, 62-53-3; glycine, 56-40-6; *tert*-butyl iodine, 558-17-8

[1] *T. L. Ho, G. A. Olah*, Angew. Chem. *88*, 847 (1976); Angew. Chem. Int. Ed. Engl. *15*, 774 (1976); *G. A. Olah, B. G. B. Gupta, S. C. Narang*, Synthesis *1977*, 583; *M. E. Jung, M. A. Lyster*, J. Chem. Soc. Chem. Commun. *1978*, 315, and references cited therein.
[2] *T. L. Ho, G. A. Olah*, Synthesis *1977*, 417.

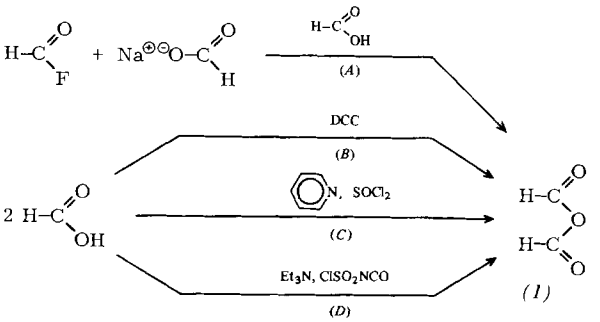
[3] M. E. Jung, T. A. Blumenkopf, Tetrahedron Lett. 1978, 3657.
[4] G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra, J. Org. Chem. 44, 1247 (1979).
[5] Benkeser et al. have observed similar catalysis. R. A. Benkeser, personal communication.
[6] (2), which is commercially available from PCR Research Chemicals, Inc., can be readily prepared from chlorotrimethylsilane and lithium; see H. Sakurai, A. Okada, J. Organomet. Chem. 36, C13 (1972); D. A. Seitz, L. Ferreira, Synth. Commun. 9, 451 (1979).

Formic Anhydride[**]

By *George A. Olah, Yashwant D. Vankar, Massoud Arvanaghi,* and *Jean Sommer*[*]

Formic anhydride *(1)*, the parent carboxylic acid anhydride, has long eluded preparation and characterization. *Olah et al.*[1] first reported in 1955 the possible formation of *(1)* in the reaction of formyl fluoride with metal formates at low temperature. No spectroscopic observations or physical data were, however, obtained. In 1964, *Muramatsu et al.*[2] assumed the intermediacy of *(1)* in the formylation of *p*-nitrophenol and L-leucine with an ethereal solution of formic acid and dicyclohexylcarbodiimide (DCC); no isolation was attempted nor were physical data obtained. *Stevens et al.*[3], in the same year, reported the formation of *(1)* by the thermal disproportionation of formic-acetic anhydride and of mixtures of formic acid and carboxylic anhydrides; proof of formation of *(1)* was based on the appearance of a ^{1}H-NMR singlet at $\delta = 9.0$, which, however, might have been due to a mixed anhydride or other species.

We now wish to report the unequivocal preparation of formic anhydride by four independent methods (*A*—*D*) and its characterization by ^{1}H-NMR, ^{13}C-NMR, and IR spectroscopy. Further, the ethereal solution of *(1)* (obtained by any of the four methods), gave *p*-nitrophenyl formate in uniformly good yield when allowed to react with *p*-nitrophenol.



In the formylation method (method *A*), formyl fluoride dissolved in anhydrous ether is reacted at −78 °C with an excess of sodium formate in the presence of formic acid. In the three dehydration methods (methods *B*—*D*), formic acid (2 mol. equiv.) was dissolved in anhydrous ether at −78 °C and treated with a base (2 mol. equiv.; no base required in case *B*) followed by one mol. equiv. of the dehydrating reagent.

[*] Prof. Dr. G. A. Olah, Dr. Y. D. Vankar, M. Arvanaghi
Hydrocarbon Research Institute, Department of Chemistry
University of Southern California
University Park, Los Angeles, California 90007 (USA)
Prof. Jean Sommer
Institute de Chimie, Université Louis Pasteur, Strasbourg (France)

[**] Support of our work by the National Institutes of Health and the National Science Foundation is gratefully acknowledged, as is a Senior U.S. Scientist Award of the Alexander von Humboldt foundation to *G. A. O.* facilitating this research.

The ^{1}H-NMR spectrum (−40 °C) of *(1)* formed by all these methods showed a singlet at $\delta = 8.45$ (TMS as external standard). The proton decoupled ^{13}C-NMR spectrum (−40 °C) of the same solution showed a singlet at $\delta = 158.54$, which on coupling displayed a doublet with $J_{^{13}CH} = 242.8$ Hz. The corresponding signals in the spectra of formic acid lie at $\delta = 8.83$ and 163.38 ($J_{^{13}CH} = 216.3$ Hz); thus the C and H atoms are, as expected, more strongly shielded in the anhydride *(1)* than in the acid. The infrared spectrum of *(1)*, recorded at −78 °C using a Beckman Instruments low temperature IR cell, shows strong carbonyl stretching frequencies at 1795 cm^{-1} and 1775 cm^{-1}, characteristic of an acid anhydride.

Attempts to isolate *(1)* from the ethereal solutions by distillation, including low temperature distillation, gave only products contaminated with formic acid.

Received: June 7, 1979 [Z 252b IE]
German version: Angew. Chem. 91, 649 (1979)

CAS Registry numbers:
(1), 1558-67-4; formyl fluoride, 1493-02-3; formic acid, 64-18-6

[1] G. A. Olah, A. Pavlath, S. Kuhn, G. Varsanyi in: Elektronentheorie der homöopolaren Bindung, Akademie Verlag, Berlin 1955, pp. 79—94; G. A. Olah, S. J. Kuhn in G. A. Olah: Friedel-Crafts and Related Reactions, Wiley-Interscience, New York 1964, Vol. III, Part II, p. 1154.
[2] I. Muramatsu, M. Itoi, M. Tsuji, A. Hagitani, Bull. Chem. Soc. Jpn. 37, 756 (1964).
[3] W. Stevens, A. Van Es, Rec. Trav. Chim. Pays-Bas 83, 863 (1964); R. Schiff, J. W. Scheeren, A. Van Es, W. Stevens, ibid. 84, 594 (1965).

[2 + 2]-Cycloaddition of a Vinyl Cation[**]

By *Günter Hammen* and *Michael Hanack*[*]

The reaction of propargyl halides and cyclopentadiene in pentane with silver trifluoroacetate has recently been reported[1]. The allenyl cations formed in the reaction undergo 1,4-addition to cyclopentadiene and, after hydrolysis of the trifluoroacetate, afford cyclopentenols; [4 + 3]-cycloaddition leads *via* vinyl cations to bicyclic products.

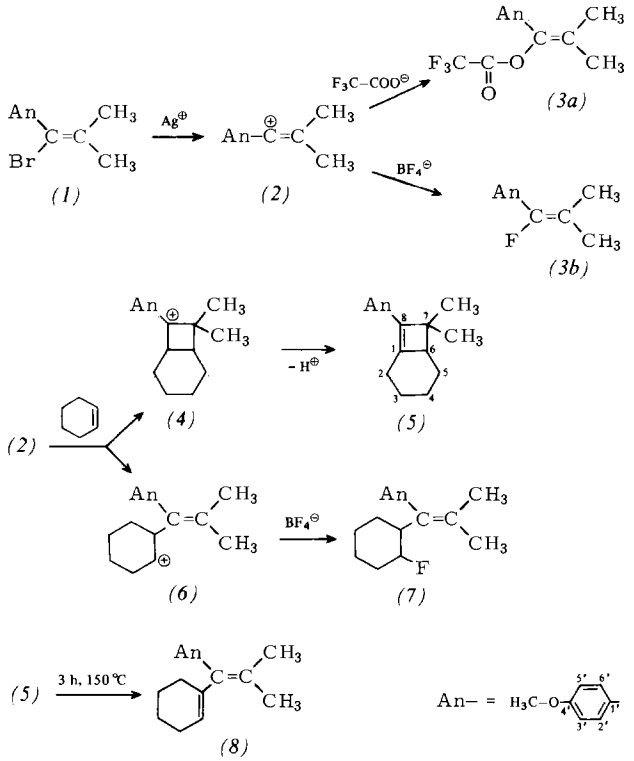
We report here on the first cycloaddition with a vinyl cation[2], which was generated from a vinyl halide by solvolysis in the presence of silver salts. The vinyl halide chosen was 1-bromo-1-(4-methoxyphenyl)-2-methyl-1-propene *(1)*, whose ready solvolysis to the vinyl cation *(2)* is well-known[3].

Reaction of *(1)* in cyclohexene with silver trifluoroacetate and pyridine as buffer at room temperature leads almost quantitatively to the vinyl ester *(3a)*. The products *(5)* and/or its isomer *(8)* expected to be formed on reaction of *(2)* with cyclohexene were obtained in only 1% yield.

On the other hand, when a solution of *(1)* in cyclohexene is allowed to react with silver tetrafluoroborate and pyridine (molar ratio 1.0:1.6:2.0) at 25 °C, subsequent workup with aqueous ammonia affords a mixture of 82% 8-(4-methoxyphenyl)-7,7-dimethylbicyclo[4.2.0]octa-1(8)-ene *(5)*, 11% 1-fluoro-1-(4-methoxyphenyl)-2-methyl-1-propene *(3b)*[4], and 7% 1-(2-fluorocyclohexyl)-1-(4-methoxyphenyl)-2-methyl-1-propene *(7)* in 70—80% yield. The structure of the products was confirmed by ^{1}H-, ^{13}C-NMR, and mass spectroscopy (Table 1). At 150 °C *(5)* isomerizes smoothly within 3 h to 1-(1-cyclohexenyl)-1-(4-methoxyphenyl)-2-methyl-1-propene

[*] Dipl.-Chem. G. Hammen, Prof. Dr. M. Hanack
Institut für Organische Chemie der Universität
Lehrstuhl für Organische Chemie II
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

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



(8) (Table 1); this is regarded as valuable additional proof of structure.

Table 1. Spectroscopic data for the products (5) and (8).

(5), ^{1}H-NMR (CCl_4): δ = 0.90—2.40 (m, 8H, H-2, 3, 4, 5), 1.21 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.50—2.94 (m, 1H, H-6), 3.69 (s, 3H, O CH_3), 6.56—7.38 (m, 4H, arom.); ^{13}C-NMR ($CDCl_3$): δ = 21.78 (CH_3), 26.42 (CH_3, superimposed), 24.63, 26.42, 27.02, 27.93 (C-2 to C-5), 44.94 (C-7), 50.43 (C-6), 55.12 (O CH_3), 113.84 (C-3', C-5'), 127.27 (C-2', C-6'), 128.63 (C-1'), 139.67, 140.52 (C-1, C-8), 157.85 (C-4'); MS: m/e = 242 (M^+, 100%), 227 (66), 199 (50), 161 (42)

(8), ^{1}H-NMR (CCl_4): δ = 0.70—2.40 (m, 8H, $4CH_2$), 1.59 (s, 3H, CH_3), 1.70 (s, 3H, CH_3), 3.69 (s, 3H, O CH_3), 5.41—5.68 (m, 1H, olefin H), 6.66—7.20 (m, 4H, arom.); MS: m/e = 242 (M^+, 100%), 227 (75), 199 (66), 187 (56), 185 (56), 119 (65), 117 (68)

The products are formed as follows: a concerted or stepwise cycloaddition[5] of (2) and cyclohexene leads to the cation (4), which by loss of a proton is stabilized to the cyclobutene derivative (5). Reaction of (2) with BF_4^- affords the vinyl fluoride (3b)[6]. Finally, (2) can also be added electrophilically to cyclohexene to give the cation (6), which reacts with BF_4^- to give (7).

The comparatively high nucleophilicity of the trifluoroacetate ion (cf. [1,7]) essentially prevents cycloaddition of (2) to cyclohexene: Reaction of (2) and F_3C COO^- in cyclohexene yields almost exclusively (3a). (2) is stable enough however to avoid stabilization by the gegenion F_3C COO^-[7] and reacts without difficulty in the presence of silver tetrafluoroborate[8].

Received: April 3, 1979 [Z 253 IE]
German version: Angew. Chem. 91, 649 (1979)

CAS Registry numbers:
(1), 40811-05-0; (3a), 57542-43-5; (3b), 52571-00-3; (5), 70891-78-0; (7), 70891-79-1; (8), 70891-80-4; cyclohexene, 110-83-8

[1] H. Mayr, B. Grubmüller, Angew. Chem. 90, 129 (1978); Angew. Chem. Int. Ed. Engl. 17, 130 (1978).

[2] Cf., e.g., K. Griesbaum, W. Naegele, G. G. Wanless, J. Am. Chem. Soc. 87, 3151 (1965); K. Griesbaum, W. Seiter, Angew. Chem. 88, 59 (1976); Angew. Chem. Int. Ed. Engl. 15, 55 (1976); J. H. Lukas, F. Baardman, A. P. Kouwenhoven, ibid. 88, 412 (1976) and 15, 369 (1976), respectively; G. A. Olah, R. J. Spear, J. Am. Chem. Soc. 97, 1845 (1975); G. A. Olah, J. S. Staral, R. J. Spear, G. Liang, ibid. 97, 5489 (1975).

[3] Z. Rappoport, A. Gal, J. Chem. Soc. Perkin Trans. II 1973, 301; Z. Rappoport, J. Kaspi, Y. Apeloig, J. Am. Chem. Soc. 96, 2612 (1974); Z. Rappoport, Acc. Chem. Res. 9, 265 (1976); P. J. Stang, Z. Rappoport, M. Hanack, L. R. Subramanian: Vinyl Cations. Academic Press, 1979, in press.

[4] Spectroscopic data of (3b): L. Eckes, M. Hanack, Synthesis 1978, 217.

[5] H.-U. Wagner, R. Gompper, Tetrahedron Lett. 1971, 4061.

[6] In the reaction of (1) with $AgBF_4$ in diethyl ether, (3b) is formed as main product: M. Hanack, G. Hammen, unpublished.

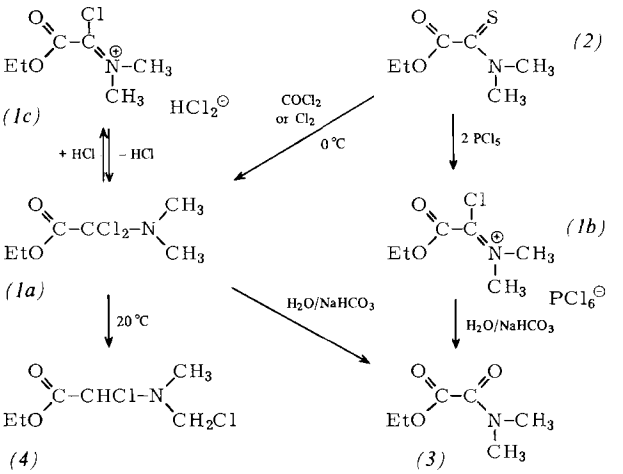
[7] H. M. R. Hoffmann, G. F. P. Kernaghan, G. Greenwood, J. Chem. Soc. B 1971, 2257.

[8] Cf. J. Marchand-Brynaert, L. Ghosez, J. Am. Chem. Soc. 94, 2871 (1972); U. M. Kempe, T. K. Das Gupta, K. Blatt, P. Gygax, D. Felix, A. Eschenmoser, Helv. Chim. Acta 55, 2187 (1972).

Synthesis and Intramolecular 1,3 Cl,H Disproportionation of Ethyl 2,2-Dichloro-2-(dimethylamino)-acetate[**]

By *Fabienne Huys, Robert Merényi, Zdenek Janousek, Lucien Stella,* and *Heinz Günter Viehe*[*]

Amide chlorides (α,α-dichloroamines), *i.e.* compounds containing the CCl_2 NR_2 partial structure, exist as electrophilic iminium salts CCl $NR_2^{\oplus}Cl^{\ominus}$ if they are substituted at the α-C atom by alkyl or aryl groups or generally by electron-donating substituents[1]. Because of our interest in geminal capto-dative substituent effects[2] we have synthesized the title compound (1) as an example of an amide chloride bearing an electron-attracting substituent. Like other amide chlorides, compound (1) can be prepared from the corresponding thiooxamate (2) and phosgene or chlorine, or PCl_5.



Depending upon the presence or absence of complexing agents such as PCl_5 or even HCl, (1) has an ionic [(1b), (1c)] or a covalent structure [(1a)] (NMR data compiled in Table 1). Chemical evidence for structure (1) is provided by its smooth hydrolysis to the oxamate (3).

The most interesting feature of (1a) is its isomerization to the glyoxalic ester derivative (4), which takes place within

[*] Prof. Dr. H. G. Viehe, Lic. Chem. F. Huys, Dipl.-Ing. R. Merényi, Dr. Z. Janousek, Dr. L. Stella
Laboratoire de Chimie Organique, Université de Louvain
Place Louis Pasteur 1, B-1348 Louvain-la-Neuve (Belgium)

[**] Capto-dative Substituent Effects, Part 3.—Part 2: ref. [2b].

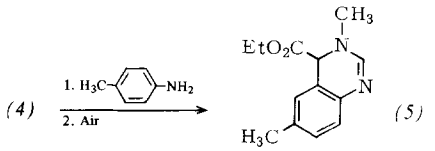
 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0615 $ 02.50/0

Table 1. NMR data (δ values) of *(1a)*—*(1c)* and *(4)* in $CDCl_3$.

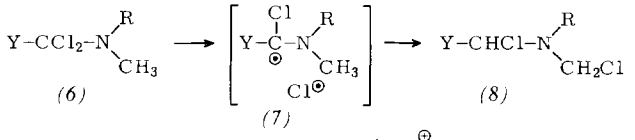
^{1}H-NMR	OCH_2	CH_3	NCH_3	NCH_2Cl	NCHCl	N CCl	COO	$^1J(NCH_3)$ [Hz]
(1a) [a]	4.45	1.25	2.98					
(1b) [b]	4.5	1.4	3.76					
(1c) [c]	4.51	1.47	4.05					
(4)	4.28	1.32	2.77	5.21	5.68			
^{13}C-NMR								
(1c)	66.7	13.3	49.6			160.9	154.2	146.7
(4)	62.5	13.9	38.4	72.9	79.9		165	138.4

[a] At −20 °C. [b] In CD_3CN. [c] If less than 1 equiv. is present on formation of *(1c)*, intermediate values are observed for $\delta(NCH_3)$ indicating occurrence of fast exchange *(1a)*⇌*(1c)*.

1 h at room temperature. *(4)* is characterized by its NMR data (Table 1); as a 1,3-biselectrophile it reacts with *p*-toluidine to give the benzpyrimidine derivative *(5)*.



Intramolecular Cl,H disproportionations such as *(1a)*→*(4)*, apparently represent a general type of reaction. Thus amide chlorides *(6)* bearing electron-withdrawing substituents isomerize to *(8)*[3].



$-Y = -CO-R', -CN, -CCl_3, -CF_3, R'-\overset{\oplus}{C}=\overset{}{N}R''_2\ X^{\ominus}$

This disproportionation formally corresponds to a 1,3 hydride shift. However, the fact that the hexachlorophosphate *(1b)* does not isomerize, and that the weakly complexed salt *(1c)* isomerizes much more slowly (several days) than *(1a)* excludes this possibility. Although a concerted or ionic mechanism cannot be ruled out, the most probable pathway involves homolysis of the C Cl bond favored by the capto-dative substitution of the presumed radical intermediate *(7)*[6].

Procedure

Synthesis of *(1b)*: Thiooxamate[4] *(2)* (0.8 g, 5 mmol) is added to a stirred suspension of PCl_5 (2.08 g, 10 mmol) in dry CH_2Cl_2 (15 ml). The resulting clear solution is stirred for 30 min, concentrated, and the residue is washed with ether. 3.95 g (98%) of *(1b)* is obtained. Hydrolysis with aqueous $NaHCO_3$ yields the known oxamate *(3)*[5] in 68% yield.

Disproportionation *(1a)*→*(4)*: Thiooxamate *(2)* (1.61 g, 10 mmol) in CH_2Cl_2 (30 ml) is treated with $COCl_2$ in 2—4 fold excess. After about 1 h at room temperature, chlorination to *(1a)* and its isomerization are complete. The solvent is removed to give 1.64 g (82%) of *(4)* as a very hygroscopic, ether-soluble oil.

Reaction *(4)*→*(5)*: *p*-Toluidine (3.21 g, 30 mmol) and *(4)* (2 g, 10 mmol) are stirred in dry CH_2Cl_2 (75 ml) for 2 h. The hydrochloride is filtered off and the solvent is evaporated. The residue is washed with benzene/ether (1:1), dried, and exposed to air for 12 h. The resulting hydrochloride of *(5)* is recrystallized from CH_3CN; yield 0.85 g (37%), m.p. 219 °C (decomp.); ^{1}H-NMR ($CDCl_3$): δ = 1.18 (3H, t), 2.32 (3H, s), 3.33 (3H, s), 4.19 (2H, q), 5.76 (1H, s), 7.17 (1H, s), 7.24 (2H, s), 8.78 (1H, s).

Received: May 21, 1979 [Z 254a IE]
German version: Angew. Chem. *91*, 650 (1979)

CAS Registry numbers:
(1a), 70941-59-2; *(1b)*, *70941-61-6*; *(1c)*, 70941-62-7; *(2)*, 16703-48-3; *(3)*, 16703-52-9; *(4)*, 70941-63-8; *(5)* · HCl, 70941-64-9; *p*-toluidine, 106-49-0

[1] *H. Böhme, H. G. Viehe:* Iminium Salts in Organic Chemistry, in Advances in Organic Chemistry. Vol. 9/1 und 9/2. Wiley-Interscience, New York 1976 and 1979.

[2] a) *L. Stella, Z. Janousek, R. Merényi, H. G. Viehe*, Angew. Chem. *90*, 741 (1978); Angew. Chem. Int. Ed. Engl. *17*, 691 (1978); b) *L. Stella, P. Tordo, Z. Janousek, R. Merényi, H. G. Viehe, A. Munoz*, J. Phys. Chem., in press.

[3] *F. Huys, M. Rover*, Part of Dissertations, Université Louvain-la-Neuve 1979; *Z. Janousek, F. Huys, L. René, M. Masquelier, L. Stella, R. Merényi, H. G. Viehe*, Angew. Chem. *91*, 651 (1979); Angew. Chem. Int. Ed. Engl. *18*, 616 (1979). For analogous sulfur compounds: *J. C. Pommelet, C. Nyns, F. L. Lahousse, R. Merényi, H. G. Viehe*, unpublished.

[4] *W. Walter, K.-D. Bode*, Justus Liebigs Ann. Chem. *660*, 74 (1962).

[5] *H. M. Atkinson*, J. Chem. Soc. *105*, 1290 (1914).

[6] *Note added in proof:* For heterocyclizations using [*(1b)*, X = $FSO_3^{\ominus}$] see *D. Bartholomew, I. T. Kay*, Tetrahedron Lett., in press.

Intramolecular Cl,H Disproportionation of an Oxamide Chloride. An Entry to Imidazole Derivatives[**]

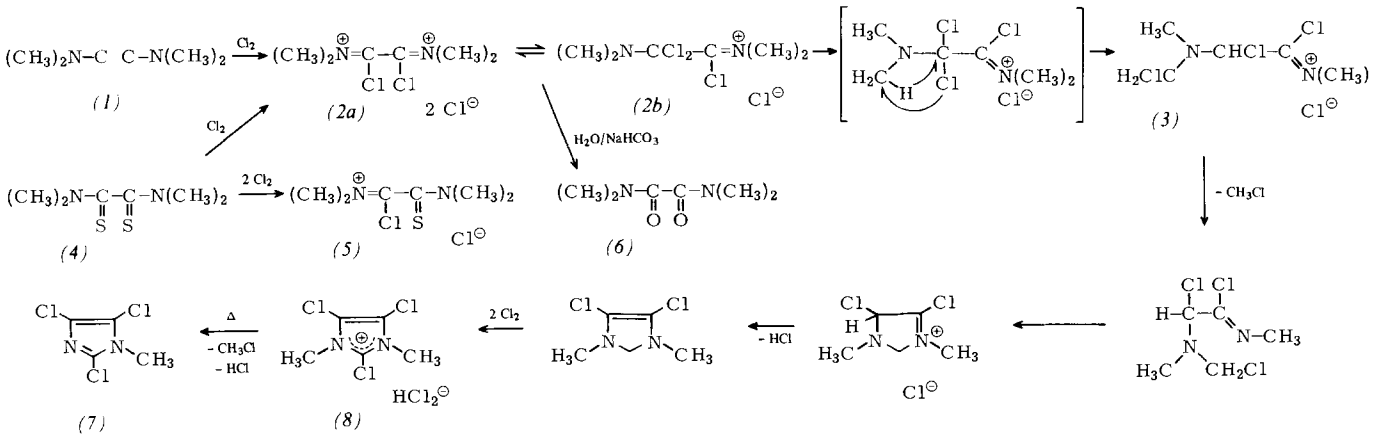
By *Zdenek Janousek, Fabienne Huys, Loïc René, Michèle Masquelier, Lucien Stella, Robert Merényi*, and *Heinz Günter Viehe*[*]

Radicals can be stabilized by capto-dative substitution[1,2]; capto-dative substitution of compounds in which the central CCl_2 moiety is linked to a dimethylamino group and an electron-withdrawing group have been observed to undergo Cl,H disproportionation[3]. Compound *(2)*, an amide chloride of oxalic acid, is a further substrate capable of such rearrangement. We have now been able to synthesize and trap, but not isolate, the highly unstable compound *(2)* and to elucidate reaction sequences in which it occurs as intermediate.

[*] Prof. Dr. H. G. Viehe, Dr. Z. Janousek, Lic. Chem. F. Huys, Dr. L. René, Lic. Chem. M. Masquelier, Dr. L. Stella, Dipl.-Ing. R. Merényi
Laboratoire de Chimie Organique, Université de Louvain
Place Louis Pasteur 1, B-1348 Louvain-la-Neuve (Belgium)

[**] Capto-dative Substitution Effects, Part 4. – Part 3: *F. Huys, R. Merényi, Z. Janousek, L. Stella, H. G. Viehe*, Angew. Chem. *91*, 650 (1979); Angew. Chem. Int. Ed. Engl. *18*, 615 (1979).

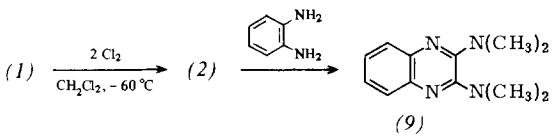
 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0616 $ 02.50/0



Attempts to synthesize *(2)* by exhaustive chlorination of tetramethyldithiooxamide *(4)* led instead to the new stable trichloroimidazolium salt *(8)*. The disproportionation *(2)*→*(3)* can be envisaged as the key step of this reaction. Although the monoamide chloride *(5)* could be detected on chlorination of *(4)* in the molar ratio 1:2, the reaction could not be stopped at the stage of *(2)*. Chemical proof for the structure of *(8)* is provided by its smooth thermolysis to the known imidazole derivative *(7)* (m.p. 76 °C; ref. [4]: 75—76 °C). This new synthesis resembles the Wallach reaction which has been employed for the synthesis of chloroimidazoles[5].

The formation of *(7)* and more highly chlorinated products on chlorination of dimethylaminoacetonitrile is already known[4]. This reaction can also be explained in terms of intramolecular Cl,H disproportionation.

We finally succeeded in preparing the oxamide chloride *(2)* by chlorination of the highly reactive bis(dimethylamino)acetylene *(1)* at −60 °C under high-dilution conditions in CH_2Cl_2. Compound *(2)* precipitates but is too unstable to be isolated. The structure of *(2)* was established by hydrolysis to tetramethyloxamide *(6)* and reaction with *o*-phenylenediamine to give the known quinoxaline derivative *(9)* (m.p. 66—67 °C).



(9)

Experimental

Synthesis of *(8)* from *(4)*: A fast stream of chlorine is passed through a solution of *(4)* (1.76 g, 10 mmol) in dry CH_2Cl_2 (30 ml) such that the solution boils under reflux. After about 30 min the precipitate is collected and washed with benzene containing some styrene to remove excess Cl_2; yield 2.26 g (96%); m.p. 186 °C (acetonitrile); ^{1}H-NMR ($SOCl_2$): $\delta = 3.85$; IR (KBr): 1580, 1510, 1390, 1330, 1155, 1070, 840 cm^{-1}.

Synthesis of *(2)*: A solution of chlorine (2.8 g, 40 mmol) in CH_2Cl_2 (250 ml) is transferred at −78 °C to a 1-l flask equipped with a dry-ice cooler and a dropping funnel. After dropwise addition of *(1)* (1.12 g, 10 mmol) in CH_2Cl_2 (250 ml) with stirring at −78 °C, a precipitate of *(2)* appears; it is hydrolyzed by aqueous $NaHCO_3$ to *(6)* (63%).

Received: May 21, 1979 [Z 254b IE]
German version: Angew. Chem. 91, 651 (1979)

CAS Registry numbers:
(1), 5907-90-4; *(2a)*, 70941-52-5; *(2b)*, 70941-53-6; *(3)*, 70941-54-7; *(4)*, 35840-78-9; *(5)*, 70941-55-8; *(6)*, 1608-14-6; *(7)*, 873-25-6; *(8)*, 70941-57-0; *(9)*, 70941-58-1; *o*-phenylenediamine, 95-54-5

[1] *L. Stella, Z. Janousek, R. Merényi, H. G. Viehe*, Angew. Chem. *90*, 741 (1978); Angew. Chem. Int. Ed. Engl. *17*, 691 (1978).
[2] *L. Stella, P. Tordo, Z. Janousek, R. Merényi, H. G. Viehe, A. Munoz*, J. Phys. Chem., in press.
[3] *F. Huys*, Part of Dissertation, Université Louvain-la-Neuve 1979.
[4] Fr. Pat. 1548390 (1969), Bayer, Chem. Abstr. *74*, 3625w (1971).
[5] *K. Shimada, J. Kurijama, T. Kanazawa, M. Satoh, S. Toyoshima*, Yakugaku Zasshi *91*, 221 (1971).

Acidity of Acetophenone Enol in Aqueous Solution[**]

By *Pavel Haspra, Alfred Sutter*, and *Jakob Wirz*[*]

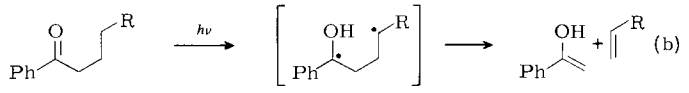
Thermodynamically unstable enols are of importance as reactive intermediates and are often the primary products of photochemical reactions. The formation of enols during the Norrish type II cleavage of ketones was first demonstrated directly by *Henne* and *Fischer*[1]. The subsequent transformation of the enols into stable ketones necessitates protonation of a carbon and proceeds much slower than the establishment of the acid-base enol-enolate equilibrium. This would suggest the possibility, hitherto not exploited, of *determining the acidity of enols directly by flash spectroscopy*. Since enolization constants, $K_e = [\text{enol}]/[\text{ketone}]$, are accessible from thermochemical[2a] or kinetic[2b] data, the α-CH acidity constant K_a of the corresponding ketone in aqueous solution can be calculated according to eq. (a).

$$pK_a(\text{ketone}) = pK_a(\text{enol}) + pK_e \qquad \text{(a)}$$

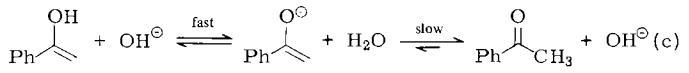
Novak and *Loudon*[3a] have recently estimated the pK_a of acetophenone enol *(1)* in aqueous solution by a somewhat tedious indirect method to be 11 ± 1, from which the pK_a of acetophenone *(2)* was calculated as 15.8 ± 1.0. Since this value deviates considerably from the result of an earlier measurement (19.2[4]) and since the pK_a value of *(1)* serves as a reference for relative measurements[3b] on derivatives of *(1)*, we decided to test the feasibility of the flash-spectroscopic "titration" method on *(1)* as an example.

[*] Priv.-Doz. Dr. J. Wirz, Dipl.-Chem. P. Haspra, Dipl.-Chem. A. Sutter
Physikalisch-chemisches Institut der Universität
Klingelbergstrasse 80, CH-4056 Basel (Switzerland)

[**] This work constitutes part of Project No. 2.012.78 of the Swiss National Science Foundation.



(3) (1) (b)



(1) $(1)^-$ (2) (c)

In order to increase the solubility of butyrophenone *(3)* (R = H) in water we used the γ-hydroxy derivative (R = OH)[5]. Figure 1 (left) shows the increase in extinction of a 10^{-4} M solution of *(3)* (R = OH) in 0.1 M air-saturated sodium hydroxide in the range 270 to 350 nm immediately after the photo-flash (1000 J, 20 μs; fresh solution used for each measurement). In neutral and acidic solutions the photo-flash effects no increase in absorption at $\lambda > 300$ nm. To interpret the results it is assumed that the increase in absorption at $\lambda > 300$ nm in basic solutions can be ascribed exclusively to the enolate $(1)^-$, while the enol *(1)* does not absorb in this region.

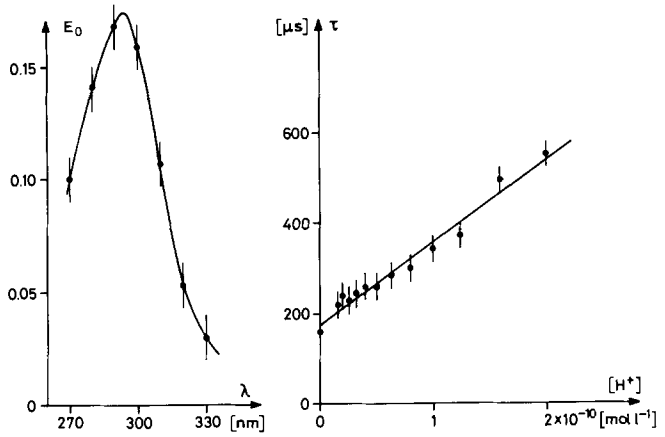


Fig. 1. Left: absorption spectrum of the enolate *(1)* in 0.1 M sodium hydroxide.—Right: lifetime of $(1)^-$ (in equilibrium with the enol *(1)*) as a function of the proton concentration [H^+]; room temp.

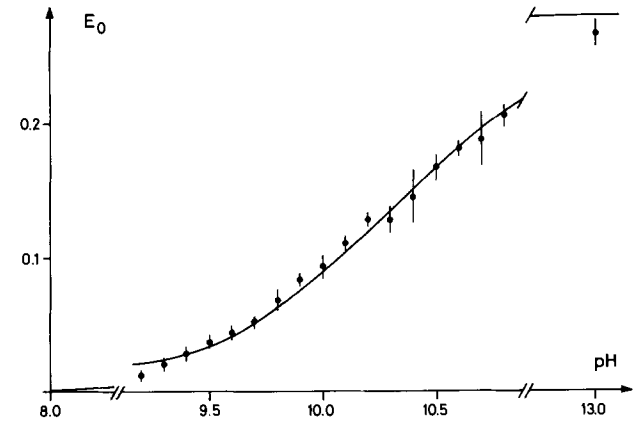


Fig. 2. Flash spectroscopic titration curve of $(1)/(1)^-$

The decrease in the concentration of enolate in equilibrium with the enol obeys a (pseudo) first-order rate law within the accuracy of measurement. On the basis of the reaction scheme (c) the dependence of the lifetime $\tau((1)^-)$ on pH can be expressed as follows

$$\tau((1)^-) = \frac{1}{k((1)^- \rightarrow (2))} + \frac{1}{K_a((1)) \cdot k((1)^- \rightarrow (2))} \cdot [H^+] \qquad (d)$$

In Figure 1 (right) the lifetime measured at room temperature is plotted against the proton concentration of a borax buffer[6] (ionic strength $I = 0.1$). At pH values below 9.5 there is a systematic deviation from the linear equation (d), caused by the acid-catalyzed decomposition of *(1)* and not taken into account in scheme (c). Consequently only an estimate of the acidity constant $K_a((1)) < 10^{-10}$ can be obtained from the ratio of the slope and intercept of the regression line. The rate constant $k((1)^- \rightarrow (2))$ for the *C*-protonation of $(1)^-$ by water is 6×10^3 s^{-1}. The acidity of *(1)* can be determined much more accurately from the "titration curve" (Figure 2), where the initial extinctions E_0 (310 nm) of $(1)^-$, obtained by linear extrapolation of the logarithmic decay curves to a reference time $t = 0$ (maximum of the photo-flash), are plotted against the pH value of the borax buffer. Each point represents the mean of three individual measurements in fresh solutions. The results were fitted by heteroscedastic regression to the linear equation

$$(E_0)^{-1} = A + A \cdot [H^+]/K_a((1)) \qquad (e)$$

where

$$A^{-1} = ([(1)]_0 + [(1)^-]_0) \cdot \varepsilon((1)^-, 310\,nm) \cdot d.$$

For weighting the measured points, the absolute mean error of E_0 was assumed to be constant. We thus obtained a value of $pK_a((1)) = 10.34 \pm 0.05$ (95%) for the acidity of acetophenone enol. With $pK_c((2)) = 6.7 \pm 1.0$[2a], equation (a) gives a value of 17 ± 1 for $pK_a((2))$. A second series of measurements with *(3)* (R = H) as starting material gave $pK_a((1)) = 10.29 \pm 0.04$ (95%); in this case 5% acetonitrile had to be added to the buffer in order to achieve sufficient solubility of butyrophenone.

The assignment of the short-lived absorption above 300 nm (Fig. 1, left) to the anion $(1)^-$ is confirmed as follows. The formation of *(1)* as a primary product of the photolysis of *(3)* ($R = CH_3$) has been demonstrated NMR spectroscopically[1]; the position of the first absorption band of $(1)^-$ is consistent with PPP-SCF-CI calculations using standard heteroparameters[7] [*(1)*: 286 nm ($\log\varepsilon = 3$), $(1)^-$: 306 nm ($\log\varepsilon = 4$)]; the evaluations of the results according to equations (d) and (e) are in agreement with each other and are consistent with the estimated value of *Novak et al.*[3a]; the absorption maximum of $(1)^-$ in basic dimethyl sulfoxide (DMSO) lies at 342 nm ($\log\varepsilon = 3.6$)[8], and in aqueous solution at *ca.* 295 nm (Fig. 1, left). Qualitatively, a hypsochromic shift of the first absorption band with increasing solvation is to be expected: according to the PPP model calculation the charge density at the oxygen atom in the first excited state is about ⅓ less than in the ground state. In the gas phase $(1)^-$ absorbs at still longer wavelengths, $\lambda_{max} \approx 420$ nm[9a]. An analogous solvatochromic shift was also observed for phenolate, $\lambda_{max} = 332$ nm (g)[9b], 287 nm (H_2O). To obtain an authentic example for the difference between such an anion in DMSO and in water we have determined the absorption spectrum of 2-naphtholate in both solvents: the first maximum shifts from 399 nm (DMSO) to 346 nm (H_2O).

Received: March 5, 1979 [Z 256 IE]
German version: Angew. Chem. 91, 652 (1979)

CAS Registry numbers:
(1), 4383-15-7; *(3)*, 495-40-9

[1] A. Henne, H. Fischer, Angew. Chem. 88, 445 (1976); Angew. Chem. Int. Ed. Engl. 15, 435 (1976).
[2] a) J. P. Guthrie, P. A. Cullimore, Can. J. Chem. 57, 240 (1979); b) J. P. Guthrie, ibid., 797 (1979).
[3] a) M. Novak, G. M. Loudon, J. Org. Chem. 42, 2494 (1977); b) J. Am. Chem. Soc. 98, 3591 (1976).
[4] R. P. Bell, Trans. Faraday Soc. 39, 253 (1943).
[5] P. J. Wagner, A. E. Kemppainen, J. Am. Chem. Soc. 94, 7495 (1972).
[6] R. C. Weast: Handbook of Chemistry and Physics, 57th Ed., D-134. The Chemical Rubber Co., Cleveland, Ohio 1976—1977.
[7] M. Tichý, R. Zahradník, J. Phys. Chem. 73, 534 (1969).
[8] F. G. Bordwell, S. Romberg (Northwestern University, Evanston, Illinois), private communication.
[9] a) A. H. Zimmerman, K. J. Reed, J. I. Brauman, J. Am. Chem. Soc. 99, 7203 (1977); b) B. S. Freiser, J. L. Beauchamp, ibid. 99, 3214 (1977).

Redox Addition/Elimination Processes of Cluster-Bound Ligands: Oxidative Elimination of CO from $Co_3(CO)_9C$—OH and Reductive Addition of Acetylene to $Co_3(CO)_9H$[**]

By *Giuseppe Fachinetti, Sergio Pucci, Pier Francesco Zanazzi,* and *Uncharee Methong*[*]

The preparation of $Co_3(CO)_9C$ OH *(1)* and its quantitative transformation at room temperature in a closed vessel into $HCo(CO)_4$ *(2)* and $Co_4(CO)_{12}$ *(3)* [eq. (a)] have recently been reported[1].

$$2\,Co_3(CO)_9C\ OH \rightarrow 2\,HCo(CO)_4 + Co_4(CO)_{12} \quad (a)$$
(1) *(2)* *(3)*

In the course of this reaction, which involves the oxidation of a C OH group to coordinated CO, a transient infrared active (ν_{CO} 1879 cm^{-1}) species was observed. In view of the current interest in redox processes involving carbon monoxide[2], a special effort was made to establish the nature of the transient carbonyl. We have now succeeded in isolating this species and characterizing it as the hydrido cluster *(4)* [eq. (b)].

$$Co_3(CO)_9C\ OH \rightarrow CO + HCo_3(CO)_9 \quad (b)$$
(1) *(4)*

(4) is a blackish green, crystalline substance which is thermally (30 °C) labile, giving $Co_4(CO)_{12}$ *(3)* in solution (verified by IR); it can be kept at 0 °C under argon without appreciable decomposition. The IR spectrum in the carbonyl stretching region (*n*-hexane, 2054, 2037, and 1879 cm^{-1} of comparable intensity) is consistent with a highly symmetrical structure, with both terminal and bridging carbonyl groups. The mass spectrum of *(4)* (*m/e* 430, M^+), and of ^{2}H-*(4)* (*m/e* 431) established the presence of a hydrogen atom in the molecule. Moreover, treatment of *(4)* with CO at atmospheric pressure and room temperature resulted in the formation of $HCo(CO)_4$ *(2)* and $Co_4(CO)_{12}$ *(3)* (with $Co_2(CO)_8$ in relative amounts depending on the rate of CO diffusion in solution) as the only IR-active species. The structure of *(4)* was confirmed by X-ray methods (Fig. 1)[3].

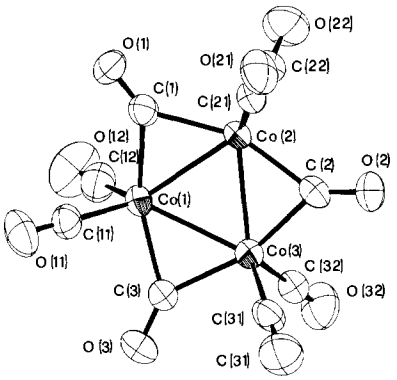
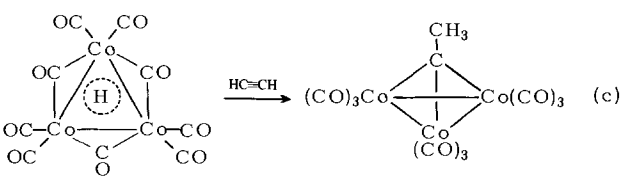


Fig. 1. The $Co_3(CO)_9$ molecular skeleton of the $HCo_3(CO)_9$ cluster *(4)*. Some important molecular parameters averaged assuming D_{3h} symmetry are: Co Co, 2.459 ± 0.008 Å; bridging CO: Co C, 1.949 ± 0.009 Å; C O 1.154 ± 0.017 Å; non-bridging CO: Co C, 1.825 ± 0.022 Å; C O, 1.122 ± 0.012 Å.

Molecular bond lengths and angles between non-hydrogen atoms show nearly perfect D_{3h} symmetry. Concerning the problem of hydrogen location, a difference Fourier map showed many peaks with electron density in the range 1.00—0.64 e/Å^3, all within 0.8 Å from cobalt atoms, except for two maxima (0.53 and 0.48 e/Å^3) near the threefold molecular axis, above and below the tricobalt plane. These could represent two possible positions for the hydrogen atom linked to the cluster of the three cobalt atoms. A reasonable hypothesis is that the hydrogen atom occupies these positions statistically with half occupancy at each site. This hypothesis is indirectly supported by the results of potential energy computations[4] which reveal two nearly equivalent minima in regions very close to those where residual electronic density was found. An attempt to refine the two positions of the H atom was carried out by imposing the constraint that all H Co distances must remain equal. The refinement converged to an *R* value of 4.26%, with H Co distances of 1.93(6) Å. However, this result is not significant from a statistical point of view.

Attachment of hydrogen to one of the oxygen atoms of the carbonyl groups is ruled out by the simplicity of the IR spectrum in the carbonyl stretching region; terminal bonding of hydrogen to one of the cobalt atoms is excluded on the same basis. Hence, a μ_3-type structure appears most likely, although it is rather uncommon among transition metal hydrides[5].

Having observed the oxidative elimination of CO from *(1)* [eq. (b)], we also verified the possibility of using the "unsaturated" cluster *(4)* as promoter of the reverse process, namely the reductive addition of a more easily reducible triply bonded molecule. Compound *(4)* reacts with acetylene at room temperature to give $Co_3(CO)_9C$ CH_3 *(5)* [eq. (c)][6] (IR, MS).



(4) *(5)* (c)

This four-electron cluster-assisted reduction of acetylene represents a step in the hydrogenation to ethane. Hydrogen-

[*] Dr. G. Fachinetti [']
Università di Pisa, Istituto Chimica Generale
Via Risorgimento 35, I-56100 Pisa (Italy)
Dr. S. Pucci
Centro di Studio del C.N.R. per le Macromolecole Stereordinate ed Otticamente Attive
Via Risorgimento 35, I-56100 Pisa (Italy)
Prof. F. P. Zanazzi, Dr. U. Methong
University of Perugia, Istituto di Mineralogia
Piazza Università, I-06100 Perugia (Italy)

[**] This work was supported by the National Research Council (C.N.R., Roma). The authors wish to thank Professor *F. Calderazzo* for helpful discussions.

[*] Author to whom correspondence should be addressed.

olysis of the cobalt-carbon bonds has already been reported[7] to occur photochemically.

Experimental

A solution of *(1)* (1.8 g, 3.93 mmol) in a *n*-hexane/toluene (50 ml + 10 ml) mixture was maintained at 15 °C/20 torr for about 10 min, and then cooled to −30 °C for about 36 h. Black crystalline *(4)* was then collected by filtration at low temperature and dried briefly *in vacuo* (0.18 g, 10%).

A solution of *(4)* (0.090 g, 0.21 mmol) in *n*-hexane was treated with an excess of acetylene at 15 °C. The brilliant green solution of the hydride immediately turned red-brown. After 0.5 h, chromatography (silica-gel, hexane) gave 0.040 g (42%) of *(5)*.

Received: April 2, 1979 [Z 258 IE]
German version: Angew. Chem. 92, 657 (1979)

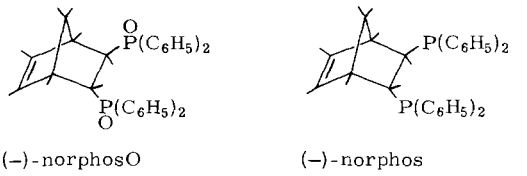
[1] *G. Fachinetti*, J. Chem. Soc. Chem. Commun., 397 (1979).
[2] *G. C. Demitras, E. L. Muetterties*, J. Am. Chem. Soc. 99, 2796 (1977); *A. K. Smith, A. Theolier, J. M. Basset, R. Ugo, D. Commereuc, Y. Chauvin, ibid.* 100, 2590 (1978).
[3] Monoclinic space group $P2_1/a$; cell dimensions (at 7 °C): $a = 17.319(2)$, $b = 6.747(2)$, $c = 11.835(2)$ Å, $\beta = 102.36(2)°$; $Z = 4$, $\rho_{calc} = 2.113$ g·cm^{-3}, $\mu = 38.3$ cm^{-1} ($Mo_{K\alpha}$), transmission factors 0.7—0.5, no absorption correction applied, $\omega/2\theta$ scan ($3 \leq \theta \leq 30°$), 3778 unique data, 2027 [$I < 3\sigma(I)$] considered as unobserved; linear correction for 4% total decay in intensity during data collection. Solution by direct methods (program SHELX-76; *G. M. Sheldrick*, SHELX-76, Program for Crystal Structure Determination, University of Cambridge, England), refinement led to $R = 4.35\%$ for all observed reflections.
[4] *A. G. Orpen*: HYDEX, 1978, A Program for Locating Hydrides, University of Cambridge, England.
[5] *M. R. Churchill, B. G. DeBoer, F. J. Rotella*, Inorg. Chem. 15, 1843 (1976), and references therein.
[6] *D. Seyferth, J. E. Hallgren, P. L. K. Hung*, J. Organomet. Chem. 50, 265 (1973).
[7] *G. L. Geoffrey, R. A. Epstein*, Inorg. Chem. 16, 2795 (1977).

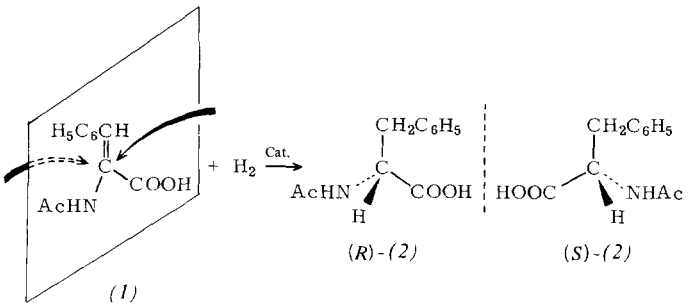
Asymmetric Hydrogenation of (*Z*)-α-(Acetylamino)-cinnamic Acid by a Rh/norphos Catalyst[**]

By *Henri Brunner* and *Willigis Pieronczyk*[*]

$RhCl[P(C_6H_5)_3]_3$ catalyzes the hydrogenation of olefins in homogeneous solutions at room temperature and atmospheric pressure[1]. If $P(C_6H_5)_3$ is replaced by optically active phosphanes, the chiral information is transferred from a small amount of catalyst to large amounts of hydrogenation products[2]. Within the last 10 years Rh complexes of about 150 different optically active phosphanes have been used for the asymmetric hydrogenation of about the same number of different prochiral substrates[3]. Especially high optical yields could be obtained using chelating phosphanes which were either derived from optically active natural products in multistep syntheses (diop[4a], prophos[4b]) or obtained *via* tedious optical resolutions (dipamp[5a], chiraphos[5b]). Taking norphos as an example, we describe a generalizable procedure for the preparation of optically active chelating phosphanes by the surprisingly facile resolution of the respective phosphane oxides, in this case norphosO, with L-(−)-dibenzoyltartaric acid, abbreviated (−)-DBT.

norphosO is obtained by Diels-Alder reaction of cyclopentadiene and *trans*-vinylenebis(diphenylphosphane oxide)[6]. When an ethanolic solution of (±)-norphosO is treated with (−)-DBT, the less soluble diastereoisomer (−)-norphosO/(−)-DBT precipitates. Treatment with KOH removes (−)-DBT from both fractions. After one separation step the optical purity of norphosO lies between 70 and 80%; it is optically pure after one repetition of the separation procedure. (+)- and (−)-norphosO can be reduced by $SiHCl_3$ to (+)- and (−)-norphos[7].





Scheme 1. Catalyst (cat.) = $Rh_2Cl_2(cod)_2$ (7 mg) and (−)-norphos (14.5 mg) in ethanol (5 ml); substrate = *(1)* (500 mg) in ethanol (10 ml); hydrogenation for 10 h at room temperature; workup, see ref. [8]; chemical yield quantitative; *(R)-(2)*:*(S)-(2)* = 2:98.

Scheme 1 shows the catalytic hydrogenation of (*Z*)-α-(acetylamino)-cinnamic acid *(1)* by $Rh_2Cl_2(cod)_2$/(−)-norphos (cod = 1,5-cyclooctadiene). The optically active catalyst differentiates so effectively between frontside and backside attack that (*R*)- and (*S*)-(*N*-acetyl)-phenylalanine *(2)* are formed in methanol (and methanol/benzene) in a ratio of 3:97, and in ethanol in a ratio of 2:98, corresponding to an optical yield of 96%. Thus, norphos is one of the most easily prepared optically active chelating phosphanes and gives one of the highest optical yields reported for asymmetric hydrogenation. In contrast to many other chelating phosphanes, both enantiomers of norphos are available and thus both configurations of the hydrogenation products can be obtained.

Like norphos, chiraphos and prophos form five-membered chelate rings with the Rh atom in the catalyst. (*S,S*)-chiraphos hydrogenates *(1)* to *(R)-(2)*[5b], whereas (*R*)-prophos gives *(S)-(2)*[4b]. Because it likewise affords *(S)-(2)*, we ascribe the (2*R*,3*R*)-configuration to (−)-norphos.

Experimental

Optical resolution of (±)-norphosO: A solution of (±)-norphosO (25.5 g) in 99% ethanol (105 ml) is added to L-(−)-dibenzoyltartaric acid monohydrate = (−)-DBT (19.5 g) in 99% ethanol (20 ml) and stirred for 2 h. The less soluble diastereomer (−)-norphosO/(−)-DBT (19.5 g) is filtered off and shaken together with a solution of KOH (4 g) in water (160 ml) until dissolution is complete. The organic phase is separated off and the aqueous phase is washed with chloroform (30 ml). The united organic phases yield 11 g of (−)-norphosO, $[\alpha]_{578}^{20} = -47°$ ($c = 1$, $CHCl_3$). Repetition of this separation step gives a further 9 g of (−)-norphosO, $[\alpha]_{578}^{20} = 62°$. — The ethanolic solution of the more soluble diaster-

[*] Prof. Dr. H. Brunner, Dr. W. Pieronczyk
Institut für Chemie der Universität
Universitätsstrasse 31, D-8400 Regensburg 2 (Germany)

[**] We thank the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and BASF AG for support of this work.

eoisomer (+)-norphosO/(−)-DBT is concentrated and the residue mixed with dry acetone (100 ml). The resulting solution contains 19.2 g (+)-norphosO/(−)-DBT from which 9.5 g of (+)-norphosO $[\alpha]_{578}^{20} = +50°$ ($c = 1$, $CHCl_3$) is isolated as above. Repetition of this separation step yields a further 5.7 g of (+)-norphosO, $[\alpha]_{578}^{20} = +58°$.

Reduction to (+)- and (−)-norphos: (−)-norphosO (9 g) is stirred in an autoclave with a solution of $HSiCl_3$ (15 g) in benzene (200 ml) for 15 h at 65—75 °C. After evaporation of the solvent the residue is dissolved in benzene (100 ml). The cooled solution is treated with 25% NaOH until the precipitate has dissolved. After separation of the aqueous phase the benzene phase is washed with water (10 ml). It contains 6.2 g of (−)-norphos (75%), which is recrystallized from acetone; $[\alpha]_{578}^{20} = -43.5°$ ($c = 1$, $CHCl_3$), m.p. 129—130 °C. (+)-norphos $[\alpha]_{578}^{20} = +45°$, m.p. 129—130 °C.

Received: March 22, 1979 [Z 261 IE]
German version: Angew. Chem. 92, 655 (1979)

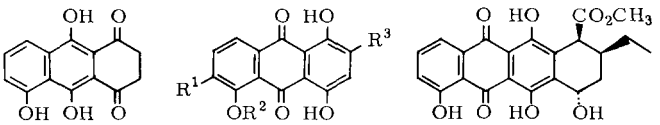
[1] *J. A. Osborn, F. H. Jardine, J. F. Young, G. Wilkinson*, J. Chem. Soc. *A 1966*, 1711.
[2] *L. Horner, H. Siegel, H. Büthe*, Angew. Chem. *80*, 1034 (1968); Angew. Chem. Int. Ed. Engl. *7*, 942 (1968); *W. S. Knowles, M. J. Sabacky*, Chem. Commun. *1968*, 1445.
[3] *D. Valentine, jr., J. W. Scott*, Synthesis *1978*, 329.
[4] a) *H. B. Kagan, T. P. Dang*, J. Am. Chem. Soc. *94*, 6429 (1972); b) *M. D. Fryzuk, B. Bosnich, ibid. 100*, 5491 (1978).
[5] a) *W. S. Knowles, M. J. Sabacky, B. D. Vineyard, D. J. Weinkauf*, J. Am. Chem. Soc. *97*, 2567 (1975); b) *M. D. Fryzuk, B. Bosnich, ibid. 99*, 6262 (1977).
[6] *N. P. Nesterova, T. Y. Medved, Y. M. Polikarpov, M. K. Kabachnik*, Izv. Akad. Nauk SSSR, Ser. Khim. *10*, 2210 (1974).
[7] *K. Naumann, G. Zon, K. Mislow*, J. Am. Chem. Soc. *91*, 7031 (1969).
[8] *R. Glaser, M. Twaik, S. Geresh, J. Blumenfeld*, Tetrahedron Lett. *1977*, 4365.

Regioselective Alkylation of 1,4,5-Trihydroxy-9,10-anthraquinone with Formaldehyde and Glyoxylic Acid[**]

By *Karsten Krohn*[*]

In addition to Diels-Alder reactions[1], intramolecular cyclizations of Marschalk type[2] are becoming increasingly important for synthesizing the tetracyclic ring system of the cytostatically active anthracycline antibiotics since they permit the synthesis of anthracyclinones bearing a methoxycarbonyl group at C-10[3] and provide a simple solution to the problem of regioselectivity[4]. Marschalk[2] alkylation of the leuco compound *(1)* with straight-chain aldehydes (C_2—C_4) gave *C*-2-alkylated products with satisfactory regioselectivity (80—90%)[5]. We now describe the reaction of *(1)* with formaldehyde or glyoxylic acid as a simple alternative to known syntheses[6] of anthracycline precursors.

Reaction of *(1)* with these aldehydes (aqueous sodium hydroxide, 50—60 °C[5]) gave polyalkylated products as well as chromatographically indistinguishable compounds alkylated at C-2 or C-3. However, on treatment at −5 to −3 °C (12 h) with alcoholic potassium hydroxide, *(1)* undergoes regioselective reaction to give 2-(hydroxymethyl)-1,4,5-trihydroxy-9,10-anthraquinone *(3)* in 18–21% yield. On filtration through a short silica gel column (3 × 20 cm, dichloromethane) about 60% of *(2)* was recovered; the polar species *(3)* could be isolated by elution with dichloromethane/2% methanol. The constitution of *(3)* is established by a downfield NMR shift of 1-OH ($\Delta\delta = 0.38$ ppm) and confirmed chemically by reduction with alkaline dithionite to give islandicin *(4)*[6]. Compound *(3)* is an attractive precursor of anthracyclinones.



(1) *(2)-(7)* *(8)*

(2)-(5), $R^1 = R^2 = H$; *(2)*, $R^3 = H$; *(3)*, $R^3 = CH_2OH$; *(4)*, $R^1 = CH_3$; *(5)*, $R^3 = CH_2CO_2CH_3$; *(6)*, $R^1 = H$, $R^2 = CH_3$, $R^3 = CH_2CO_2CH_3$; *(7)*, $R^1 = R^3 = CH_2CO_2CH_3$, $R^2 = H$

The analogous reaction of *(1)* with glyoxylic acid and subsequent reduction and esterification of the initially formed α-hydroxy acid gave the monoester *(5)* in 33% overall yield. Small amounts (<5%) of the anthraquinone substituted at C-3 could be eliminated by recrystallization from chloroform. The constitution has again been assigned by means of the NMR chemical shift of 1-OH ($\Delta\delta = 0.40$ ppm). The diester *(7)* could also be isolated in about 1% yield from some runs. Methylation of *(5)* with an excess of diazomethane[7] led selectively in 55% yield to the monomethyl ether *(6)*, suitable as starting material for a second alkylation at C-3 and further transformation into ε-rhodomycinone[3a]. It was possible to synthesize 9-deoxy-ε-rhodomycinone *(8)* in only two steps from *(5)*[3c].

Procedure

Synthesis of *(5)*: A solution of glyoxylic acid hydrate (3.68 g, 40 mmol) in methanol (100 ml) is added dropwise (6 h) to a solution of *(1)* (10.16 g, 40 mmol) [prepared from *(2)* by reduction with alkaline dithionite and precipitation with dilute sulfuric acid] in 0.5 N methanolic KOH (500 ml) cooled in an ice/salt mixture (internal temperature −5 to −3 °C). After a total of 12 h the mixture is acidified with 1 N HCl (500 ml), the precipitate is filtered off, dissolved in 1 N aqueous NaOH (400 ml), treated under N_2 with 85% sodium dithionite (8.30 g, 40 mmol), and heated under reflux for 2 h. A vigorous current of air is then passed through the solution at room temperature for 3 h; the precipitate is filtered off and dried *in vacuo* at 80 °C. Crude *(5)* is boiled in a mixture of chloroform (1 l), methanol (10 ml), and conc. sulfuric acid (5 ml) for *ca.* 12 h. The solution is washed twice with water, dried ($NaSO_4$), and filtered over a short silica gel column (3 × 20 cm). Some 2.20 g of *(2)* is recovered from the first fraction (chloroform) and then *(5)* is eluted; m.p. 197—200 °C (chloroform); yield 4.33 g (33%); IR (KBr): 1730 (C=O), 1598 cm^{-1} (quinone, chelated); ^{1}H-NMR ($CDCl_3$, 270 MHz): $\delta = 3.75$ (s; 3H, CO_2CH_3), 3.79 (s; 2H, CH_2), 7.36 (dd, $J_{6,7} = 8.1$, $J_{6,8} = 1.1$ Hz; 1H, 6-H), 7.71 (t; 1H, 7-H), 7.89 ($J_{7,8} = 7.4$, $J_{6,8} = 1.1$ Hz; 1H, 8-H), 12.21, 12.26 (each s, 2H, 2OH), 13.44 (s; 1H, 1-OH).

Received: May 8, 1979 [Z 262 IE]
German version: Angew. Chem. 91, 658 (1979)

[*] Dr. K. Krohn
Institut für Organische Chemie und Biochemie,
Abt. Biochemie, der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

[**] Synthetic Anthracyclinones, Part 9. I wish to thank Dr. *R. Merten*, Bayer AG, for kindly supplying 1,4,5-trihydroxy-9,10-anthraquinone.—Part 8: *K. Krohn, K. Tolkiehn*, Chem. Ber., in press.

[1] Review: *T. R. Kelly*, Annu. Rep. Med. Chem., in press.
[2] *C. Marschalk, F. Koenig, N. Ouroussof*, Bull. Soc. Chim. Fr. *3*, 1545 (1936).
[3] a) *K. Krohn, M. Radeloff, Chem. Ber. 111*, 3823 (1978); b) *K. Krohn*, J. Chem. Res. (S) *1978*, 394; (M) *1978*, 4762; c) *ibid.*, in press.

[4] *F. Suzuki, S. Trenbeath, R. D. Gleim, C. J. Sih*, J. Org. Chem. *43*, 4159 (1978).
[5] *L. H. Harwood, L. C. Hodgkinson, J. K. Sutherland*, J. Chem. Soc. Chem. Commun. *1978*, 712.
[6] a) *M. Braun*, Angew. Chem. *90*, 1000 (1978); Angew. Chem. Int. Ed. Engl. *17*, 945 (1978); b) *C. J. Sih et al.*, J. Chem. Soc. Chem. Commun. *1978*, 242.
[7] *R. J. Blade, P. Hodge*, J. Chem. Soc. Chem. Commun. *1979*, 85.

Competition in the Three-Component System Triphenylphosphane/Azo Ester/3-Hydroxy-Carboxylic Acid: OH- *versus* COOH-Activation

By *Johann Mulzer, Gisela Brüntrup,* and *Alexander Chucholowski*[*]

The question of hydroxy group activation (HGA) *vs.* carboxy group activation (CGA) always arises when dehydrating agents react with hydroxy carboxylic acids; this problem is of particular importance in the synthesis of macrolides[1] (stereocontrol[2] of a chiral center at the lactone-O) and peptides[3] (problem of hydroxy protection on preparing the active ester derivatives of hydroxyamino acids). It has generally remained unclear so far whether a given dehydrating agent exclusively effects HGA or CGA, or whether a variation of the substituents in the substrate may lead to a change in the activation mode.

In the case of the adduct *(1)* of triphenylphosphane and diethyl azodicarboxylate, a frequently employed dehydrating agent[4], only HGA was known in the system alcohol-carboxylic acid[5]. We now report on the first CGA reactions of *(1)* and reveal the factors determining the HGA/CGA competition.

As can been seen from the formula scheme our model system—the reaction of *(1)* with *threo*-3-hydroxycarboxylic acids *(2)*[6]—allows a simple and unambiguous differentiation between CGA and HGA. Proton transfer generates the ion pair *(3)*, from which the zwitterions *(A)* or *(B)* are formed by elimination of hydrazo ester. Of the reaction products, *(4)* and *(5)* can be unequivocally assigned to *(A)*, while *(6)* can only be formed from *(B)*; the alternative *(B)*→*(7)*+*(8)* is about 30 kcal/mol[7] less favorable and can be ruled out. The ratio HGA/CGA can thus be expressed by the quotient $Q=[(4)]+[(5)]/[(6)]$ (Table 1).

The relationship between Q and R^1/R^2 is attributed to the fact that the energy levels of *(A)* and *(B)* are shifted relatively to each other under steric effects. For small R^1 and R^2 *(A)* is much more stable than *(B)* due to the high resonance energy of its carboxylate function; so exclusively HGA is observed in cases *(a)*—*(e)*. On the other hand, bulky R^1 and R^2 in *(A)* strongly interact with each other and the $P(C_6H_5)_3$ group, whereas the steric interference is far less in *(B)*; hence, in the systems *(f)*—*(l)* the reaction path *via (B)*, and thus CGA, is progressively preferred. This interrelationship can be described semiquantitatively by correlating Q with the expression $\sum E_s = E_s(R^1) + 2E_s(R^2)$ [Table 1; E_s = steric parameter according to *Taft*[8].—Owing to its immediate proximity to the hydroxy group greater consideration must be given to R^2 than R^1 in $\sum E_s$; this is taken care of by an arbitrarily chosen

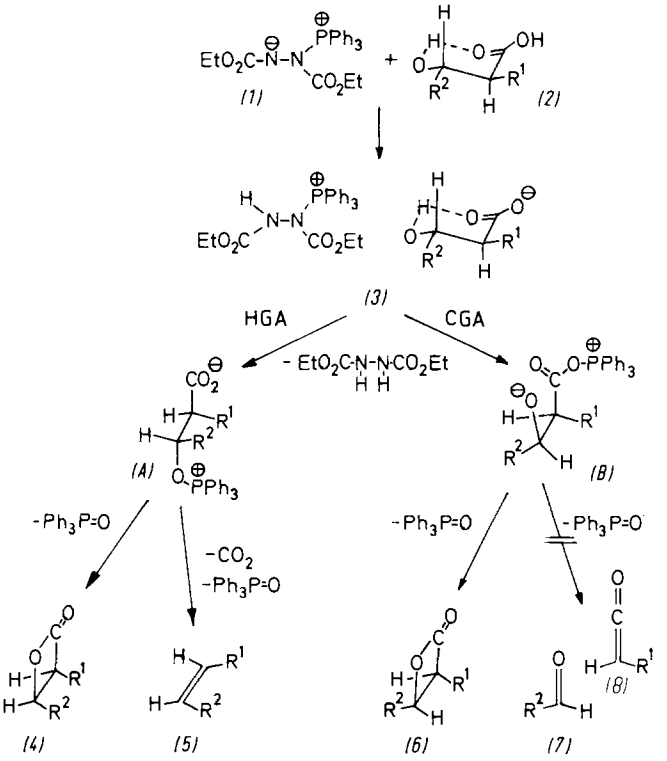


Table 1. Ratio Q = HGA/CGA in the reaction of *(1)* with *(2)*. The systems are listed according to falling $\sum E_s$ values.

System	R^1	R^2	Rel. yield [%] [a] *(4)*	*(5)*	*(6)*	Total yield [b] [%]	$\sum E_s = E_s(R^1)+2E_s(R^2)$ [c]	$Q=((4)+(5))/(6)$
(a)	OPh	Et	0	100	0	75	−3.2	100/0
(b)	Ph	Me	12	88	0	85	−3.5	100/0
(c)	Ph	Et	17	83	0	82	−3.6	100/0
(d)	SPh	Et	0	100	0	73	−3.7	100/0
(e)	OPh	*i*Pr	0	100	0	67	−4.0	100/0
(f)	Ph	*i*Pr	0	80	20	92	−4.4	80/20
(g)	SPh	*i*Pr	0	50	50	78	−4.5	50/50
(h)	*t*Bu	Et	44	12	44	90	−5.4	56/44
(i)	OPh	*t*Bu	0	44	56	91	−6.1	44/56
(j)	*t*Bu	*i*Pr	0	0	100	83	−6.2	0/100
(k)	Ph	*t*Bu	0	0	100	92	−6.6	0/100
(l)	*t*Bu	*t*Bu	0	0	100	90	−8.3	0/100

[a] ^{1}H-NMR analysis of the crude product; structural assignments see [6].
[b] After TLC (silica gel, pentane/ether 3:1).
[c] With $E_s(Ph) = -1.0$, $E_s(OPh) = E_s(OMe)$, $E_s(SPh) = E_s(SMe)$.

[*] Dr. J. Mulzer, G. Brüntrup, A. Chucholowski
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

factor 2]. Table 1 shows that the transition from HGA to CGA occurs in the range $-6.2 < E < -4.2$. If the smaller tri-*n*-butylphosphane is employed instead of triphenylphos-

phane CGA is only found in the heavily crowded systems *(k)* ($Q = 33/67$) and *(l)* ($Q = 0/100$), quite in accordance with the interpretation given above.

The preference of *(1)* to react with the sterically least hindered OH group is further demonstrated by the fact that it transforms *(2f)* and *(2k)* exclusively into the methyl esters if one equivalent of methanol is present. Apparently, of all the OH groups in the system that of the methanol is most rapidly activated, thus leading to an *inter*molecular reaction.

That the problem hydroxy-group *versus* carboxy-group activation plays a decisive role in biochemistry is clearly demonstrated by the transformation of mevalonic diphosphate into isopentenyl diphosphate, the key step in the terpene- and cholesterol-biosynthesis[9]. The enzyme, which utilizes a positively charged pentavalent phosphorus like *(1)*, apparently succeeds in avoiding steric congestion at the hydroxy function. The undesirable carboxy group activation thus is completely suppressed.

Received: March 19, 1979 [Z 259 IE]
German version: Angew. Chem. *91*, 654 (1979)

CAS Registry numbers:
(1), 58477-00-2; *(2a)*, 70982-74-0; *(2b)*, 33398-46-8; *(2c)*, 70982-75-1; *(2d)*, 70982-76-2; *(2e)*, 70982-77-3; *(2f)*, 33398-49-1; *(2g)*, 70982-78-4; *(2h)*, 70982-79-5; *(2i)*, 70982-80-8; *(2j)*, 70982-81-9; *(2k)*, 33398-52-6; *(2l)*, 70982-82-0; *(4b)*, 70982-83-1; *(4c)*, 70982-84-2; *(4h)*, 70982-85-3; *(5a)*, 33746-78-0; *(5b)*, 766-90-5; *(5c)*, 1560-09-4; *(5d)*, 21106-26-3; *(5e)*, 70982-86-4; *(5f)*, 15325-56-1; *(5g)*, 33923-89-6; *(5h)*, 3123-93-1; *(5i)*, 70982-87-5; *(6f)*, 70982-88-6; *(6g)*, 70982-89-7; *(6h)*, 70982-90-0; *(6i)*, 70982-91-1; *(6j)*, 70982-92-2; *(6k)*, 69974-12-5; *(6l)*, 70982-93-3

[1] *K. C. Nicolaou*, Tetrahedron *33*, 683 (1977).
[2] Cf. also synthesis and assignment of configuration of pyrenophorin and vermiculin: *D. Seebach, B. Seuring, H. O. Kalinowski, W. Lubosch, B. Renger*, Angew. Chem. *89*, 270 (1977); Angew. Chem. Int. Ed. Engl. *16*, 264 (1977).
[3] *E. Wünsch* in Houben-Weyl: Methoden der Organischen Chemie, Vol. XV/1, p. 568ff. Thieme, Stuttgart 1974.
[4] Summaries: *R. Mengel, M. Bartke*, Angew. Chem. *90*, 725 (1978); Angew. Chem. Int. Ed. Engl. *17*, 679 (1978); *F. di Ninno*, J. Am. Chem. Soc. *100*, 3251 (1978).
[5] *E.g.* [2]; cf. also *H. Loibner, E. Zbiral*, Helv. Chim. Acta *59*, 2100 (1976); *T. Kurihara, Y. Nakajima, O. Mitsunobu*, Tetrahedron Lett. *1976*, 2455; and references cited therein.
[6] *J. Mulzer, A. Pointner, A. Chucholowski, G. Brüntrup*, J. Chem. Soc. Chem. Commun. *1979*, 52.
[7] *S. W. Benson:* Thermochemical Kinetics, Wiley, New York 1968; *J. D. Cox, G. Pilcher:* Thermochemistry of Organic and Organometallic Compounds. Academic Press, New York 1970.
[8] *S. H. Unger, C. Hansch*, Prog. Phys. Org. Chem. *12*, 91 (1976).
[9] *E. D. Beytia, J. W. Porter*, Annu. Rev. Biochem. *45*, 123 (1976).

Complexes of γ-Cyclodextrin with Crown Ethers, Cryptands, Coronates, and Cryptates[**]

By *Fritz Vögtle* and *Walter M. Müller*[*]

The cyclodextrins (CD) have a lipophilic cavity which enables them to incorporate guest molecules and perform enzyme-analogous reactions[1]. Space-filling models show that smaller crown ethers and cryptands[2] just fit into the conical cavity of γ-CD enclosed by eight glucose units (Fig. 1).
For example, mixing of aqueous solutions of γ-CD and [12]crown-4 *(1)* in various stoichiometric ratios at room temperature or slightly elevated temperatures leads, within a few minutes or few hours, to crystallization of a 1:1 complex.

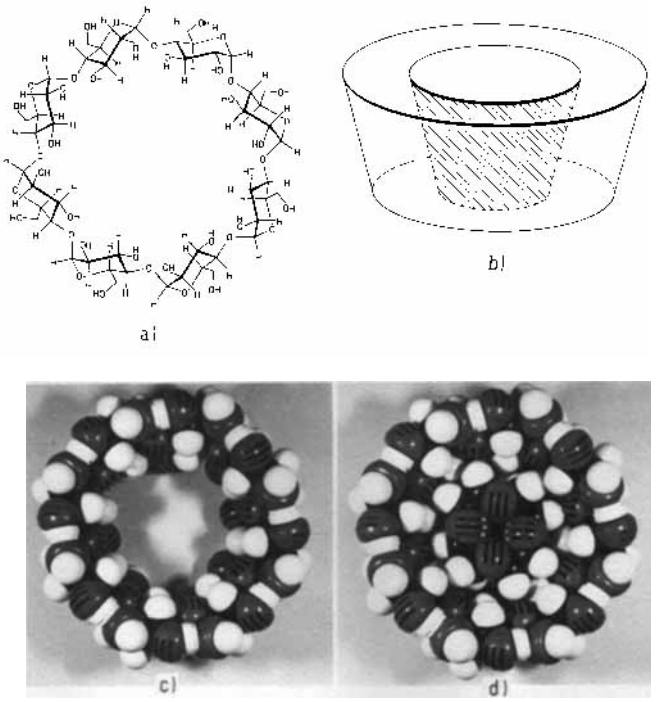


Fig. 1. a) Formula of γ-cyclodextrin (γ-CD); b) conical cavity in γ-CD; c) space-filling model of γ-CD; d) space-filling model of γ-CD with [12]crown-4 *(1)* in the cavity.

A similar ease of cavity accommodation (cf. Fig. 1[3]) is demonstrated by models of the γ-CD complexes of [2.1.1]cryptand *(9)* and of [1.1.1]cryptand *(8)*. The complexes form colorless needles and are so stable that they can be recrystallized from water.

Table 1 lists a series of further CD ⊂ crown ether and CD ⊂ cryptand combinations[4] whose elemental analyses indicate exact 1:1 or 2:1 stoichiometry. IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectra confirm the presence of both components. According to model considerations crown ether—metal ion complexes (coronates)[2], though much more rigid, should also be capable of being accommodated in the CD cavity. Reaction of aqueous solutions, *e.g.* of the [12]crown-4-LiSCN complex *(1a)*, or of the [2.2.2] ⊂ $Ca(SCN)_2$- or [2.2.2] ⊂ $Ba(SCN)_2$-cryptates *(10a)* and *(11a)* at room temperature with aqueous solutions of γ-CD leads to crystallization of "cascade complexes"[5] with the stoichiometric ratios 1:1, 2:1 and 2:1, respectively, whose thiocyanate anions are easily detectable by IR spectroscopy (2070 cm^{-1}). Since the changeover from 1:1 to 2:1 stoichiometry coincides with the transition from smaller to larger host molecules, such as from [2.1.1]- to [2.2.2]-cryptands, it can be assumed that if the guest molecule is too large, an arrangement is preferred in which it is enclosed by two CD molecules from opposite sides[6]. This also applies if the guest molecule contains several lipophilic groups suitable for accommodation, as in *(6)* and *(7)*. On the other hand, we have so far been unable to isolate complexes with the bulky molecules[8] dibenzo[24]crown-8 and $[2_B.2_B.2]$cryptand[7]. CD-crown ether complexes could also be useful for the transport of ions through cellulose membranes[9].

Procedure

γ-Cyclodextrin-[1.1.1]cryptand complex γ-CD · *(8)*: A solution of *(8)* (27.0 mg, 0.11 mmol) in 1 ml water is heated to

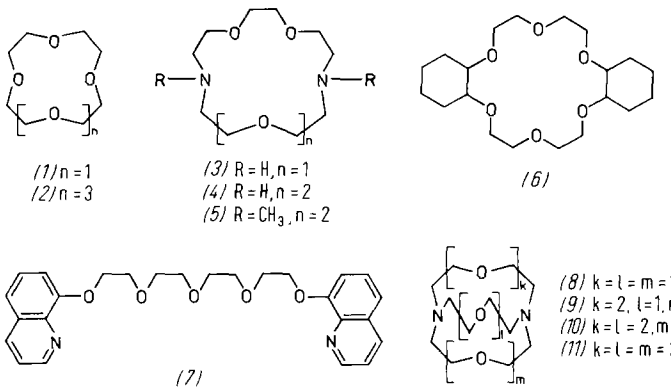
[*] Prof. Dr. F. Vögtle, W. M. Müller
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Str. 1, D-5300 Bonn (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We thank Prof. Dr. *W. Saenger*, Dr. *M. Noltemeyer*, and Dr. *G. Weber*, MPI Göttingen for valuable discussions.

Table 1. Synthesized γ-CD ⊂ crown ether and γ-CD ⊂ cryptand complexes and γ-CD ⊂ coronate and γ-CD ⊂ cryptate cascade complexes (γ-CD = γ-cyclodextrin).

Guest species		γ-CD:guest:H_2O (cryst. form)	Darkening, decomp. above [°C] [a]
[12]Crown-4	*(1)*	1:1 (platelets)	308—321
(1)·LiSCN	*(1a)*	1:1 (needles)	273
[18]Crown-6	*(2)*	2:1 (platelets)	306—309
1,4,10-Trioxa-7,13-diaza-cyclopentadecane	*(3)*	2:1 (platelets)	289
1,4,10,13-Tetraoxa-7,16-diazacyclooctadecane	*(4)*	2:1 (platelets)	291—299
7,16-Dimethyl-1,4,10,13-tetraoxa-7,16-diazacyclo-octadecane	*(5)*	2:1 (platelets)	289
Dicyclohexano[18]crown-6	*(6)*	2:1 (needles)	278—286
1,13-Bis(8-quinolyl)-1,4,7,10,13-pentaoxatridecane	*(7)*	2:1 (needles)	306—332
[1.1.1]Cryptand	*(8)*	1:1:2 (needles)	235
[2.1.1]Cryptand	*(9)*	1:1:1 (needles)	264
(9)·$LiClO_4$	*(9a)*	1:1:1 (platelets)	283—288
[2.2.1]Cryptand	*(10)*	2:1 (needles)	246
(10)·$Ca(SCN)_2$	*(10a)*	2:1 (platelets)	276
[2.2.2]Cryptand	*(11)*	2:1:1 (needles)	252
(11)·$Ba(SCN)_2$	*(11a)*	2:1 (platelets)	281—292

[a] Difficulties have been experienced in determining the melting points and decomposition points of CD complexes.



boiling, whereupon drops of the ligand form on the walls of the vessel. On addition of a hot solution of γ-cyclodextrin (50.0 mg, 0.045 mmol) in 0.5 ml water a clear solution is obtained which on further warming turns cloudy within 30 seconds; the complex crystallizes out spontaneously as fine colorless needles; yield 55.0 mg (90.5% yield).

Received: February 28, 1979 [Z 263 IE]
supplemented: March 30, 1979
German version: Angew. Chem. *91*, 676 (1979)

CAS Registry numbers:
(1), 294-73-9; *(1)*-γ-cyclodextrin, 71040-60-3; *(2)*, 17455-13-9; *(2)*-γ-cyclodextrin, 71010-20-3; *(3)*, 31249-95-3; *(3)*-γ-cyclodextrin, 71010-21-4; *(4)*, 23918-55-9; *(4)*-γ-cyclodextrin, 71010-22-5; *(5)*, 31255-13-7; *(5)*-γ-cyclodextrin, 71010-23-6; *(6)*, 16069-36-6; *(6)*-γ-cyclodextrin, 71010-24-7; *(7)*, 57310-75-5; *(7)*-γ-cyclodextrin, 71010-25-8; *(8)*, 37095-49-1; *(8)*-γ-cyclodextrin, 71010-26-9; *(9)*, 31250-06-3; *(9)*-γ-cyclodextrin, 71010-27-0; *(10)*, 31364-42-8; *(10)*-γ-cyclodextrin, 71010-28-1; *(11)*, 23978-09-8; *(11)*-γ-cyclodextrin, 71010-29-2; γ-cyclodextrin, 17465860

[1] Review: *M. L. Bender, M. Komiyama:* Cyclodextrin Chemistry, Springer, Berlin 1978; *W. Saenger* in *B. Pullman:* Environmental Effects on Molecular Structure and Properties, D. Reidel, Dordrecht 1976, p. 265ff.; cf. *M. F. Czarniecki, R. Breslow*, J. Am. Chem. Soc. *100*, 7771 (1978).
[2] Reviews: *F. Vögtle, E. Weber*, Kontakte (Merck) *1/77*, 11; *2/77*, 16; *3/77*, 36; *2/78*, 16; *F. Vögtle, E. Weber, U. Elben, ibid. 3/78*, 32; *1/79*, 3.
[3] A non-coaxial arrangement of the crown ether in the CD cavity is also conceivable [6b].
[4] The symbol ⊂ was suggested for cryptates by *Lehn*; it signifies that the compound preceding the symbol encloses that following it. *J.-M. Lehn, J. P. Sauvage*, J. Am. Chem. Soc. *97*, 6700 (1975).
[5] *J.-M. Lehn*, Pure Appl. Chem. *50*, 871 (1978); *J.-M. Lehn, J. Simon, A. Moradpour*, Helv. Chim. Acta *61*, 2407 (1978).
[6] Cf. also a) The "dimeric β-CD complex" with *n*-propanol and *p*-iodophenol: *J. J. Stezowski, K. H. Jogun, E. Eckle, K. Bartels*, Nature *274*, 617 (1978); b) The channel structure of the α-CD-*m*-nitrophenol 1:2 complex: *K. Harata, H. Uedaira, J. Tanaka*, Bull. Chem. Soc. Jpn. *51*, 1627 (1978).
[7] *B. Dietrich, J.-M. Lehn, J. P. Sauvage*, J. Chem. Soc. Chem. Commun. *1973*, 15.
[8] This finding can possibly be exploited for the separation of crown ether and/or cryptand mixtures.
[9] Cf. *B. Siegel, D. Eberlein, D. Rifkin, K. A. Davis*, J. Am. Chem. Soc. *101*, 775 (1979).

Colloidal Redox Catalysts for Evolution of Oxygen and for Light-Induced Evolution of Hydrogen from Water[**]

By *John Kiwi* and *Michael Grätzel*[*]

Redox catalysts such as PtO_2 and IrO_2 are known to promote the evolution of oxygen[1] and the light-induced evolution of hydrogen[2,3] from water. The ultimate aim of such studies is the production of systems in which water is decomposed into its components in high yield by visible light. We have now found that colloidal ruthenium (oxide) and other colloidal metals catalyze the evolution of oxygen and the light-induced evolution of hydrogen from water more efficiently than less finely divided substances.

The colloids were characterized by light scattering measurements[4]. Figure 1 shows autocorrelation functions obtained with poly(vinyl alcohol) (PVA) alone and with Ru in the presence of PVA as protective colloid. The hydrodynamic radius can be calculated from the correlation times (Table 1); the substances are therefore present as colloidal dispersions.

Table 1. Evaluation of correlation measurements by Stokes-Einstein equation. D = diffusion coefficient; τ = decay time; r_h hydrodynamic radius (at 25 °C)

$D = kT/(6\pi\eta r_h)$; $D = 1/(2K^2\tau)$, $K = 1.039 \times 10^4$ cm^{-1} [4]

Substance	D [cm²/s]	τ [ms]	r_h [Å]
Poly(vinyl alcohol) (PVA) (mol. wt. 60000)	2.3×10^{-7}	19.7	101
Ru colloid (from $RuCl_3$) PVA	8.5×10^{-8}	56.0	280
Pd colloid (from $PdCl_2 \cdot H_2O$) PVA	4.7×10^{-8}	101.2	500
Pt colloid (from H_2PtCl_6) PVA	3.6×10^{-8}	132.1	564

[*] Prof. Dr. M. Grätzel, Dr. J. Kiwi
Institut de chimie physique, Ecole Polytechnique Fédérale
CH-1015 Lausanne (Switzerland)

[**] Support of this work by the Swiss National Foundation (Grant No. 4.061.076.04) and by Ciba-Geigy, Basel (Switzerland), is gratefully acknowledged.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0624 $ 02.50/0

The test system used for O_2 evolution was an aqueous cerium(IV) sulfate solution in 1 N H_2SO_4[1,3a]. The kinetically inhibited reaction

$$4Ce^{4+} + 2H_2O \rightarrow O_2 + 4Ce^{3+} + 4H^+ \quad (1)$$

is known to be accelerated by dispersed noble metal oxides; $k = 0.3\ h^{-1}$ was observed with 5×10^{-3} mol/l of RuO_2 at room temperature[1b].

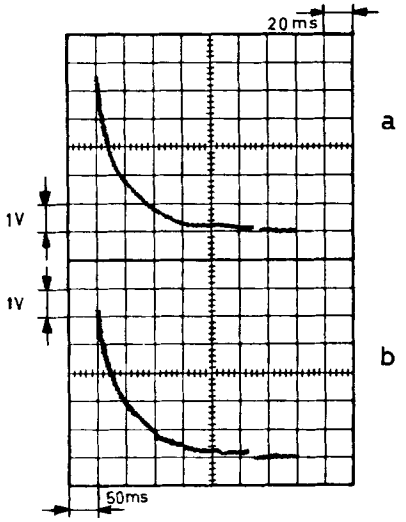


Fig. 1. Autocorrelation function for (a) poly(vinyl alcohol) (PVA, mol. wt. 60000, $\theta = 4.5°$) and (b) ruthenium with PVA as protective colloid. Measuring time 2 ms; data acquisition time 10 minutes; Ru concentration 3.3×10^{-4} mol/l. 1 V on the ordinate is equivalent to 0.2×10^{20} (autocorrelator, resolution 0.1 μm, 64 channels).

The catalytic activity of colloidal Ru in reaction (1) follows from Figure 2. The spectrum of the Ce^{4+} ions is completely transformed into that of Ce^{3+} ions within 4 min. Oxygen is liberated in the course of this process[5]. The differential concentration ratio $-d[Ce^{4+}]/d[O_2]$ falls from an initial high value of about 6 to the calculated value of 4 during the reaction. The physical properties of the colloidal system change during the initial phase of the reaction. The solution becomes pale red ($\lambda_{max} = 460$ nm). According to *Mie*[6] this corresponds to spherical particles having a narrow size distribution centered around 140 Å. Under the conditions of pH and potential required for the oxygen evolution step RuO_2 is the stable oxidation state of Ru[7]. Hence the active form of the catalyst may be considered to be Ru particles covered by a thin layer of RuO_2, the colloid being stabilized by PVA. This accounts for the oxygen deficiency found at the onset of the reaction.

These entities act as microelectrodes: electron transfer to Ce^{4+} ions leads to anodic polarization until the potential of the particle is sufficiently positive for oxygen evolution to occur. The low overvoltage[8] allows the redox process to occur quantitatively and at high speed even though the free energy for reaction (1) is only −200 mV under standard conditions.

The transformation of Ce^{4+} into Ce^{3+} is a first order reaction. The rate constant obtained at a Ru concentration of 1.3×10^{-4} mol/l is $k = 0.5\ min^{-1}$ ($\approx 28\ h^{-1}$). This value is about 100 times higher than that obtained with RuO_2 powder at the same temperature[1b] although in the latter case about 40 times higher concentrations had to be used. A similar increase in activity was observed on evolution of O_2 from $Ru(bpy)_3^{3+}/H_2O$[1b]. These results demonstrate convincingly the advantage of employing colloidal systems as redox catalysts.

The advantage of colloidal catalysts becomes apparent in light-induced H_2-evolution from water. In order to examine the activity of various catalysts we employed a homogeneous test system consisting of an aqueous solution of tris(bipyridine)ruthenium(II) ($Ru(bpy)_3^{2+}$), methylviologen (MV^{2+}), and EDTA (the kinetics and mechanistic details of these light-induced processes have been elaborated previously[3]). In the presence of suitable redox catalysts, MV^+ reduces water according to

$$2MV^+ + 2H_2O \rightarrow 2MV^{2+} + 2OH^- + H_2 \quad (2)$$

Since under standard conditions this process is thermodynamically favorable only by several millivolts, we restricted our choice to materials for which the hydrogen overvoltage is low. The relative efficiencies of the catalysts are seen in Figure 3. Experimental conditions were not optimized with respect to maximum H_2 yields. Once again, the rate increases drastically when the macrodispersions are replaced by colloidal systems. In very recent work we obtained 12 l H_2 per day and per l solution with a colloidal Pt catalyst of very high dispersity[1c].

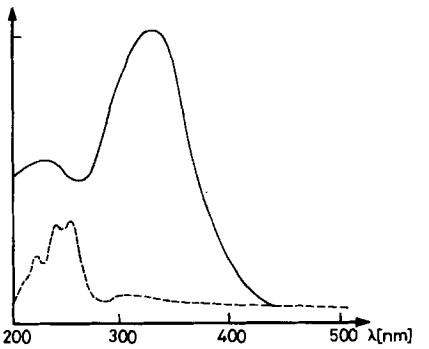


Fig. 2. Absorption spectra of $Ce(SO_4)_2 \cdot 2H_2O$ (8×10^{-3} mol/l) in 1 N H_2SO_4 solutions before (—) and 4 min after (---) addition of colloidal Ru catalyst.

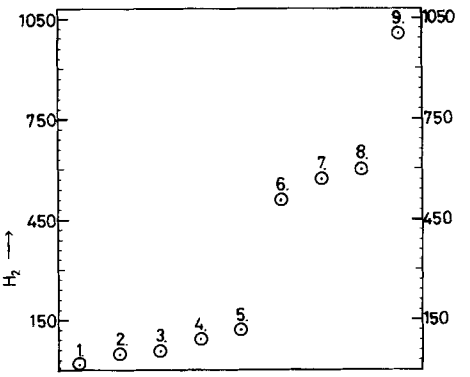


Fig. 3. Evolution of hydrogen in ml per day and per liter of aqueous solution containing 4×10^{-5} mol/l of $Ru(bpy)_3^{2+}$, 2×10^{-3} mol/l of methylviologen (*N,N*-dimethylbipyridine dication) (MV^{2+}), 2.5×10^{-2} mol/l ethylenediaminetetraacetic acid (EDTA). Catalysts: 1, PdO_2 powder; 2, IrO_2 powder; 3, Ru powder; 4, Ru powder, irradiated; all 5×10^{-3} mol/l. 6, colloidal Pd; 7, colloidal Ru (from $RuCl_3$); 8, colloidal Ru (from $(NH_4)_2(Ru_2OCl_{10})$); 9, colloidal Pt; all 1.3×10^{-4} mol/l. pH = 5, $\lambda > 400$ nm (cut off filter), optical pathlength 3.2 cm, hydrogen detected by gas chromatography, irradiation with Osram XBO 450-W lamp.

Experimental

Colloidal Ru: A 2% solution of PVA of mol. wt. 60000 (12.5 g) was dissolved in water (11 ml). To this solution was added $RuCl_3$ (41.4 mg) or $(NH_4)_4[RuOCl_{10}]$ (56 mg) and the pH adjusted to 8 with NaOH. After warming to 100 °C for 30 min the volume was made up to 42 ml and the Ru^{3+} reduced

to the metal by H_2. 3 ml of this stock solution was added to 100 ml of the reaction mixture; this corresponds to 1.4 mg Ru/100 ml or 10^{-4} mol/l.—The production of colloidal Pt and Pd is described in ref. [9].

Received: March 30, 1979;
revised: June 1, 1979 [Z 264 IE]
German version: Angew. Chem. 91, 659 (1979)

CAS Registry numbers:
Ce, 7440-45-1; Pd, 7440-05-3; Pt, 7440-06-4; Ru, 7440-18-8; H, 12385-13-6; O, 17778-80-2; $Ru(bpy)_3^{2+}$, 15158-62-0; EDTA, 60-00-4; methylviologen, 1910-42-5; poly(vinyl alcohol), 9002-89-5

[1] a) *J. Kiwi, M. Grätzel*, Angew. Chem. *90*, 900 (1978); Angew. Chem. Int. Ed. Engl. *17*, 860 (1978); b) Chimia, in press; J. Am. Chem. Soc., in press.
[2] *A. Piccini, L. Marino*, Z. Anorg. Chem. *32*, 55 (1902); *B. V. Koryakin, T. S. Dzhabiev, A. E. Shilov*, Dokl. Akad. Nauk SSSR *238*, 620 (1977); *J. M. Lehn, J. P. Sauvage*, Nouveau J. Chim. *1*, 449 (1977).
[3] a) *K. Kalyanasundaram, J. Kiwi, M. Grätzel*, Helv. Chim. Acta *61*, 2720 (1978); *A. Moradpour, E. Amouyal, P. Keller, H. Kagan*, Nouveau J. Chim. *2*, 547 (1978).
[4] KMX-6 Chromatix instrument; see Chromatix Application Note LS8 (1978), 560 Oakmead Parkway, Sunnyvale, Calif. 94086 (USA).
[5] Quantitative oxygen analysis was performed with an "end-0-mess" model D instrument (Friedrichsfeld GmbH, Mannheim, Germany). The method of detection is selective, being based on the response of the potential of a Zr/ZrO_2 (solid electrolyte) electrode to O_2.
[6] *G. Mie*, Ann. Phys. (Leipzig) *25*, 377 (1908).
[7] *M. Pourbaix:* Atlas d'Equilibres Electrochimiques, Gauthier-Villars, Paris 1963.
[8] *M. H. Miles, E. A. Klaus, B. P. Gunn, J. R. Locker, W. E. Serafin*, Electrochim. Acta *23*, 521 (1978).
[9] *L. D. Rampino, F. F. Nord*, J. Am. Chem. Soc. *63*, 2745 (1941).

CS_2- and CS_3-Bridged Transition Metal Complexes—Directed Synthesis of Metallodithiocarboxylato-Metal Complexes[**]

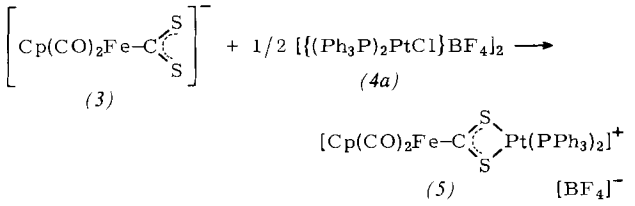
By *Wolf Peter Fehlhammer, Andreas Mayr,* and *Heribert Stolzenberg*[*]

In 1975 the preparation and X-ray characterization[1] of a dinuclear CS_2-bridged platinum complex was reported combining the structural features of a dithiocarbenemetal *(1)* and a metal *S,S'*-dithiolate *(2)*. Attempts to prepare other compounds having the same interesting kind of linkage proved unsuccessful.



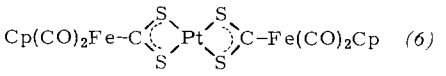
(1) *(2)*

Studies on the *basic metal/heteroallene/acid* or *Lewis acid metal* system[2] have now enabled us to prepare a series of such stable dinuclear and trinuclear "metallodithiocarboxylato-metal complexes". The adduct[3] obtained from carbon disulfide and sodium dicarbonyl(cyclopentadienyl)ferrate



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

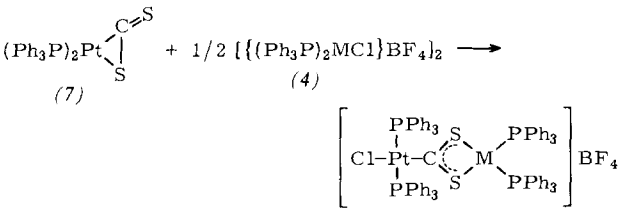
reacts with *(4a)* in tetrahydrofuran (THF) to give the CS_2-bridged dinuclear complex *(5)*. A platinum complex *(6)* having two of the same "ferriodithiocarboxylatochelate ligands" can be obtained as red crystals on reaction of *(3)* with $PtCl_2$ in the molar ratio 2:1.



(6)

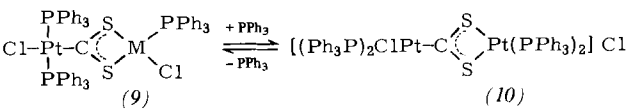
IR spectra [(KBr) *(5):* 2042, 1998 vs [ν(CO)], 870 s [$\nu(CS_2)$]; *(6):* 2028, 1973 vs [ν(CO)], 870 s [$\nu(CS_2)$] cm^{-1}], elemental analysis, molecular weight determination, and synthesis support the proposed structures[3].

Another electron-rich adduct which, like *(3)*, should be able to react with electrophilic metal compounds is η^2-(carbon disulfide)bis(triphenylphosphane)platinum *(7)* described in 1966 by *Wilkinson et al.*[4]. Indeed, its reaction in dichloromethane with the chlorine bridged complex cation *(4a)* immediately and quantitatively leads to *Angelici's* complex *(8a)* which was formed in an *unexplained* manner on decomposition of $[(Ph_3P)_2Pt(Cl)(CS)]BF_4$[1]. The tendency of formation of the *hetero*metallic dinuclear complex *(8b)*, on the other hand, is much less pronounced.



(7) *(4)* *(8a)*, M = Pt; *(8b)*, M = Pd

Prolonged times are also required for reactions of $(Ph_3P)_2Pt(CS_2)$ with neutral dichlorobis(triphenylphosphane)nickel(II), -palladium(II), and -platinum(II); the nickel and palladium compounds exclusively giving respectively the red-brown and orange neutral complexes *(9)*, whereas *cis*-$(Ph_3P)_2PtCl_2$ also gives rise to the yellow cationic complex *(10)* which in solution readily eliminates triphenylphosphane to form *(9)* with M = Pt.



(9) *(10)*

A remarkably constant band pattern (*ca.* 930 s, 870 m [ν_{as}, $\nu_s(CS_2)$] cm^{-1}), which seems to be characteristic of the Pt CS_2M group, is found in the IR spectra of the complexes *(8)*—*(10)*.

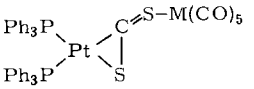
The ^{31}P-NMR spectra prove the *trans* configuration at the *C*-bonded platinum and the equivalence of the *cis*-triphenylphosphane ligands on the chelated metal in *(8)* and *(10)*, which in turn provides evidence for the equivalent nature of the two *S* ligands in *trans* position.

We suspect the first step of formation of these platiniothiocarboxylato complexes to consist in coordination of the electropositive metal to the "exo-sulfur atom" of *(7)*, which is followed by intra- or intermolecular halogen transfer between the metals with concomitant opening of the PtCS three-membered ring and chelatization at the entering metal.

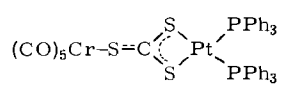
In the absence of mobile halogen ligands in the Lewis acid metal component the reaction with *(7)* ceases at the stage of primary coordination. The complexes *(11)* obtained in high

[*] Prof. Dr. W. P. Fehlhammer, Dr. A. Mayr, Dipl.-Chem. H. Stolzenberg
Institut für Anorganische Chemie der Universität Erlangen-Nürnberg
Egerlandstrasse 1, D-8520 Erlangen (Germany)

[**] Isocyanide- and Heteroallene-Bridged Metal Complexes, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 1: [2b].



(11), M = Cr, W



(12)

yield from (7) and $M(CO)_5THF$ (M = Cr, W) apparently contain the same kind of CS_2 bridge as considered for the known compounds
$Cp(CO)_2Mn(SCS)Mn(CO)_2Cp$[5],
$(R_3P)_2(CO)_2Fe(SCS)Mn(CO)_2Cp$[6],
and $Cp(Me_3P)_2Co(SCS)Cr(CO)_5$[7].

A variant of the *basic metal/CS_2* interaction is found in the reaction of $Na_2Cr(CO)_5$ with CS_2 and $(Ph_3P)_2PtCl_2$. The compound isolated as yellow crystals (37% yield) on work-up is not an isomer of (11) as would be expected from the method of preparation. Instead it contains more sulfur and is to be formulated as the trithiocarbonate-bridged species (12) (IR (KBr): 1040 m [$\nu(CS_3)$] cm^{-1}). CS_3 bridge formation has also been observed on reaction of pentacarbonylmanganate(−I) and -rhenate(−I) with CS_2[8].

Experimental

CS_2 (0.15 ml, 2.5 mmol) in THF (50 ml), and then $[(Ph_3P)_2PtCl]_2(BF_4)_2$[9] (2.1 g, 1.25 mmol), are added to a 0.1 M solution of $Na[CpFe(CO)_2]$ in THF (25 ml) [prepared from $[CpFe(CO)_2]_2$ (3.54 g) and $NaK_{2.8}$ (1.35 ml) in THF (200 ml)] at −70 °C under N_2. A clear light-orange solution arises on warming to 0 °C. The solvent is evaporated at this temperature, the residue dissolved in dichloromethane (*ca.* 50 ml), and the solution filtered through cellulose. After concentration of the filtrate to half the volume, the product crystallizes on addition of *n*-pentane. The yellow platelets of (5) (yield 76%, dec. pt. 170 °C) can be stored indefinitely at −20 °C.

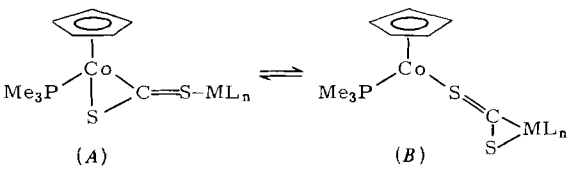
Received: March 9, 1979 [Z 265 IE]
German version: Angew. Chem. 91, 661 (1979)

[1] *J. M. Lisy, E. D. Dobrzynski, R. J. Angelici, J. Clardy*, J. Am. Chem. Soc. 97, 656 (1975).
[2] a) *W. P. Fehlhammer, A. Mayr, M. Ritter*, Angew. Chem. 89, 660 (1977); Angew. Chem. Int. Ed. Engl. 16, 641 (1977); b) *W. P. Fehlhammer, A. Mayr, G. Christian, ibid.* 90, 920 (1978) and 17, 866 (1978).
[3] In contrast, (3) and $CpFe(CO)_2I$ form a CS_2-bridged complex in which ferriodithiocarboxylate functions as a *monohapto S* ligand: *J. E. Ellis, R. W. Fennell, E. A. Flom*, Inorg. Chem. 15, 2031 (1976).
[4] *M. C. Baird, G. Wilkinson*, J. Chem. Soc. Chem. Commun. *1966*, 514.
[5] *M. Herberhold, M. Süss-Fink, C. G. Kreiter*, Angew. Chem. 89, 191 (1977); Angew. Chem. Int. Ed. Engl. 16, 193 (1977).
[6] *U. Oehmichen, T. G. Southern, H. LeBozec, P. Dixneuf*, J. Organomet. Chem. 156, C29 (1978).
[7] *H. Werner, K. Leonhard, Ch. Burschka*, J. Organomet. Chem. 160, 291 (1978).
[8] *I. B. Benson, J. Hunt, S. A. R. Knox, V. Oliphant*, J. Chem. Soc. Dalton Trans. *1978*, 1240.
[9] *W. Beck, K. v. Werner*, Chem. Ber. 104, 2901 (1971); *C. Eaborn, N. Farrell, J. L. Murphy, A. Pidcock*, J. Chem. Soc. Dalton Trans. *1976*, 58.

$(C_5H_5)_3Co_3(CS)(S)$; The First Complex to Have a μ_3-Thiocarbonyl Bridge[1]

By *Helmut Werner* and *Konrad Leonhard*[*]

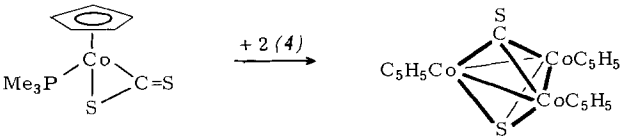
The complex $C_5H_5(PMe_3)Co(\eta^2\text{-}CS_2)$ (1) readily obtained from $C_5H_5Co(PMe_3)_2$ and CS_2 reacts with the tetrahydrofuran (THF) adducts $Cr(CO)_5THF$ and $C_5H_5Mn(CO)_2THF$ to give the dinuclear complexes $C_5H_5(PMe_3)Co(SCS)Cr(CO)_5$ (2) and $C_5H_5(PMe_3)Co(SCS)Mn(CO)_2C_5H_5$ (3) in which the CS_2 ligand bridges two different metal atoms[2]. The carbon disulfide moiety of (2) and (3) is rigidly fixed [as in (A)], *i.e.* isomerization according to



(A) (B)

is not detectable.

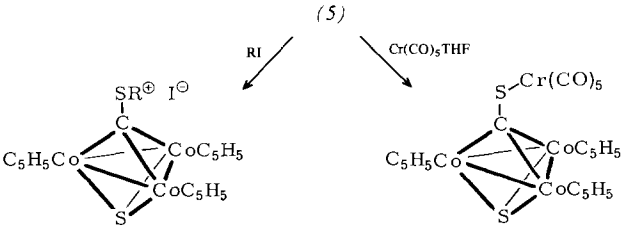
We expected a *non-rigid* structure (*i.e.* a flexible CS_2 bridge) for the analogous *symmetrical* dinuclear complex having $ML_n = Co(PMe_3)C_5H_5$. *Herberhold et al.*[3] observed a flexibility of this kind in $C_5H_5(CO)_2Mn(SCS)Mn(CO)_2C_5H_5$ which is completely frozen in at low temperature (210 K). However, reaction of (1) with $C_5H_5(PMe_3)Co(\mu\text{-}CO)_2Mn(CO)C_5H_4Me$ (4), which we used as a source for the 16-electron fragment $C_5H_5CoPMe_3$[4], followed a completely different course. Instead of the expected product $C_5H_5(PMe_3)Co(SCS)Co(PMe_3)C_5H_5$ we obtained the trinuclear complex $(C_5H_5)_3Co_3(CS)(S)$ (5) as black crystals that are only slightly air-sensitive. On reaction of (1) and (4) in a molar ratio of 1:2, compound (5) is isolated in *ca.* 80% yield.



(1) (5)

Crystal structure analysis[5] shows that the three cobalt atoms form an equilateral triangle with the two bridging ligands located above and below its midpoint. An analogous trigonal-bipyramidal arrangement of the skeletal atoms occurs in the complexes $(C_5H_5)_3Co_3(CO)(O)$[6] and $(C_5H_5)_3Co_3(CO)(S)$[7], which are obtained in very low yield by photolysis of $C_5H_5Co(CO)_2$ and by reaction of $C_5H_5Co(CO)_2$ with $S(N\text{-}tBu)_2$, respectively.

(5) behaves as a Lewis base and reacts smoothly with methyl and ethyl iodide and with $Cr(CO)_5THF$ to give the complexes (6)—(8). The sulfur atom of the CS bridge is apparently the site of maximum nucleophilicity, in accord with the results of X-ray crystal structure analysis (relatively long C S distance[5]).



(6), R = Me
(7), R = Et

(8)

A notable feature of the synthesis of (5) is the ease with which the carbon disulfide coordinated very strongly in (1) is cleaved to CS and S. Numerous carbon monosulfide (or thiocarbonyl) complexes having terminal CS ligands are known[8], and several dinuclear compounds of manganese,

[*] Prof. Dr. H. Werner, Dr. K. Leonhard
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

iron, and ruthenium containing bridging μ_2-CS groups have recently also been described[9]. To our knowledge, *(5)* is the first complex in which carbon monosulfide links *three* metal atoms together, and thus represents an example of the hitherto missing last member of the series $L_nM{-}CS$, $L_nM_2(\mu_2\text{-CS})$, $L_nM_3(\mu_3\text{-CS})$ established over 20 years ago in the case of the CO ligand.

Table 1. Spectroscopic data of complexes *(5)*—*(8)*.

(5): ^{1}H-NMR ([D$_6$]-benzene): $\delta = 4.50$ (s). IR (KBr): 1075 (s), 1039 (s) cm^{-1} (region expected for μ_3-C–S stretching vibrations). MS: $m/e = 448$ (M^+ with correct isotopic satellites).

(6): ^{1}H-NMR ([D$_3$]-nitromethane): $\delta = 5.11$ (15H; s), 3.89 (3H; s). IR (KBr): 1008 (s), 997 (s) cm^{-1}.

(7): ^{1}H-NMR ([D$_3$]-nitromethane): $\delta = 5.16$ (15H; s), 4.45 (2H; q, $J_{HH} = 7$ Hz), 1.95 (3H; t, $J_{HH} = 7$ Hz).

(8): ^{1}H-NMR ([D$_6$]-acetone): $\delta = 4.95$ (s). IR (THF): ν(CO) = 2050, 1970 (sh), 1925, 1895 cm^{-1}.

Experimental

A solution of *(1)* (330 mg, 1.2 mmol) and *(4)* (1 g, 2.4 mmol) in benzene (15 ml) is heated under gentle reflux for 5 h. A first crop of *(5)* crystallizes on cooling. The solvent is stripped off completely under vacuum, the residue washed several times with hexane, and recrystallized from THF/hexane. *(5)*, black crystals, dec. pt. = 289 °C; yield 450 mg.

Received: March 28, 1979 [Z 267 IE]
German version: Angew. Chem. *91*, 663 (1979)

[1] Basic Metals. Part 18. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and by gifts of chemicals from BASF. Ludwigshafen.—Part 17: *H. Werner, W. Hofmann*, Angew. Chem. *91*, 172 (1979); Angew. Chem. Int. Ed. Engl. *18*, 158 (1979).

[2] *H. Werner, K. Leonhard, Ch. Burschka*, J. Organomet. Chem. *160*, 291 (1978).

[3] *M. Herberhold, M. Süss-Fink, C. G. Kreiter*, Angew. Chem. *89*, 191 (1977); Angew. Chem. Int. Ed. Engl. *16*, 193 (1977).

[4] *K. Leonhard, H. Werner*, Angew. Chem. *89*, 656 (1977); Angew. Chem. Int. Ed. Engl. *16*, 649 (1977).

[5] *E. Röttinger, H. Vahrenkamp*, unpublished results.

[6] *V. A. Uchtman, L. F. Dahl*, J. Am. Chem. Soc. *91*, 3763 (1969).

[7] *S. Otsuka, A. Nakamura, T. Yoshida*, Justus Liebigs Ann. Chem. *719*, 54 (1968); *P. D. Frisch, L. F. Dahl*, J. Am. Chem. Soc. *94*, 5082 (1972).

[8] *I. S. Butler*, Acc. Chem. Res. *10*, 359 (1977).

[9] *M. H. Quick, R. J. Angelici*, J. Organomet. Chem. *160*, 231 (1978); references cited therein.

$[\{Cu_3WS_3Cl\}(PPh_3)_3O]$, Directed Synthesis of a Compound Containing Different Metal Atoms in a Cubane-like Skeleton

By *Achim Müller, Theng Khing Hwang*, and *Hartmut Bögge*[*]

Synthetic approaches for the linking of different metals *via* sulfur in cluster structures are of special importance in current studies on polynuclear transition metal-sulfur complexes[1,2]. We are presently investigating the directed synthesis of compounds of this type with thiometalates such as MoS_4^{2-} and WS_4^{2-}. Polynuclear Cu^I-cage and -cluster compounds are of particular interest as regards structural variancy. However, although compounds with, *inter alia*, the central moieties $\{Cu_4S_4\}$ (ring structure), $\{Cu_4S_6\}$ (adamantane structure), and $\{Cu_8S_{12}\}$ (Cu_8 cube) are well-known[3] all attempts to synthesize cubane-like variants—including those containing other metals besides Cu^I—have so far failed.

We have now been able to synthesize yellow, crystalline $[\{Cu_3WS_3Cl\}(P(C_6H_5)_3)_3O]$ *(1)* having a cubane-like $\{CuWS_3Cl\}$ core and to characterize it by elemental analysis, IR spectroscopy, and a complete crystal structure analysis.

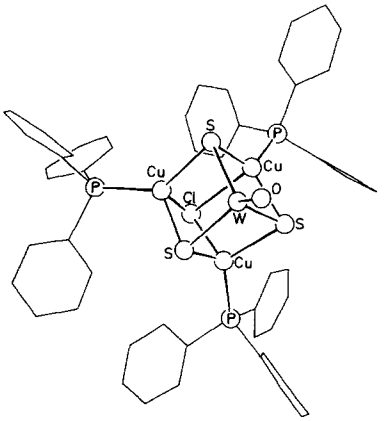


Fig. 1. Molecular structure of *(1)* in the crystalline state.

The structure of *(1)* was determined from single-crystal diffractometer data (Syntex $P2_1$, MoK_α radiation, 5349 independent reflections, $R = 0.088$). The compound crystallizes in the orthorhombic space group $P2_12_12_1$ ($a = 12.825(2)$, $b = 17.529(4)$, $c = 22.711(4)$ Å, $V = 5105.5$ Å^3; $\rho_{calc} = 1.70$ g cm^{-3}; $Z = 4$). The central unit corresponds to a highly distorted cube (average W–S, Cu–S, Cu–Cl distances 2.241, 2.315 and 2.610 Å, respectively). W and Cu are in a tetrahedral and a strongly distorted tetrahedral environment (with O and PPh_3 as terminal ligands, and W–O and average Cu–P bond lengths of 1.752(14) and 2.202 Å, respectively). The metal atoms form a distorted tetrahedral Cu_3W central unit[4].

The significance of metal-metal interaction in *homotetranuclear* clusters having a cubane structure has already been demonstrated[5]. The IR spectrum (solid, Nujol) also clearly indicates the presence of three W–S bridge bonds and a terminal W–O bond [ν(WO) = 929, ν(WS) = 436/432 cm^{-1}, cf. Ref.[6]].

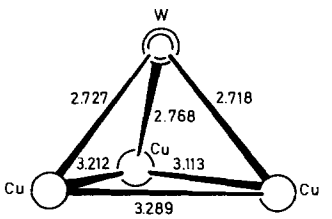


Fig. 2. Central Cu_3W unit in *(1)*.

(1) could be obtained by the first directed synthesis of a cubane unit starting from a partly formed cage: the formation of a compound with a cubane-like structure was to be expected on using the synthon OWS_3^{2-} (preferred formation of Cu–S over Cu–O bonds, preferred triple-bonding of S[1]).

Procedure

Solutions of $CuCl_2 \cdot 2H_2O$ (0.17 g) in H_2O (5 ml) and $(C_6H_5)_3P$ (0.4 g) in CH_2Cl_2 (25 ml) are mixed by vigorous stirring and treated with a freshly prepared solution of

[*] Prof. Dr. A. Müller, Dr. T. K. Hwang, Dipl.-Chem. H. Bögge
Fakultät für Chemie der Universität
Universitätsstrasse, D-4800 Bielefeld 1 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0628 $ 02.50/0

Cs_2WOS_3 (0.35 g) in H_2O (100 ml). After briefly shaking, the aqueous phase is separated off and the organic phase is covered with a mixture of *n*-pentane (50 ml) and acetone (10 ml). After *ca.* 3—4 d orange-yellow crystals of *(1)* separate out (yield 0.05 g).

Received: December 21, 1978 [Z 268 IE]
revised: April 20, 1979
German version: Angew. Chem. *91*, 656 (1979)

[1] *H. Vahrenkamp*, Angew. Chem. *87*, 363 (1975); Angew. Chem. Int. Ed. Engl. *14*, 322 (1975).
[2] For the synthesis of biochemically interesting iron-sulfur-molybdenum cage systems cf. *T. E. Wolff, J. M. Berg, C. Warrick, K. O. Hodgson, R. H. Holm, R. B. Frankel*, J. Am. Chem. Soc. *100*, 4630 (1978); *G. Christou, C. D. Garner, F. E. Mabbs, T. J. King*, J. Chem. Soc. Chem. Commun. *1978*, 740.
[3] *D. M. L. Goodgame, G. A. Leach, A. C. Skapski, K. A. Woode*, Inorg. Chim. Acta *31*, L375 (1978); *E. H. Griffith, G. W. Hunt, E. L. Amma*, J. Chem. Soc. Chem. Commun. *1976*, 432; *D. Coucouvanis, D. Swenson, N. C. Baenziger, R. Pedelty, M. L. Caffery*, J. Am. Chem. Soc. *99*, 8097 (1977); and references cited therein.
[4] On the problem of metal-metal bonding of Cu^I with its closed valency shell cf. *P. K. Mehrotra, R. Hoffmann*, Inorg. Chem. *17*, 2187 (1978).
[5] *B. A. Averill, T. Herskovitz, R. H. Holm, J. A. Ibers*, J. Am. Chem. Soc. *95*, 3523 (1973).
[6] *K. H. Schmidt, A. Müller*, Coord. Chem. Rev. *14*, 115 (1974).

Existence and Bond Energy of the Cesium Auride Molecule

By *Bernd Busse* and *Konrad G. Weil*[*]

As prototypes of the metal-metal bond, isolated dimeric and oligomeric metallic species are investigated primarily by matrix isolation techniques[1]. This method, however, has the disadvantage that the properties of the species investigated can be strongly influenced in an, as yet, unclear manner by interaction with the matrix material. Mass spectrometry of metal vapors permits observation of not only the metal atoms but also dimers and oligomers. Investigations on binary systems can thus afford valuable information on the existence and properties of heterometallic molecules. We have therefore started a series of studies on systems in which there is a large difference in electronegativity of the metal partners—in anticipation of finding molecules having predictable bonding character in such systems.

As the phase diagram of cesium-gold[2] shows, this system forms an intermetallic compound with a 1:1 composition which crystallizes with a CsCl-type structure and has a melting point of 590 °C. In the liquid state it exists as a purely ionicmelt[3]. A stable molecule CsAu can be expected to exist in the vapor phase. In our experiments we used a MM 30 K mass spectrometer (VG-Micromass) especially developed for investigations by the Knudsen method (collector system with conversion dynodes, no mass discrimination). The ionization was achieved by electron impact. For preparation of the intermetallic compound stoichiometric amounts of the components—pure cesium, packed and stored under high vacuum (Merck), and pure gold (Degussa), cut into small pieces—were weighed under pure argon into a molybdenum Knudsen cell. The cell, sealed by a screw-top lid, was heated briefly in an evacuated oven at the melting temperature of gold and then annealed for 5—6 h at 700 °C. After cooling, an effusion orifice in the cell was rapidly opened in a stream of argon and the cell then directly attached to the mass spectrometer.

The mass spectrum obtained at 60 eV and 70 μA showed in addition to Cs^+, Cs^{2+}, and Au^+ a distinct signal for $CsAu^+$. In the temperature range 1200—1500 K the intensity of the signal at $m/e = 330$ is weaker by a factor of about 10^3 than that of the Cs^+ signal. Figure 1 shows plots of the ionization curves of $CsAu^+$ and Au^+ obtained at a Knudsen cell temperature of 1490 K.

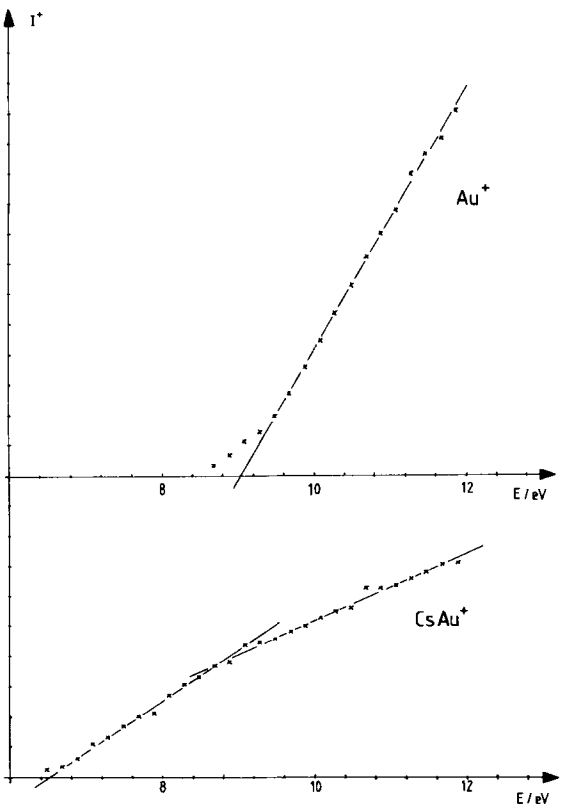


Fig. 1. Ionization curves of $CsAu^+$ and Au^+. Ion current in arbitrary units.

Extrapolation of the curves gave appearance potentials of 6.6 ± 0.3 eV for $CsAu^+$ and 9.0 ± 0.3 eV for Au^+. As a rule of thumb, an appearance potential near to the mean value of the ionization potentials of its atoms can be expected for molecules without free valence electrons. For Cs and Au this leads to 6.55 eV. The experimental value for Au^+ agrees within the limits of error with the ionization potential of Au (9.22 eV).

A decrease in the slope of the ionization curve of $CsAu^+$ at 8.7 eV can be interpreted in terms of the fragmentation process

$$CsAu + e^- \rightarrow Cs^+ + Au + 2e^-; \quad \Delta E^* = 8.7 \pm 0.3 \text{ eV}$$

A corresponding increase in the slope of the ionization curve of Cs^+ is not observable since the differences in intensity of the two reaction channels for formation of Cs^+ are too great.

Conclusions on the bond energy of the molecule can be drawn from the fragmentation energy if the ionization potentials of the fragment ions are known and if it can be assumed that the fragmentation products are formed without additional kinetic energy.

[*] Prof. Dr. K. G. Weil, Dipl.-Ing. B. Busse
Institut für Physikalische Chemie der Technischen Hochschule
Petersenstrasse 20, D-6100 Darmstadt (Germany)

Thus, from a thermodynamic cycle we obtain for the bond energy

$$D(\mathrm{CsAu}) = \Delta E^* - I(\mathrm{Cs}) = 8.7\ \mathrm{eV} - 4.0\ \mathrm{eV} = 4.7\ \mathrm{eV}$$
$$\approx 460 \pm 30\ \mathrm{kJ/mol}$$

At first sight this value appears astonishingly high; however, it is consistent with the expected formation of an ionic bond due to the difference in electronegativities of gold and cesium. Calculation of the bond energy from the electronegativities and known dissociation energies of the dimers Cs_2 and Au_2 according to *Pauling*[4] gives a value of 430 kJ/mol. Also interesting is a comparison with the isostructural CsCl, for which the value $D(\mathrm{CsCl}) = 444$ kJ/mol was found[5].

Our findings clearly indicate that the stability of the cesium auride molecule is essentially determined by ionic bonding, with cesium acting as the donor and gold as the acceptor.

Received: April 24, 1979 [Z 269 IE]
German version: Angew. Chem. *91*, 664 (1979)

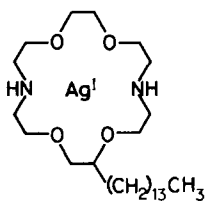
CAS Registry number:
CsAu, 12256-37-0

[1] *B. Meyer*, Ber. Bunsenges. Phys. Chem. *82*, 24 (1978).
[2] *R. P. Elliot:* Constitution of Binary Alloys, 1st Suppl. McGraw-Hill, New York 1965.
[3] *H. Hoshino, R. W. Schmutzler, F. Hensel*, Phys. Lett. *51 A*, 7 (1975).
[4] *L. Pauling:* Die Natur der chemischen Bindung. Verlag Chemie, Weinheim 1973.
[5] *L. Brewer, E. Bracket*, Chem. Rev. *61*, 425 (1961).

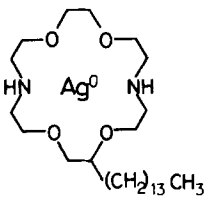
Complexes of Nitrogen-Containing Crown Ether Surfactants with Stable Silver Atoms[**]

By *Robin Humphry-Baker, Michael Grätzel, Pietro Tundo,* and *Ezio Pelizzetti*[*]

Nitrogenous crown ethers bearing long alkyl chains as substituents, such as *(1)*, are surfactants, form micelles, and complex cations[1,3]. We have now succeeded in reducing the complex *(1)*·Ag^+ photochemically and thermally to *(1)*·Ag^0. The complexed silver atoms do not aggregate to form clusters or crystalline silver.



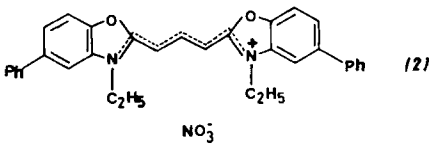
(1)·Ag^+



(1)·Ag^0

The complex *(1)*·Ag^+ is formed spontaneously on treatment of 2-tetradecyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane *(1)* (see ref. [2] for synthesis) with equimolar amounts of $AgNO_3$. The binding constant of Ag^+ ion with the crown ether containing no alkyl side chain has been reported[3] to be $\approx 7 \times 10^7$. Since alkyl substitution is not expected to change this value significantly, it may safely be assumed that practically all the Ag^+ ions are in the complexed state. All the experiments were carried out at concentrations above the CMC of *(1)*·Ag^+, *i.e.* 3.3×10^{-4} mol/l. The molecular weight of the relatively large micellar aggregates (6.3×10^6) was determined by quasielastic light scattering.

In the photochemical reduction of Ag^+ in *(1)*·Ag^+, the cyanine dye *(2)* was used as a sensitizer. This dye absorbs in



(2)

the visible region[4] ($\lambda_{max} = 500$ nm) and due to its hydrophobic nature is expected to associate quantitatively with *(1)*·Ag. In solutions of simple micelles such as sodium laurylsulfate *(2)* displays a strong fluorescence ($\phi_F = 0.45$). This emission is totally quenched ($\phi_F < 10^{-6}$) in micellar solutions of *(1)*·Ag^+. On illumination with visible light, rapid bleaching of the cyanine and formation of a new stable absorption band with a maximum at $\lambda = 415$ nm is observed (Fig. 1). The hydrophobic species produced is hence readily extracted into a chloroform solution ($\lambda_{max} = 410$ nm; Fig. 1).

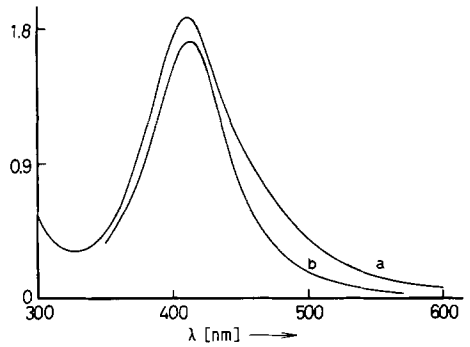


Fig. 1. Absorption spectra of *(1)*·Ag^0 (a) 8.5×10^{-4} M in $CHCl_3$ and (b) 8.5×10^{-4} M in H_2O.

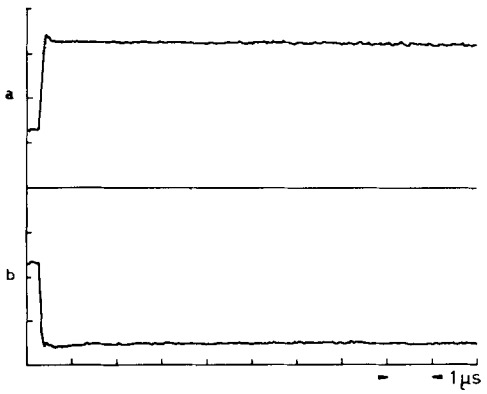


Fig. 2. Transient traces recorded on laser excitation (532 nm) of 1.0×10^{-6} mol/l of *(2)* in *(1)*·Ag^+ micelles. (a) Absorption of *(1)*·Ag^0 (415 nm) and (b) bleaching of the ground-state absorption of *(2)* (500 nm).

The dynamics of the photoreaction of *(2)* with *(1)*·Ag^+ were examined by laser photolysis. A 15 ns pulse of a Q-switched Nd-laser was used to excite the cyanine and resulting changes in the absorbance of the solution were monitored by kinetic spectroscopy (Fig. 2). An irreversible bleach-

[*] Prof. Dr. M. Grätzel, Dr. R. Humphry-Baker
Institut de chimie physique, École Polytechnique Fédérale
CH-1015 Lausanne (Switzerland)
Prof. Dr. P. Tundo
Istituto di Chimica Organica, Università di Torino (Italy)
Prof. Dr. E. Pelizetti
Istituto di Chimica Analitica, Università di Torino (Italy)

[**] Support of this work by the Swiss National Foundation (Grant No. 4.061.076.04) and Ciba-Geigy, Basel (Switzerland) is gratefully acknowledged.

ing is observed at 500 nm, while at 415 nm a stable absorption is produced. These events are so fast that they both occur within the duration of the laser pulse. The end-of-pulse spectrum is identical with that observed after steady-state illumination.

These observations are rationalized in terms of the one-electron reduction of the complexed silver ion according to:

$$(2)^* + Ag^+ \rightarrow Ag^0 + \text{products} \qquad (1)$$

where *(2)** stands for the excited cyanine dye. The spectrum in Figure 1 is attributed to silver atoms stabilized by the macrocyclic ligand *(1)*. This may be compared with the absorption of single silver atoms (matrix isolation spectroscopy)[5]. It appears that in our system Ag^0 is prevented from aggregation through insertion in the crown ether cavity.

Photoinduced reduction of Ag^+ can also be performed with a number of other donor chromophores, such as porphyrins, $Ru(bpy)_3^{2+}$, and pyrene[6]. In all those cases no back reaction between oxidized donor and Ag^0 is observed. Apparently, the donor cation is ejected from the positively charged aggregates by electrostatic interactions before back transfer of electrons can take place[7]. Once in the aqueous phase, re-entry of the donor cation into the micelle is prevented by the repulsive surface charge. We conclude that in the photoinduced reduction of Ag^+ to silver atoms the functional macrocyclic ligand *(1)* serves three important purposes: i) by permitting high local concentration of acceptor Ag^+ it drastically accelerates the forward rate—and hence the yield—of reaction (1); ii) it stabilizes the silver atoms; and iii) it prevents back transfer of electrons by means of a microscopic electrostatic barrier (lipid/water interface).

Quantitative conversion of *(1)*·Ag^+ into *(1)*·Ag^0 can be achieved, for example, by using $NaBH_4$ as a reductant. The spectrum of the product obtained is identical with that shown in Figure 1. The *(1)*·Ag^0 complex has reducing properties and is quantitatively reoxidized to *(1)*·Ag^+ by acceptors such as Cu^{2+} and $Fe(CN)_6^{3-}$.

The redox processes may be accomplished electrochemically. A reversible cathodic wave with a half-wave potential around 0.1 V (NHE) is observed[8]. Controlled potential electrolysis at −0.5 V produces a species with an absorption spectrum identical with that presented in Figure 1.

It is interesting to note that the standard potential $E^0(Ag^+/Ag^0)$ calculated from the silver electrode potential and the Ag sublimation energy is −1.25 V. A binding constant of 10^{21} would thence be calculated for complexation of Ag atoms by the macrocyclic ligand *(1)*. It is probably a consequence of the considerable increase in size on going from Ag^+ to Ag^0 that the stability of the complex increases in such a drastic manner.

Received: May 30, 1979 [Z 270 IE]
German version: Angew. Chem. *91*, 669 (1979)

CAS Registry numbers:
(1)·Ag^+, 71042-56-3; *(1)*·Ag^0, 71042-57-4; *(2)*, 71032-75-2

[1] *M. Cinquini, F. Montanari, P. Tundo*, J. Chem. Soc. Chem. Commun. *1975*, 393; *J. Le Moigne, P. Gramain, J. Simon*, J. Colloid Interface Sci. *60*, 565 (1977); *Y. Moroi, E. Promauro, M. Grätzel, E. Pelizzetti, P. Tundo*, J. Coll. Interface Sci. *64*, 341 (1974).

[2] *M. Cinquini, P. Tundo*, Synthesis *1976*, 516.

[3] For binding of metal ions to nitrogen-containing crown ethers, see, *e.g., J. M. Lehn, J. P. Sauvage, B. Dietrich*, J. Am. Chem. Soc. *92*, 2916 (1970); *H. K. Frensdorf, ibid. 93*, 600 (1971).

[4] *R. Humphry-Baker, M. Grätzel, R. Steiger*, J. Am. Chem. Soc., in press.

[5] *W. Schulze, H. N. Becker, H. Abe*, Chem. Phys. *35*, 177 (1978).

[6] *R. Humphry-Baker, M. Grätzel, P. Tundo*, J. Am. Chem. Soc., in press.

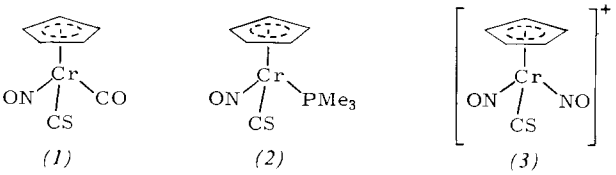
[7] *Ch. Wolff, M. Grätzel*, Chem. Phys. Lett. *52*, 542 (1977).

[8] *A. Delay*, unpublished results.

η^5-Cyclopentadienylchromium Complexes with Thiocarbonyl and Nitrosyl Ligands[**]

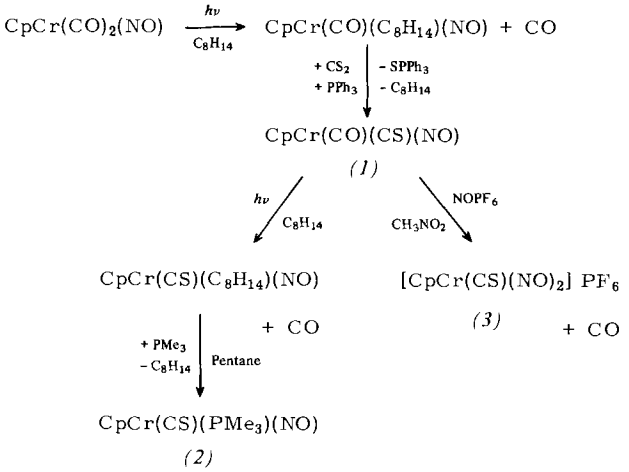
By *Max Herberhold* and *Paul D. Smith*[*]

Comparison of the acceptor properties of diatomic ligands (L = CO, CS, NO) requires the availability of model complexes containing different ligand combinations. We now report the new chromium complexes *(1)*—*(3)* containing the rare combination CS/NO hitherto found only in cations[1].



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

Incorporation of a CS ligand into the parent complex $CpCr(CO)_2(NO)$ can be accomplished by a method previously developed[2a] for the isosteric compound $CpMn(CO)_3$ which involves reaction of the *cis*-cyclooctene derivative $CpCr(CO)(C_8H_{14})(NO)$[3] with both CS_2 and a sulfur atom acceptor such as PPh_3. No carbon disulfide intermediate "$CpCr(CO)(CS_2)(NO)$" could be detected although a labile $CpMn(CO)_2(CS_2)$ complex is known[2].



The CO ligand remaining in *(1)* is more firmly bonded than that in the cation $[CpMn(CO)(CS)(NO)]^+$[1b] but can be replaced photolytically by two-electron ligands such as cyclooctene or by the nitrosyl cation ($L = NO^+$). Table 1 lists some spectroscopic data of the thiocarbonyl complexes *(1)*—*(3)* and of the corresponding carbonyl complexes. As a general rule, the stretching frequencies [ν(CO), ν(CS), ν(NO)] increase and the NMR signals of the cyclopentadienyl protons [δ(Cp)] are shifted downfield as the electron deficit on the metal increases.

Both the ν(NO) and $\delta(C_5H_5)$ values indicate that the thiocarbonyl group (L = CS) is a much more effective acceptor ligand than the carbonyl group (L = CO) in the neutral complexes CpCr(CO)(L)(NO). The thionitrosyl group in $CpCr(CO)_2(NS)$[4] is also superior as an acceptor to the nitro-

[*] Prof. Dr. M. Herberhold [+], Dr. P. D. Smith
Anorganisch-chemisches Institut der Technischen Universität
Lothstrasse 17, D-8000 München 2 (Germany)

[+] Present address: Laboratorium für Anorganische Chemie der Universität, Universitätsstrasse 30, D-8580 Bayreuth (Germany)

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

Table 1. IR stretching absorptions ν(CO), ν(NO), and ν(CS) and chemical shifts δ(Cp) of the cyclopentadienyl ring protons.

Complex	IR [a] ν(CO) [c]	ν(NO) [c]	ν(CS) [d, e]	k(CO) [f]	^{1}H-NMR [b] δ(Cp) [c]
$CpCr(CO)_2(NO)$	2025, 1948	1693	—	15.94	5.24
$CpCr(CO)(CS)(NO)$ *(1)*	2010	1705	1253	16.31	5.39
$CpCr(PMe_3)(CO)(NO)$	1907	1629	—	14.69	4.98 [g]
$CpCr(PMe_3)(CS)(NO)$ *(2)*	—	1654	1205	—	5.16 [h]
$[CpCr(CO)(NO)_2]PF_6$	2142	1875, 1789	—	18.53	6.25
$[CpCr(CS)(NO)_2]PF_6$ *(3)*	—	1867, 1779	1352	—	6.14

[a] Perkin-Elmer 297; cm^{-1}. [b] Jeol C-60-HL; δ values rel. to TMS int., calibration with TMS/$CHCl_3$. [c] Nitromethane solution. [d] KBr. [e] The ν(CS) absorption in nitromethane solution appears at 1258 and 1221 cm^{-1} for *(1)* and *(2)*; ν(CS) for *(3)* could not be observed in the 1620—1340 cm^{-1} region because of the strong absorption of the solvent. [f] Stretching force constants [N/cm] according to *F. A. Cotton, C. S. Kraihanzel*, J. Am. Chem. Soc. *84*, 4432 (1962). [g] Doublet, J(P,H) = 2.45 Hz. [h] Doublet, J(P,H) = 2.1 Hz.

syl group in $CpCr(CO)_2(NO)$, even though the difference is only slight. In the cations $[CpCr(L)(NO)_2]^+$ (L = CO, CS), on the other hand, spectroscopic criteria show CO to be the better acceptor ligand. These results are in accord with a rule first stated by *Andrews*[5] which stipulates that the ratio of the π-acceptor to the $(\sigma+\pi)$-donor behavior, *i.e.* the acceptor capacity of the CS ligand in thiocarbonyl complexes of the $M(CO)_n(CS)$ type, exceeds that of the CO ligand only if the Cotton-Kraihanzel force constant k(CO) of the corresponding carbonyl complex $M(CO)_{n+1}$ lies below *ca.* 17.1 N/cm^{-1}.

Experimental[6]

Photolysis of a solution of $CpCr(CO)_2(NO)$[7] (*ca.* 1 g, 4.9 mmol) in *cis*-cyclooctene (250 ml) for 2 h proceeds with elimination of CO to form $CpCr(CO)(C_8H_{14})(NO)$[3]. The solvent is stripped off and the complex is dried for 2 h at 35 °C *in vacuo*. The dry olefin complex is then treated with triphenylphosphane (*ca.* 1.3 g, 5 mmol) and CS_2 (30 ml); once the IR spectrum of the green solution indicates completion of reaction after *ca.* 60 h, the CS_2 is stripped off. Purification is accomplished by filtration of *(1)*, first in benzene/pentane (1:5) and then in pure pentane, over a G3 frit covered with a layer of silica gel/pentane. *(1)* is finally crystallized from pentane (50 ml) at −78 °C. Yield *ca.* 0.43 g (40%) of green crystals, m.p. 42 °C (under argon).

A solution of *(1)* (0.175 g, 0.80 mmol) in *cis*-cyclooctene (200 ml) is irradiated for 1 h and then evaporated to dryness (0.1 torr, 25 °C). The residue is stirred for 24 h with pentane (50 ml) and trimethylphosphane (1 ml). After removal of the pentane and the PMe_3, the residue is taken up in benzene and filtered over a G3 frit covered with a layer of silica gel/pentane. The green complex *(2)* crystallizes from pentane (−78 °C). Yield 0.1 g (50%), m.p. 101 °C (under argon).

To a solution of *(1)* (0.19 g, 0.87 mmol) in nitromethane (30 ml) is added dropwise a solution of $NOPF_6$ (0.15 g, 0.87 mmol) in nitromethane (4 ml) at −25 °C (evolution of gas and change in color). After filtration (filter flocks) into cold ether (150 ml) the resulting precipitate of olive green *(3)* is washed once again with cold ether and with pentane, and dried at −30 °C. Yield 0.20 g (63%), dec. (in a sealed tube under Ar) 125 °C with liberation of gas.

Received: March 19, 1979 [Z 266 IE]
German version: Angew. Chem. *91*, 662 (1979)

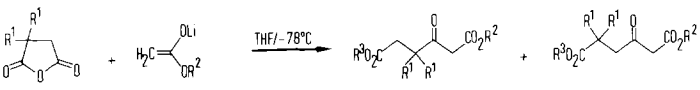
CAS Registry numbers:
(1), 71032-39-8; *(2)*, 71032-40-1; *(3)*, 71032-42-3; $CpCr(CO)_2(NO)$, 36312-04-6; $CpCr(CO)(C_8H_{14})(NO)$, 38816-33-0; $CpCr(PMe_3)(CO)(NO)$, 71032-43-4; $[CpCr(CO)(NO)_2]PF_6$, 69439-82-3

[1] a) *M. J. Mays, F. P. Stefanini*, J. Chem. Soc. *A 1971*, 2747; b) *A. Efraty, R. Arneri, J. Sikora*, J. Organomet. Chem. *91*, 65 (1975).
[2] a) *A. E. Fenster, I. S. Butler*, Inorg. Chem. *13*, 915 (1974); b) *M. Herberhold, M. Süss-Fink, C. G. Kreiter*, Angew. Chem. *89*, 191 (1977); Angew. Chem. Int. Ed. Engl. *16*, 193 (1977).
[3] *M. Herberhold, H. Alt*, J. Organomet. Chem. *42*, 407 (1972); *M. Herberhold, H. Alt, C. G. Kreiter*, Justus Liebigs Ann. Chem. *1976*, 300.
[4] *B. W. S. Kolthammer, P. Legzdins*, J. Am. Chem. Soc. *100*, 2247 (1978).
[5] *M. A. Andrews*, Inorg. Chem. *16*, 496 (1977).
[6] All operations performed under protective gas (Ar).
[7] For the preparation cf. *J. L. Atwood, R. Shakir, J. T. Malito, M. Herberhold, W. Kremnitz, W. P. E. Bernhagen, H. G. Alt*, J. Organomet. Chem. *165*, 65 (1979).

Reaction of α-Lithioacetic Acid Esters with Succinic Anhydrides

By *Franz-Peter Montforts* and *Silvio Ofner*[*]

β-Ketoadipic acid esters have been prepared in relatively low overall yields as intermediates for the synthesis of natural products in multistep reaction sequences involving tedious purification operations *via* malonic ester and acetic ester syntheses[1]. We have now found that succinic anhydride *(1)* reacts with α-lithioacetic acid esters *(2)* in a single reaction step to give the corresponding readily crystallizing β-ketoadipic acid monoesters:



(1a), R^1 = H *(2a)*, R^2 = $CH_2C_6H_5$
(1b), R^1 = CH_3 *(2b)*, R^2 = $C(CH_3)_3$

(3) *(4)*

(3a)=*(4a)* : R^1=R^3=H, R^2= $CH_2C_6H_5$
(3b)=*(4b)* : R^1=R^3=H, R^2= $C(CH_3)_3$
(3c)≠*(4c)* : R^1=R^3=CH_3, R^2= $C(CH_3)_3$

Starting cpds.	Products	Product ratio	Yield [%]
(1a) + *(2a)*	*(3a)* = *(4a)*	—	62
(1a) + *(2b)*	*(3b)* = *(4b)*	—	78
(1b) + *(2b)*	*(3c)* + *(4c)*	71:29 [a]	96 [b]

[a] The isomeric esters *(3c)* and *(4c)* were identified by their 270-MHz ^{1}H-NMR spectra ($CDCl_3$/TMS) as well as by trifluoroacetic acid degradation affording (preparative gas chromatography) methyl 3,3-dimethyl-4-oxopentanoate *(5a)* and methyl 2,2-dimethyl-4-oxopentanoate *(5b)*. The product ratio was determined by GC analysis of the methyl esters *(3c)* and *(4c)* on 5% OV 210 Chromosorb W-AW-DMCS 80—100 (60 ml N_2/min) and ^{1}H-NMR spectroscopically. [b] After esterification with diazomethane and bulb-to-bulb distillation of the mixture of diesters.

The geminally dimethylated anhydride *(1b)* reacts preferably at the higher substituted carbonyl function. This finding is consistent with experiments on the reduction of geminally

[*] Dr. F. P. Montforts
Institut für Organische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Dipl.-Chem. S. Ofner
Laboratorium für Organische Chemie, ETH-Zentrum
Universitätstr. 16, CH-8006 Zürich (Switzerland)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0808-0632 $ 02.50/0

disubstituted succinic anhydrides and succinimides[2] and can be explained in terms of *Bürgi*'s and *Dunitz*'s hypothesis[3], according to which the angle of nucleophilic attack at the carbonyl group is greater than 90°, thereby favoring reaction path *B* over *A* (cf. Fig. 1).

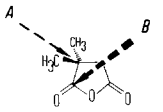


Fig. 1. Possible reaction paths for nucleophilic attack at the carbonyl group of geminally dimethylated succinic anhydride *(1b)*.

To our knowledge this is the first example of regioselective addition of a carbon nucleophile in such a system where there are two possible modes of attack.

Procedure

A solution of *n*-butyllithium (43.5 ml, 0.100 mol) in hexane (2.3 M) is added dropwise (within 30 min) at 0 °C under argon to a stirred solution of hexamethyldisilazane (21.3 ml, 0.102 mol) in anhydrous tetrahydrofuran (40 ml). After cooling to −78 °C, 0.101 mol of the ester *(2a)* or *(2b)* is added within 15 min to the solution and stirring continued for a further 45 min. To the resulting α-lithioacetic ester solution is added dropwise over 20 min a solution of the anhydride *(1a)* or *(1b)* (0.05 mol) in tetrahydrofuran (60 ml). The mixture is stirred for 2.5 h in a methanol/dry-ice bath while the temperature is allowed to increase to −20 °C. After treatment with 8 ml conc. hydrochloric acid and 50 ml water, it is then concentrated by evaporation in a rotary evaporator. The neutral solution is adjusted to pH 2 with conc. hydrochloric acid and extracted with ether (5 × 50 ml). The combined extracts are dried over sodium sulfate and the solvent removed in a rotary evaporator. The β-ketoadipic acid esters *(3a)* and *(3b)* crystallize from ether/hexane. The products obtained on reaction of *(1b)* with *(2b)* are esterified with ethereal diazomethane solution in the usual way and the esters *(3c)* and *(4c)* are purified by bulb-to-bulb distillation.

Received: March 19, 1979 [Z 260 IE]
German version: Angew. Chem. *91*, 656 (1979)

CAS Registry numbers:
(1a), 108-30-5; *(1b)*, 17347-61-4; *(2a)*, 71010-30-5; *(2b)*, 53503-61-0; *(3a)*, 71010-31-6; *(3b)*, 71010-32-7; *(3c)*, 71010-33-8; *(4c)*, 71010-34-9

[1] *G. W. Kenner, J. Rimmer, K. M. Smith, J. F. Unsworth*, J. Chem. Soc. Perkin Trans. 1 *1977*, 332; *D. K. Banerjee, K. M. Sivanandaiah*, J. Org. Chem. *26*, 1634 (1961).

[2] *D. M. Bailey, R. E. Johnson*, J. Org. Chem. *35*, 3574 (1970); *J. B. P. A. Wijneberg, H. E. Schoemaker, W. N. Speckamp*, Tetrahedron *34*, 179 (1978).

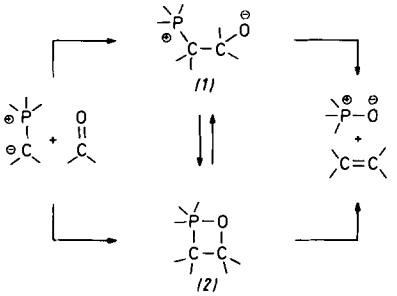
[3] *H. B. Bürgi*, Angew. Chem. *87*, 461 (1975); Angew. Chem. Int. Ed. Engl. *14*, 460 (1975); *R. E. Rosenfield jr., J. D. Dunitz*, Helv. Chim. Acta *61*, 2176 (1978).

New Evidence for Zwitterionic Intermediates in the Wittig Reaction[**]

By *Manfred Schlosser* and *Huynh Ba Tuong*[*]

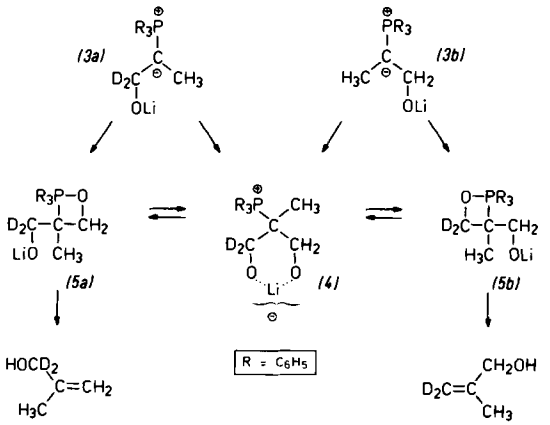
Dedicated to Professor André S. Dreiding on the occasion of his 60th birthday

For a long time open-chain "P-betaïnes" *(1)* were considered the decisive and momentarily stable intermediates of the Wittig reaction[1], whereas the four-membered heterocyclic oxaphosphetanes *(2)* were regarded as high-energy species too short-lived for detection. After low temperature NMR studies had revealed the presence of—fairly stable—oxaphosphetanes rather than the expected betaines[2], a new hypothesis emerged claiming that oxaphosphetanes would always form directly from the components, ylid and aldehyde, bypassing a zwitterionic precursor[2].



This simplification of the reaction mechanism has, however, one great drawback: the postulated[2] $[2_s+2_a]$-cycloaddition does not unequivocally account for the *cis*-stereoselectivity[3] of the Wittig reaction in "salt-free media" nor in any way explain the salt effect[3] on the stereochemistry and reaction rate. Therefore, we support the original view that adduct formation proceeds *via* a betaine-like transition state and that an equilibrium is rapidly established between the betaines *(1)* and the—generally but not always—more stable oxaphosphetanes *(2)*. Electrophilic reagents such as lithium iodide[4], formaldehyde[5], and triphenylborane[5] trap betaïnes from the equilibrium. We have now obtained further evidence for the fast and reversible transition between oxaphosphetanes and betaines by means of isotopic labeling.

A solution of salt-free triphenylphosphonioethylid in tetrahydrofuran was treated at −75 °C consecutively with formaldehyde solution[6] and *sec*-butyllithium. Dideuterioformaldehyde was then added to the resulting "betaine-ylid" *(3b)*. After subsequent addition of potassium *tert*-butoxide and warming to 25 °C, 2-methylallyl alcohol could be separated in 80% yield, being doubly deuteriated equally at the carbon adjacent to oxygen or at the terminal olefinic carbon (NMR results). The same product mixture was formed when deuterium-free formaldehyde was added to the deuteriated betaine-ylid *(3a)*.



The ^{31}P-NMR spectrum of the adduct formed from the zwitterion *(3)* and formaldehyde shows a major signal at $\delta = -55$ (accompanied by a weaker signal at $\delta = -51$, rel. to

[*] Prof. Dr. M. Schlosser, Dr. Huynh Ba Tuong
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung (Project 2.467.0.75 and 2.693.0.76).

85% H_3PO_4), compatible with an oxaphosphetane structure *(5)*. The question remains whether this intermediate is formed directly on combining the reaction partners or whether it is formed indirectly *via* a betaine precursor, formulated as the chelate *(4)*. In either respect, the two species (*(4)* and *(5a)/(5b)*) must be in an equilibrium with each other, which apparently is very mobile even at $-80\,^{\circ}C$. For, on addition of acetyl chloride, which reacts spontaneously with lithium alkoxides at $-80\,^{\circ}C$, to the betaine-ylid/formaldehyde adduct, we obtained 2-methylallyl acetate in which once again both types of methylene groups were isotopically labeled in equal distribution.

The reaction of aliphatic or aromatic aldehydes with betaine-ylids to give allyl alcohols usually proceeds with high regio- or stereoselectivity[6, 7]. This in no way contradicts the postulated betaine/oxaphosphetane equilibrium. On the contrary, due to this equilibrium the reaction can proceed *via* the sterically least hindered oxaphosphetane (no bulky groups in *cis* position) to give the energetically most favorable product[8].

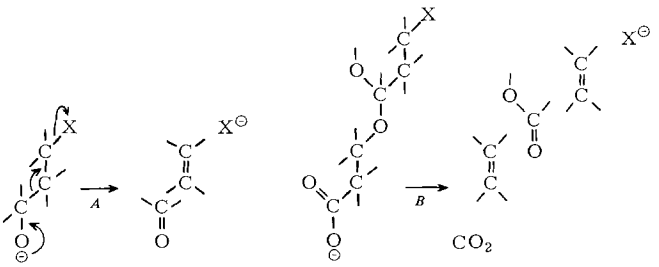
Received: June 6, 1979 [Z 257 IE]
German version: Angew. Chem. *91*, 675 (1979)

CAS Registry numbers:
(3a), 71010-07-6; *(3a)*, (ionic form), 71010-08-7; *(3b)*, 71010-09-8; *(3b)*, (ionic form), 71010-10-1; *(4)*, 71032-51-4; *(5a)*, 71010-11-2; *(5b)*, 71010-12-3; 1,1-dideuterio-2-methyl-2-propen-1-ol, 71010-13-4; 3,3-dideuterio-2-methyl-2-propen-1-ol, 71010-14-5

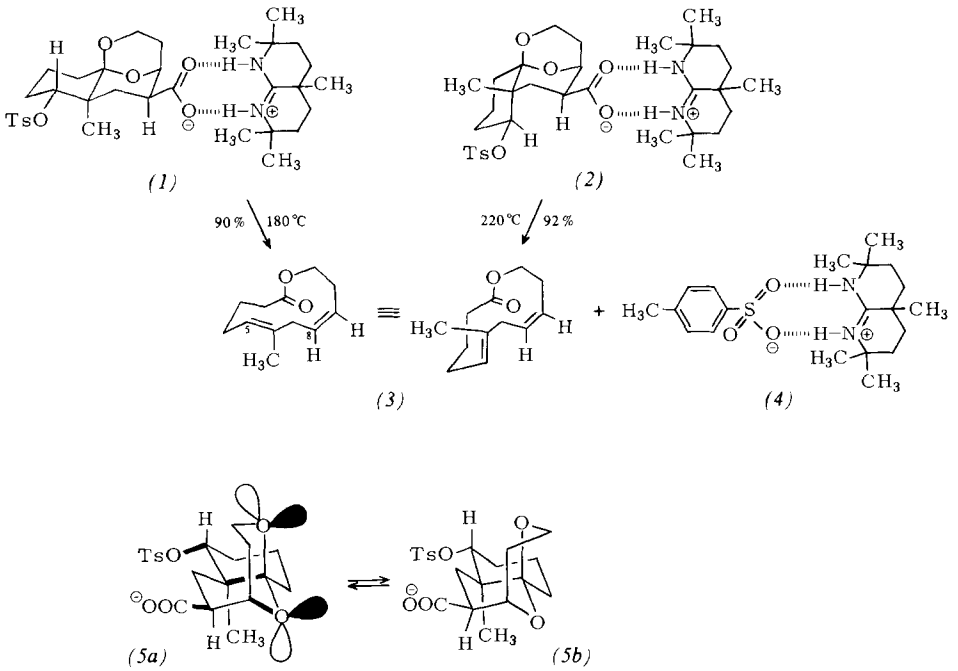
A Fragmentational Approach to Macrolides: (5-*E*, 8-*Z*)-6-methyl-5,8-undecadien-11-olide[**]

By *Daniel Sternbach, Masayuki Shibuya, Fritz Jaisli, Marco Bonetti*, and *Albert Eschenmoser*[*]

The cleavage of C C single bonds according to the general scheme A[1] has proved to be an effective method for the modification of carbon frameworks and indeed constitutes the preparatively most useful reaction available today in



heterolytic fragmentations[2]. This type of process has found specific application especially in the synthesis of cyclic compounds of medium ring size[3]. Using the title compound *(3)* as an example, we demonstrate here the application of this reaction principle in the preparation of unsaturated macrolides[4], the key step being a decarboxylative double fragmentation of the type *B*.



Scheme 1. The yields are based on analytically pure products.

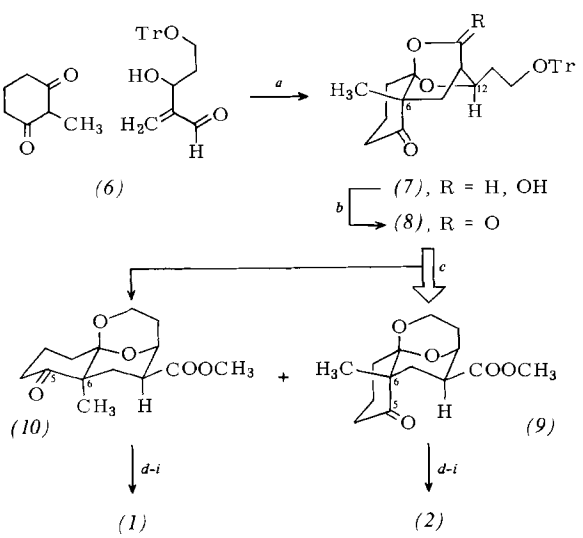
[1] Reviews: *A. W. Johnson:* Ylid Chemistry. Academic Press, New York 1966; *M. Schlosser*, Top. Stereochem. 5, 1 (1970); *M. Schlosser* in *F. Korte, H. Zimmer, K. Niedenzu:* Methodicum Chimicum. Vol. 7, pp. 529–552. Thieme, Stuttgart 1976.
[2] *E. Vedejs, K. A. Snoble*, J. Am. Chem. Soc. *95*, 5778 (1973).
[3] *M. Schlosser, K. F. Christmann*, Justus Liebigs Ann. Chem. *708*, 1 (1967).
[4] *M. Schlosser, Huynh Ba Tuong, C. Tarchini*, Chimia *31*, 219 (1977).
[5] *Huynh Ba Tuong, M. Schlosser*, unpublished; cf. Dissertation *Huynh Ba Tuong*, Université de Lausanne 1976, pp. 16–17.
[6] *M. Schlosser, D. Coffinet*, Synthesis *1971*, 380.
[7] *E. J. Corey, H. Yamamoto*, J. Am. Chem. Soc. *92*, 3523 (1970); *M. Schlosser, K. F. Christmann, A. Piskala, D. Coffinet*, Synthesis *1971*, 29; *M. Schlosser, D. Coffinet, ibid. 1972*, 575; *E. J. Corey, P. Ulrich, A. Venkatesvarlu*, Tetrahedron Lett. *1977*, 3231.
[8] In this context a metalloxy group has to be considered a very bulky substituent due to solvation and, even more, to aggregation.

[*] Prof. Dr. A. Eschenmoser, Dr. D. Sternbach, dipl. Ing.-Chem. F. Jaisli, dipl. sc. nat. M. Bonetti
Organisch-chemisches Laboratorium der ETH
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Prof. Dr. M. Shibuya
Faculty of Pharmaceutical Sciences, Tokushima University
Tokushima (Japan)

[**] 14th Communication on Synthetic Methods. This work was supported by the Anniversary Funds of the ETH Zürich. *Dr. D. Sternbach* thanks the Schweizerischer Nationalfonds for a postdoctoral study grant. Preliminary experiments on the work described here were performed by Dr. *M. Jung* (1974). We thank *S. Denmark* (ETH) for his help with the translation of the German manuscript. 13th Communication ref. [13].

Heating either of the diastereomeric amidinium salts *(1)* or *(2)* for three minutes at their melting points under argon affords uniformly in both cases under vigorous evolution of CO_2 the title substance *(3)* and the amidinium tosylate *(4)* (Scheme 1). The structural formula of the anion *(5a)* of the *trans* isomer *(1)* illustrates how the educts are programmed to undergo a double fragmentation: The central C–C bridge in *(5a)* is antiperiplanar[5, 3c] to the equatorial tosylate group as well as to the two "equatorial" electron pair sp^3 axes of the acetal function[6], and the equatorial carboxyl group is antiperiplanar to one of the two acetal linkages. The overall process most likely involves at least two reaction steps, *i.e.* proceeds *via* the corresponding bicyclic dioxonium ion as an intermediate: in any event, the two reaction planes are askew to each other.

Compounds *(1)* and *(2)* are prepared as outlined in Scheme 2. Condensation of β-trityloxypropionaldehyde[7] with α-lithioacrolein diethyl acetal[8] readily affords 2-(1-hydroxy-3-trityloxy) acrolein *(6)*. The aldehyde *(6)* reacts in good yield with 2-methyl-1,3-cyclohexanedione to afford a Michael-adduct in which the free aldehyde remarkably cyclizes to give a diastereomeric mixture of hemiacetals of the type *(7)* (with the requisite boat conformation of one of the rings). Oxidation of *(7)* with sodium metaperiodate and a catalytic amount of ruthenium dioxide produces a mixture of lactone diastereomers in which the crystalline lactone *(8)* is present to an extent of 86%[9]. Compound *(8)* can be converted in high yield by acid-catalyzed methanolysis into the crystalline ketoacetal esters *(9)* and *(10)*. Under conditions of predominantly kinetic control (0.05 equiv. *p*-toluenesulfonic acid in methanol, 60 °C, 3 h), *(9)* and *(10)* are formed in a ratio of 1:2; under more drastic conditions (0.3 equiv. *p*-toluenesulfonic acid, 7 h), the ratio inverts to approx. 5:1. The structure of the *trans* compound *(10)* (mp. 123 °C) is secured by X-ray crystallography[11].

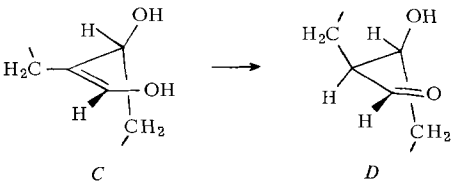


Scheme 2 [10]. The yields are based on analytically pure products. *a:* $(C_2H_5)_3N$, *t*-BuOH, 20 °C (77%).—*b:* $NaIO_4$, RuO_2, CCl_4/H_2O, 20 °C (69%).—*c:* TsOH, CH_3OH, 60 °C [72% *(9)* + 13% *(10)*].—*d:* 4 N KOH, dioxane, CH_3OH, 20 °C.—*e:* Li, NH_3, −33 °C.—*f:* CH_2N_2, ether, CH_3OH [81% hydroxyacetal ester based on *(9)*].—*g:* TsCl, pyridine, 20 °C (90%).—*h:* 4 N KOH, dioxane, CH_3OH, 20 °C (91%).—*i:* 3,3,6,9,9-pentamethyl-2,10-diazabicyclo[4.4.0]dec-1-ene [13], CH_2Cl_2 [96% *(2)*].

The structure of the fragmentation product *(3)* is in accord with all spectral and microanalytical data (see Table 1). The assignment of the *Z*-configuration for the C-8, C-9 double bond is supported by the observed ^{1}H-NMR coupling constant of the two vinyl protons (10.8 Hz; see ref. [12a]), while the *E*-configuration for the double bond between C-5 and C-6 follows from the usual interpretation of stereospecific fragmentation processes[3c, 2c]. The selection of the special bicyclic amidine[13] used in *(1)* and *(2)* is based on the ready crystallizability, solubility and convenient melting properties of the salts derived therefrom. The simplicity of the experimental procedure and the high yields obtained from the fragmentation are consequences of the use of this amidine; the ability of the tosyloxycarboxylic acids to suffer fragmentation is, however, independent.

Table 1. Analytical data of *(3)* [10]. *(3)* is a liquid under normal conditions.

^{1}H-NMR ($CDCl_3$, 360 MHz): δ = 1.63 (s/3 H/CH_3 at C-6), 1.82–1.90 (m/2 H/H_2C-3), 2.07–2.18 (m/4 H/H_2C-2 and H_2C-4), 2.34–2.42 (m/2 H/H_2C-10), 2.64 (d/J = 8 Hz/2 H/H_2C-7), 4.17–4.21 (m/2 H/H_2C-11), 5.09 (t/1 H/J = 7 Hz with fine coupling/HC-5), 5.51–5.61 (m/1 H/HC-9), 5.71–5.80 (m/1 H/HC-8). Decoupling: 2.38 → 5.56 (d/J = 11.2 Hz) and 4.19 (s), 2.64 → 5.76 (d/J = 10.7 Hz).—^{13}C-NMR ($CDCl_3$, 25 MHz): δ = 16.1 (q), 24.0 (t), 27.4 (t), 28.0 (t), 34.1 (t), 36.3 (t), 63.9 (t), 122.7 (d), 128.9 (d), 129.4 (d), 136.7 (s), 174.4 (s).—IR ($CHCl_3$): *e.g.* 1722 (sharp) cm^{-1}.—MS (200 °C): *m/e* = *e.g.* 195 (5%), 194 (44%, M^+), 93 (100%)



The synthesis of the tricyclic fragmentation reactants according to the sequence shown in Scheme 2 is relatively simple and amenable to structural variation[12]. The steric pathway of the protonation of the enol (or enolate) formed by Michael-addition of 2-methyl-1,3-cyclohexanedione on *(6)* is decisive for the success of the reaction sequence. The protonation must proceed in the sense shown (C→D) so that the carboxyl function in *(9)* and *(10)* (as precursors for *(2)* and *(1)*, resp.), comes to rest in an equatorial orientation. The desired steric pathway prevails. This can possibly be explained in terms of a C-protonation antiperiplanar to the hydroxyl group (cf. *D*).

Received: May 3, 1979 [Z 255a IE]
German version: Angew. Chem. *91*, 670 (1979)

CAS Registry numbers:
(1), 70968-71-7; *(2)*, 71030-33-6; *(3)*, 70968-72-8; *(4)*, 70968-73-9; *(6)*, 70968-74-0; *(7)*, 70968-75-1; *(8)* (isomer A), 70968-76-2; *(8)* (isomer B), 71030-34-7; *(9)*, 70968-59-1; *(10)*, 71030-24-5; β-trityloxypropionaldehyde, 67057-68-5; α-lithioacrolein dithyl acetal, 54780-30-2; 2-methyl-1,3-cyclohexanedione, 1193-55-1

[1] *A. Eschenmoser, A. Frey*, Helv. Chim. Acta *35*, 1660 (1952).
[2] a) *C. A. Grob, W. Baumann*, Helv. Chim. Acta *38*, 594 (1955); *C. A. Grob*, Experientia *13*, 126 (1957); b) *C. A. Grob, P. Schiess*, Angew. Chem. *79*, 1 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1 (1967); c) *C. A. Grob, ibid. 81*, 543 (1969) and *8*, 535 (1969).
[3] a) *G. Stork, H. K. Landesmann*, J. Am. Chem. Soc. *78*, 5129 (1956); b) *P. S. Wharton*, J. Org. Chem. *26*, 4781 (1961); c) *P. S. Wharton, G. A. Hugel, ibid. 30*, 3254 (1965); *P. S. Wharton, Y. Sumi, R. A. Kretchmer, ibid. 30*, 234 (1965); d) *E. J. Corey, R. B. Mitra, H. Hota*, J. Am. Chem. Soc. *85*, 362 (1963); *86*, 485 (1964); *G. Ohloff, J. Becker, K. H. Schulte-Elte*, Helv. Chim. Acta *50*, 705 (1967); *A. Eschenmoser, D. Felix, G. Ohloff, ibid. 50*, 708 (1967); *D. Felix, J. Schreiber, G. Ohloff, A. Eschenmoser*, ibid. *54*, 2896 (1971); *A. Fischli, Q. Branca, J. Daly, ibid. 59*, 2442 (1976).
[4] Survey: *S. Masamune, G. S. Bates, J. W. Corcoran*, Angew. Chem. *89*, 602 (1977); Angew. Chem. Int. Ed. Engl. *16*, 585 (1977); *K. C. Nicolaou*, Tetrahedron *33*, 683 (1977); *Th. G. Back, ibid. 33*, 3041 (1977).
[5] *G. Gamboni, H. Schinz, A. Eschenmoser*, Helv. Chim. Acta *37*, 964 (1954); *A. Eschenmoser, L. Ruzicka, O. Jeger, D. Arigoni, ibid. 38*, 1890 (1955).
[6] *P. Deslongchamps*, Tetrahedron *31*, 2463 (1976).
[7] M.p. = 101 °C; prepared by oxidation of 3-trityloxy-1-propanol (m.p. 120 °C) with pyridinium chlorochromate (see *M. G. Bonetti*, Dissertation No. 6360, ETH Zürich, 1979, p. 122). The synthesis of the aldehyde had been worked out by *R. K. Müller* and *S. Baumberger* (ETH).
[8] *J. Ficini, J. C. Depezay*, Tetrahedron Lett. *1969*, 4797; *J. C. Depezay, Y. Le Merer, ibid. 1974*, 2751; *1978*, 2865.
[9] Isolated from the mother liquors of *(8)* by HPL chromatography: *(8a)*, m.p. 142 °C (11%), epimer of *(8)* at C-12; *(8b)*, m.p. 183 °C (2%), epimer at C-12 and C-6. The assignment of the configuration of *(8)* follows from the con-

version of *(8)* into *(9)* and *(10)* [with *(8a)* and *(8b)* this conversion is not possible]. The assignment of a *cis*-ring fusion in compound *(8)* resulting from the fact that reduction of *(8)* with sodium borohydride, trans-acetalation with methanol, and tosylation afforded the *cis*-tosyloxyacetal methyl ester (corresponding to *(2)*) in 48% yield. A *trans*-ring fusion would have led to the derivative corresponding to *(1)*[10].

[10] The intermediates were characterized by elemental and spectroscopic analysis (IR, ^{1}H- and ^{13}C-NMR, MS). Experimental details to be published: *F. Jaisli*, planned Dissertation, ETH Zürich.

[11] *G. Procter, F. Nesme, J. D. Dunitz*, unpublished data. According to crystal structure analysis, the 1,3-dioxane ring of *(10)* is in the boat conformation [analogous to structure *(5b)*]. The same holds true for the respective hydroxyacetal ester with an axial hydroxy group [see ref. [12b], structure *(9)*]. We would like to thank *Prof. Dunitz* for allowing us to use these data here (see also ref. [12a]).

[12] a) *M. Shibuya, F. Jaisli, A. Eschenmoser*, Angew. Chem. *91*, 672 (1979); Angew. Chem. Int. Ed. Engl. *18*, 636 (1979); b) *F. Jaisli, D. Sternbach, M. Shibuya, A. Eschenmoser, ibid. 91*, 673 (1979) and *18*, 637 (1979); c) *N. R. A. Beeley, P. R. Jenkins, V. G. Matassa, M. Bonetti*, unpublished.

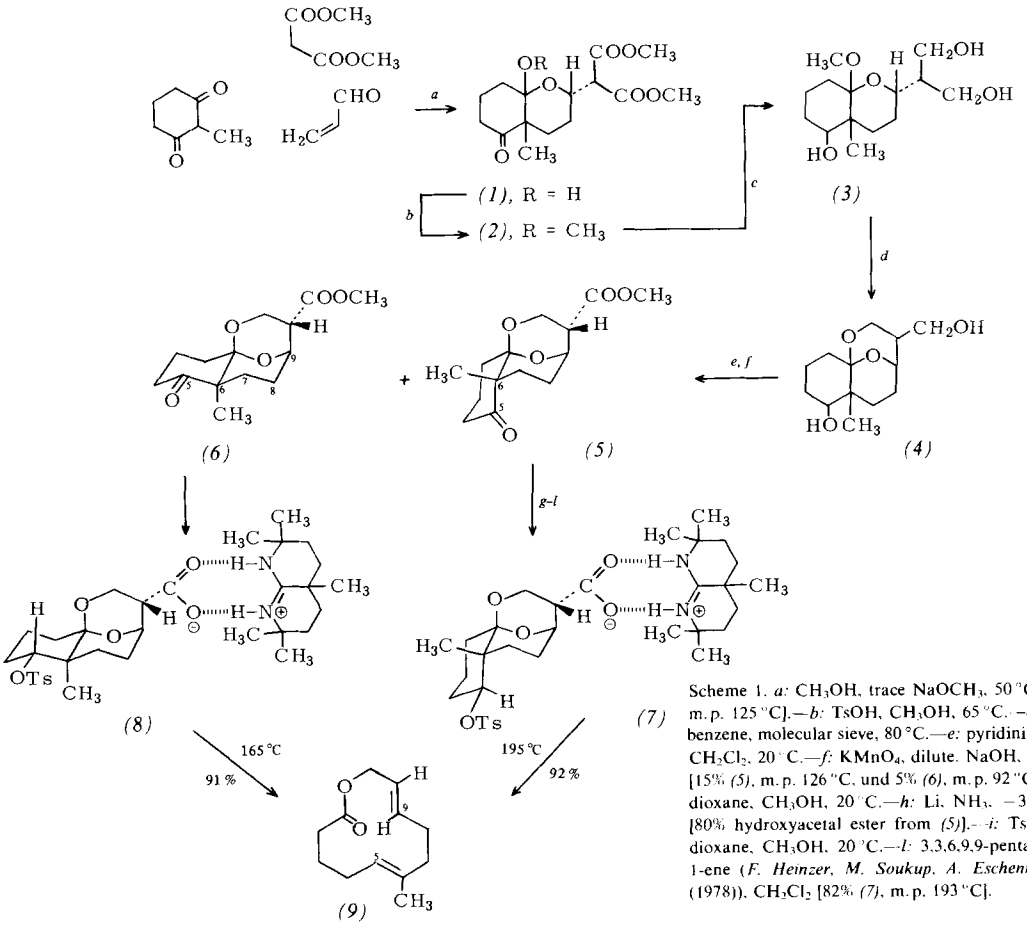
[13] *F. Heinzer, M. Soukup, A. Eschenmoser*, Helv. Chim. Acta *61*, 2851 (1978).

A Fragmentational Approach to Macrolides: (5-*E*, 9-*E*)-6-methyl-5,9-undecadien-11-olide[**]

By *Masayuki Shibuya, Fritz Jaisli,* and *Albert Eschenmoser*[*]

The principle for the synthesis of unsaturated macrolides through decarboxylative double fragmentation[1] offers fundamentally the possibility to vary the position of the C=C double bonds in the macrolide ring by changing the site of both the tosylate and carboxyl groups in the reactants. We report herein the realization of one of these possibilities.

Michael-addition of acrolein to 2-methyl-1,3-cyclohexanedione in methanol in the presence of a catalytic amount of sodium methoxide directly followed by condensation with dimethyl malonate in the same reaction medium afforded a crystalline ketohemiacetal diester *(1)*[2] in 60% yield (Scheme 1). Protection of the hemiacetal function by methanolysis, $LiAlH_4$ reduction of the ketoacetal diester *(2)*, intramolecular transacetalization of the mixture of diastereomeric trihydroxyacetals *(3)*, oxidation and esterification of *(4)* afforded a chromatographically separable 3:1 mixture of crystalline ketoacetal esters *(5)* and *(6)*. Starting from *(1)*, it is not necessary to purify the intermediate diastereomeric mixtures in order to prepare *(5)* and *(6)* in pure form (yield based on *(1)* is 20%)[3]. The assignment of configuration for the ring fusion in *(5)* and *(6)* is based on distinct configuration-specific differences in the ^{13}C-NMR spectra[4] of the two ketoacetal esters as well as the corresponding hydroxy derivatives[5]. Such differences run parallel to those observed in the series of isomers[1] in which the configurational assignment of the corresponding ketoacetal esters is established by X-ray crystallography[6]. From a stereochemical point of view, the key step is the transacetalization *(3)*→*(4)*; here we expect that the thermodynamic control of this step causes a differentiation of the diastereotopic hydroxymethyl groups such that the remaining hydroxymethyl group (which becomes the carboxylate function of *(5)* and *(6)* as well as of *(7)* and *(8)*) can occupy an equatorial position. This corresponds to the *endo*-configuration when the 1,3-dioxane ring exists in the chair form (as originally expected[7]) or, contrariwise, the *exo*-configura-

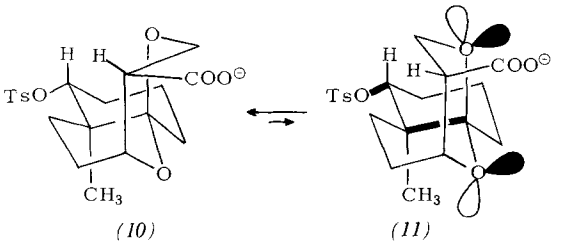


Scheme 1. *a:* CH_3OH, trace $NaOCH_3$, 50 °C; $CH_2(COOCH_3)_2$, 65 °C [60% *(1)*, m.p. 125 °C].—*b:* TsOH, CH_3OH, 65 °C.—*c:* $LiAlH_4$, ether, 20 °C.—*d:* TsOH, benzene, molecular sieve, 80 °C.—*e:* pyridinium chlorochromate, sodium acetate, CH_2Cl_2, 20 °C.—*f:* $KMnO_4$, dilute NaOH, 20 °C, followed by CH_2N_2, CH_3OH [15% *(5)*, m.p. 126 °C, und 5% *(6)*, m.p. 92 °C; yield based on *(1)*].—*g:* 4N KOH, dioxane, CH_3OH, 20 °C.—*h:* Li, NH_3, −33 °C, followed by CH_2N_2, CH_3OH [80% hydroxyacetal ester from *(5)*].—*i:* TsCl, pyridine, 20 °C.—*k:* 4N KOH, dioxane, CH_3OH, 20 °C.—*l:* 3,3,6,9,9-pentamethyl-2,10-diazabicyclo[4.4.0]dec-1-ene (*F. Heinzer, M. Soukup, A. Eschenmoser*, Helv. Chim. Acta *61*, 2851 (1978)), CH_2Cl_2 [82% *(7)*, m.p. 193 °C].

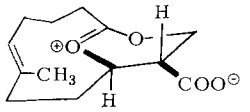
[*] Prof. Dr. A. Eschenmoser, Dipl. Ing.-Chem. F. Jaisli
Organisch-chemisches Laboratorium der ETH
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Prof. Dr. M. Shibuya
Faculty of Pharmaceutical Sciences, Tokushima University
Tokushima (Japan)

[**] 15th Communication on Synthetic Methods. This work was supported by the Anniversary Funds of the ETH Zürich.—For the 14th Communication see ref. [1].

tion (compare *(5)* and *(6)*) if the ring prefers the boat conformation. According to an X-ray crystallographic analysis performed by *Dunitz et al.*[6], the 1,3-dioxane ring in the isomeric ketoacetal esters[1] prefers the boat form. Thus, the carboxyl function, as shown in *(5)* and *(6)*, probably exists in the *exo* configuration. This assignment is compatible with the ^{1}H-NMR data[8] and, above all, is in agreement with the stereochemical outcome of the fragmentation to *(9)* (see Schemes 1 and 2).



(10) *(11)*



Scheme 2 *(12)*

Heating the amidinium carboxylates *(7)* and *(8)* prepared from *(5)* and *(6)* respectively, for 1 minute at their melting points afforded the title compound *(9)* in stereochemically homogeneous form (see Table 1). That the disubstituted double bond takes up the *E*-configuration is evidenced by the ^{1}H-NMR coupling constant (15.5 Hz)[9] for the two adjacent vinyl protons. This corresponds to the *exo*-arrangement of the carboxyl group in *(7)* and *(8)* as illustrated by the conformational formulas in Scheme 2 for the carboxylate ion of the *trans* isomer *(8)*. Of the two reactant conformations *(10)* and *(11)*, the latter satisfies the stereochemical requirements for the first step of the fragmentation[10]. From the formula of the intermediate zwitterion *(12)* it is seen how this configuration of the carboxyl group can lead to the *E*-configuration of the C-9, C-10 macrolide double bond in a second step of the fragmentation[11].

Table 1. Analytical data of *(9)*. Experimental details, see ref. [3]. Compound *(9)* is a liquid under normal conditions.

^{1}H-NMR ($CDCl_3$, 360 MHz): $\delta = 1.49$ (s/3H/CH_3 an C-6), 1.77—1.86 (m/2H/H_2C-3), 2.06—2.11 (m/6H/H_2C-4, H_2C-7, H_2C-8), 2.21—2.24 (m/2H/H_2C-2), 4.48 (d/J = 7.4 Hz/2H/H_2C-11), 4.98 (t, J = 7.4 Hz/1H/HC-5), 5.42 (dt/J = 15.3 und 7.4 Hz/1H/HC-10), 5.67—5.76 (m/1H/HC-9). Decoupling: 4.48 ppm → 5.42 (d/J = 15.1 Hz); 2.09 → 5.73 (d/J = 15.5 Hz), 4.98 (doubled s/J = 1.2 Hz) and 1.49 (d/J = 1.2 Hz).—^{13}C-NMR ($CDCl_3$, 25 MHz): $\delta = 14.8$ (q), 24.5 (t), 28.7 (2t), 35.4 (t), 39.5 (t), 62.8 (t), 125.3 (d), 127.5 (d), 132.5 (s), 139.1 (d), 173.4 (s).—IR ($CHCl_3$): *e.g.* 1727 (sharp), 1670 w cm^{-1}.—MS (200 °C): m/e = 195 (3%), 194 (15%, M^+), 140 (100%)

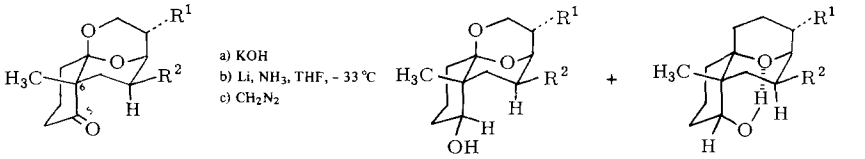
CAS Registry numbers:
(1), 70968-63-7; *(2)*, 70968-64-8; *(3)*, 70968-65-9; *(4)*, 70968-66-0; *(5)*, 70968-61-5; *(6)*, 71030-27-8; *(7)*, 70968-68-2; *(8)*, 71030-31-4; *(9)*, 70968-69-3; 2-methyl-1,3-cyclohexanedione, 1193-55-1; acrolein, 107-02-8; dimethyl malonate, 108-59-8

[1] *D. Sternbach, M. Shibuya, F. Jaisli, M. Bonetti, A. Eschenmoser*, Angew. Chem. *91*, 670 (1979); Angew. Chem. Int. Ed. Engl. *18*, 634 (1979).
[2] Presumably the *cis* diastereomer; compare the isomer pair *(5)* and *(6)*.
[3] In preliminary work, most of these intermediates were isolated isomer-free and characterized (*F. Jaisli*, planned Dissertation, ETH Zürich).
[4] For ^{13}C-NMR signals see ref. [5], Table 1.
[5] *F. Jaisli, D. Sternbach, M. Shibuya, A. Eschenmoser*, Angew. Chem. *91*, 673 (1979); Angew. Chem. Int. Ed. Engl. *18*, Nr. 8 (1979).
[6] *G. Procter, F. Nesmé, J. D. Dunitz*, to be published; cf. ref. [1], footnote [11].
[7] *M. Dobler, J. D. Dunitz*, Helv. Chim. Acta *47*, 695 (1964); *W. A. C. Brown, J. Martin, G. A. Sim*, J. Chem. Soc. *1965*, 1844.
[8] ^{1}H-NMR coupling constants from decoupling experiments: *(5)*: H(C-9) 4.47/H(C-10) 2.87, $J_{10,9}$ = 4 Hz; H(C-10)/H_2(C-11), $J_{10,11}$ = 10 and 8 Hz; corresponding values for *(6)*: 4.45/2.90, $J_{10,9}$ = 4Hz; $J_{10,11}$ = 11.5 and 8 Hz.
[9] The assignment of configuration was confirmed by opening of the lactone ring with methanol, oxidation of the terminal hydroxy group of the α,β-unsaturated aldehyde group (coupling constant between the adjacent olefinic protons: 15.3 Hz) and reduction to the alcohol [$Zn(BH_4)_2$].
[10] *P. Deslongchamps*, Tetrahedron *31*, 2463 (1976).
[11] The connection between the *E* configuration of the C^9 C^{10} double bond in *(9)* and the *exo* configuration of the carboxylate group in *(7)* and *(8)* is unequivocal only if the formation of the product does not involve a [3,3]-sigmatropic equilibration of the allylic lactone group (*via* a 10-membered ring). In analogous cases with 12- and 14-membered rings we did not observe a thermal equilibration of this kind at 220 °C but at 400 °C. *P. R. Jenkins, N. Beeley*, unpublished results.

Steric Course of the Reduction of Ketoacetal Esters with Alkali Metals in Liquid Ammonia[**]

By *Fritz Jaisli, Daniel Sternbach, Masayuki Shibuya*, and *Albert Eschenmoser*[*]

The most productive method of preparing the hydroxyacetal esters *(2)* and *(5)* starting with the two *cis*-ketoacetal esters *(1)*[1a] and *(4)*[1b] respectively, was found to be the following sequence of reactions: ester hydrolysis with potassium hydroxide in water/methanol/dioxane at ambient temperature, reduction of the crude ketoacetal carboxylic acids with *ca.* 5 equivalents of lithium in liquid ammonia/tetrahydrofuran at −33 °C (reaction quenched by addition of solid ammonium chloride) and re-esterification with diazomethane in methanol. Column chromatographic separation of the products afforded, along with a small amount of starting material, the hydroxyacetal ester *(2)* or *(5)* with an equatorial hydroxy group in 81 or 80% yield respectively. As expected[2] only trace amounts of the axial epimers *(3)* or *(6)* were formed[3] (see Scheme 1).



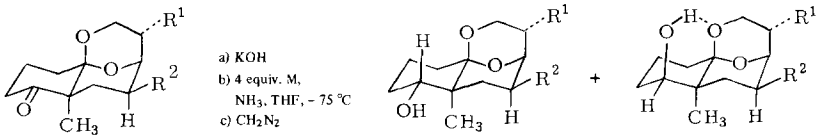
R^1	R^2			
(1), H	$COOCH_3$	⟶	*(2)*, 81%	*(3)*, 1% (+ 5% educt)
(4), $COOCH_3$	H	⟶	*(5)*, 80%	*(6)*, 2% (+ 3% educt)

Scheme 1

Received: May 3, 1979 [Z 255b IE]
German version: Angew. Chem. *91*, 672 (1979)

[*] Prof. Dr. A. Eschenmoser, dipl. Ing.-Chem. F. Jaisli, Dr. D. Sternbach
Organisch-chemisches Laboratorium der ETH
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Prof. Dr. M. Shibuya
Faculty of Pharmaceutical Sciences, Tokushima University
Tokushima (Japan)

[**] 16th Communication on Synthetic Methods.—For 15th Communication, see ref. [1b].

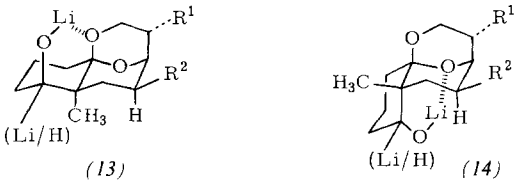


	R^1	R^2			
(7),	H	$COOCH_3$	⟶	*(8)*	*(9)*
(10),	$COOCH_3$	H	⟶	*(11)*	*(12)*

M	*(8)*:*(9)*	*(11)*:*(12)*
Li	1:3.1 (77%)	1:2.5 (74%)
	1:2.6 (83%) [a]	
Na	3.1:1 (81%)	2.6:1 (72%)
K	6.2:1 (79%) [b]	3.0:1 (56%) [c]

Scheme 2: Product ratio (yields). [a] Reduction in the presence of ten equivalents of water in liquid ammonia at −75 °C. [b] 10% reactant recovered. [c] 15% reactant recovered.

An unexpected inversion in the stereochemistry of the reaction has been observed in the case of the *trans*-ketoacetal esters *(7)*[1a] and *(10)*[1b] under otherwise identical conditions (see Scheme 2). Reduction of *(7)* or *(10)* with lithium in liquid ammonia affords mainly the axial alcohol *(9)* or *(12)* respectively, independent of reaction temperatures of ca. −30° or −75 °C and the presence or absence of moisture[4]. An equatorial/axial ratio between 1:2.5 and 1:3 was reproducibly obtained in several experiments[5]. We have interpreted these findings by the assumption that the lithium alkoxides which arise as intermediates on the path to the axial alcohols are stabilized by intramolecular lithium ion bridging as illustrated in the structural formula *(13)* (Scheme 3). The behaviour of the *cis*-compounds *(1)* and *(4)* could then be attributed to greater steric hindrance in the region of the alkoxide oxygen and the lithium bridge (see *(14)*[6]). If this interpretation is correct, then the steric course of the reduction in the *trans*-series must be correspondingly sensitive to the nature of the metal employed. This proved to be the case. As suspected on the basis of the larger ionic radii and the weaker complexation tendency of sodium and potassium ions compared to lithium ions, the reduction of *(7)* and *(10)* (*trans*-series) with sodium or potassium in liquid ammonia provided the equatorial alcohols *(8)* and *(11)* as the principle products (see Scheme 2).



(13) *(14)*

Scheme 3

The assignment of configuration for the hydroxyacetal esters *(2)*, *(3)*, *(5)*, *(6)*, *(8)*, *(9)*, *(11)*, and *(12)* rests on the X-ray structure determinations by *Dunitz et al.*[7] of the ketoacetal ester *(7)*[1a] and the corresponding axial alcohol *(9)*[8]. For the four axial alcohols *(3)*, *(6)*, *(9)*, and *(12)* an intramolecular hydrogen bond between the hydroxyl and acetal oxygen is documented by IR spectroscopy (concentration independent OH-stretching vibration at 3560 cm^{-1} in CCl_4). In light of the previously found correlations between the generalized anomeric effect and ^{13}C-NMR shifts[9] it should be emphasized that for these four alcohols the ^{13}C-NMR signals of the angular methyl groups (antiperiplanar to the axial hydroxyl group) are shifted *ca.* 7 ppm *downfield* as compared to the corresponding signals of the epimeric (equatorial) alcohols (see Table 1).

Table 1. ^{13}C-NMR spectroscopic data for compounds *(1)*—*(12)* [a].

Cpd.	C-5	CH_3 at C-6	OH/CH_3-Conf. [b]
cis series:			
(1)	211.3	22.5	
(2)	69.2	15.6	sc
(3)	78.9	23.2	ap
(4)	211.8	22.8	
(5)	68.7	15.7	sc
(6)	78.8	23.4	ap
trans series:			
(7)	211.9	19.6	
(8)	73.7	12.8	sc
(9)	74.9	19.7	ap
(10)	212.7	19.3	
(11)	73.9	12.4	sc
(12)	75.1	19.3	ap

[a] Chemical shifts based on (TMS) = 0; broad band decoupled spectra in $CDCl_3$. [b] sc = synclinal, ap = antiperiplanar.

Our results illustrate how neighboring oxygen substituents can influence the steric course of the reduction of a carbonyl group and also indicate the possibility of directing the stereochemistry in such cases[10].

Received: May 3, 1979 [Z 255c IE]
German version: Angew. Chem. *91*, 673 (1979)

CAS Registry numbers:
(1), 70968-59-1; *(2)*, 70968-60-4; *(3)*, 71030-22-3; *(4)*, 70968-61-5; *(5)*, 70968-62-6; *(6)*, 71030-23-4; *(7)*, 71030-24-5; *(8)*, 71030-25-6; *(9)*, 71030-26-7; *(10)*, 71030-27-8; *(11)*, 71030-28-9; *(12)*, 71030-29-0

[1] a) *D. Sternbach, M. Shibuya, F. Jaisli, M. Bonetti, A. Eschenmoser*, Angew. Chem. *91*, 670 (1979); Angew. Chem. Int. Ed. Engl. *18*, 634 (1979); b) *M. Shibuya, F. Jaisli, A. Eschenmoser, ibid. 91*, 672 (1979) and *18*, 636 (1979).

[2] *D. H. R. Barton*, Experientia 6, 316 (1950); J. Chem. Soc. *1953*, 1027; *D. H. R. Barton, C. H. Robinson, ibid. 1954*, 3045.

[3] Compounds *(3)* and *(6)* are formed in a much higher proportion (34 from 82% and 25 from 65% respectively) by the $NaBH_4$ reduction of *(1)* and *(4)* respectively, in methanol at 0 °C.

[4] An example of how the steric course of a metal/ammonia reduction depends upon the amount of water in the ammonia is found in *J. E. McMurry, L. C. Blaszek, H. A. Johnson*, Tetrahedron Lett. *1978*, 1633.

[5] Product ratio of the reduction of *(7)* with $NaBH_4$ in methanol at 0 °C: 13% *(8)* and 83% *(9)*.

[6] In this connection, one should consider supplementary solvation of the only twice coordinated lithium ions that are depicted in *(13)* and *(14)*.

[7] *G. Procter, F. Nesmé, J. D. Dunitz*, to be published; compare ref. [1a], footnote [11].

[8] The configuration of the methoxycarbonyl group R^2 in *(1)*—*(12)* is certain; the assignment for R^1 has not yet been proven (compare ref. [1b]).

[9] Cf., *e.g. E. L. Eliel, W. F. Bailey, L. D. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Duch, E. Wenkert, F. M. Schell, D. W. Cochran*, J. Am. Chem. Soc. 97, 322 (1975).

[10] For the formation of the thermodynamically unstable epimeric alcohols by the reduction of the ketones with metals/ammonia, compare *e.g. J. W. Huffman, J. T. Charles*, J. Am. Chem. Soc. *90*, 6486 (1968), and references cited therein.

The Chemistry of Functional Groups. The Chemistry of the Carbon-Carbon Triple Bond. Ed. by *S. Patai.* John Wiley & Sons, London, 1978. Part 1: xiv, 522 pp.; Part 2: xiv, pp. 523—1065, bound, together £ 70.00.

These two volumes on the chemistry of the acetylene bond have been written by a total of 31 authors. The advantage of such collective works is that experts can report on their own particular field, but generally there is a price to pay: uneven emphasis is given to individual aspects, which normally does not make for uniformity and causes many topics to be overemphasized. The present work, however, gives an over-all impression of uniformity, and in particular the wealth of literature references gives access to practically all work in this field. As might be expected, the approach does lead to a certain amount of overlap, and a number of aspects are omitted. With the great wealth of material, however, one could hardly expect a book of this size to give an exhaustive treatment. Since consideration is given to both the theoretical and the purely preparative aspects, the book will certainly be of interest to a wide circle of readers.

Ferdinand Bohlmann [NB 469 IE]

Megawatt Infrared Laser Chemistry. By *E. Grunwald, D. F. Dever,* and *Ph. M. Keehn,* John Wiley & Sons, New York 1979. xii, 107 pp., bound, $ 21.50.

Currently there is a considerable interest in the applications of lasers, and in particular of high-power infrared lasers, in chemistry, and a large number of reviews have already appeared. The present book with its 107 pages looks rather thin in comparison. It is designed to meet the interests of the preparative chemist. In five chapters it offers some basic information, together with a quite comprehensive collection of individual examples. The level corresponds to that of an advanced chemistry student, which is perhaps only to be expected from the brevity of the chapters. The basic approach of the book derives from the authors' field of study; it is aimed less at a detailed understanding of the physical and spectroscopic aspects and more at an interpretation of laser-induced reactions in the gas phase at relatively high pressures, on the basis of the products and product distributions.

The collection of examples is undoubtedly useful. It includes the dissociations and eliminations of halogenated hydrocarbons, cyclizations and rearrangements, sensitized reactions, and reactions such as chloroboration, displacement of the chemical equilibrium, and isotope separation. But apart from this, the book has little new to offer. The material could have been covered in a review article, and the price seems far too high. It is certainly time that we had a chemically oriented review of laser-induced reactions, but an account at a higher level than this would be desirable.

Karl L. Kompa [NB 470 IE]

Infrared and Raman Spectra of Inorganic and Coordination Compounds. By *Kazuo Nakamoto.* John Wiley & Sons, New York—Chichester—Brisbane—Toronto 1978. 3rd edit., xv, 448 pp., bound, $ 31.15.

After the first (1963) and second (1970) editions of Nakamoto we now have the third, considerably modified edition. This shows that vibrational spectroscopy is still a technique in current use by inorganic and organometallic chemists, although in the past 15 years other physical techniques have come to the fore and it has been possible to simplify greatly the use of X-ray single-crystal structure analysis.

The basic framework of the book remains unchanged. Chapter I gives an introduction to the theory of vibrational spectroscopy and deals with topics such as Raman intensities, resonance Raman spectra, vibrational spectra in the gas phase, matrix-isolation spectroscopy, and crystal spectra, Chapter II deals with inorganic compounds, Chapter III with coordination compounds, and Chapter IV (new) with organometallic compounds. In order to take account of developments over the past years, problems such as metal-isotope techniques, metal-ligand interactions, and the fixation of diatomic molecules are discussed. The present reviewer found Chapter III to be the most interesting, since the author reports among other things on his own field of work and discusses current problems in the chemistry of complexes.

This book may be recommended without any reservations. It is intended for anyone interested in becoming acquainted with the fundamentals of the theory of vibrational spectroscopy, and for the preparative chemist working in the fields of complex and organometallic chemistry who wishes to become familiar with the information content of the vibrational spectra measured. For chemists involved with elements in the main groups, Chapter II can serve as a reference work for characteristic vibrations.

Achim Müller [NB 473 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Tensid-Taschenbuch. Edited by *H. Stache.* Carl Hanser Verlag, München 1979. viii, 581 pp., sewed, DM 98.00.—ISBN 3-446-12581-7

Organic Reaction Mechanisms—1977. Edited by *A. C. Knipe* and *W. E. Watts.* John Wiley & Sons, New York 1978. 741 pp., bound, $ 110.00.—ISBN 0-471-99666-1

Antiviral Mechanisms in the Control of Neoplasia. Edited by *P. Chandra.* Plenum Press, New York 1979. xiv, 757 pp., bound, $ 69.00.—ISBN 0-306-40063-4

Highly Conducting One-Dimensional Solids. Edited by *J. T. Devreese, R. P. Evrard,* and *V. E. van Doren.* Plenum Press, New York 1979. xiii, 422 pp., bound, $ 51.00.—ISBN 0-306-40099-5

Studienbücher Chemie. Chemische Affinität. By *A. Markert.* Verlag Diesterweg/Salle Verlag, Frankfurt; Verlag Sauerländer, Aarau 1978. 168 pp., sewed, DM 9.90.—ISBN 3-425-05364-7 (Diesterweg/Salle); 3-7941-1673-9 (Verlag Sauerländer)

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 9
September 1979
Pages 641–706

August Kekulé—The Architect of Chemistry Commemorating the 150th Anniversary of His Birth[**]

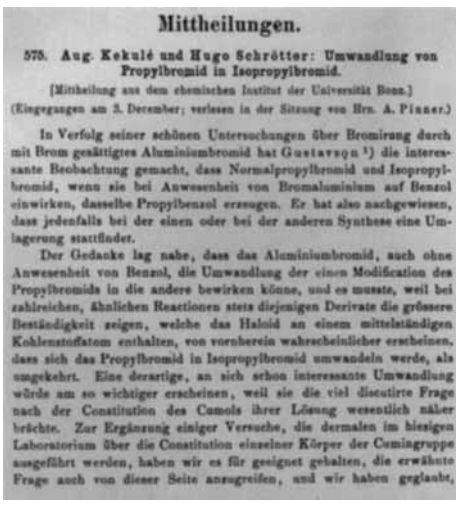
By Klaus Hafner[*]

Imagination, daring, and critical understanding are the sources of the impulses still felt today which chemistry received from the theoretical studies of *Kekulé*. "Let us learn to dream, gentlemen, then perhaps we shall discover the truth; but let us beware of publishing our dreams abroad before they have been scrutenized by our vigilant intellect ... Let us always allow the fruit to hang until it is ripe. Unripe fruit brings even the grower but little profit; it damages the health of those who consume it; it endangers particularly the youth which cannot yet distinguish between ripe and unripe." (*Kekulé* 1890).

"Eine Geschichte zu schreiben, ist immer eine bedenkliche Sache. Denn bei dem redlichsten Vorsatz kommt man in Gefahr, unredlich zu sein; ja, wer eine solche Darstellung unternimmt, erklärt im voraus, daß er manches in Licht, manches in Schatten setzen werde." (J. W. von Goethe, Introduction to the didactic part of the theory of colors)

Many scientific discoveries of bygone centuries have meanwhile become so commonplace that the achievement of their discoverer is often underestimated in spite of all the appreciation it receives. Yesterday's genius becomes today's banality. Pertinent examples are the foundation of organic structural chemistry and the proposal of the benzene formula by *August Kekulé* who, although of comparable genius with *Justus Liebig*, likewise born at Darmstadt, received far less recognition than the latter. The 150th anniversary of his birth provides an opportunity to call to mind his importance in the history of chemistry and for development of the chemical industry, and his part in the teaching of chemistry as viewed from a modern standpoint, and thus to reflect upon a great, almost unique scientific tradition, extending far into the present century, which is hardly known to the present generation.

When Kekulé published his paper on the isomerization of *n*-propyl bromide to isopropyl bromide in the presence of aluminum bromide[1] a hundred years ago and therein, without knowing it, provided one of the first experimental proofs of the existence of carbenium ion intermediates, he had



Mittheilungen.

575. Aug. Kekulé und Hugo Schrötter: Umwandlung von Propylbromid in Isopropylbromid.

[Mittheilung aus dem chemischen Institut der Universität Bonn.]

(Eingegangen am 3. December; verlesen in der Sitzung von Hrn. A. Pinner.)

In Verfolg seiner schönen Untersuchungen über Bromirung durch mit Brom gesättigtes Aluminiumbromid hat Gustavson [1]) die interessante Beobachtung gemacht, dass Normalpropylbromid und Isopropylbromid, wenn sie bei Anwesenheit von Bromaluminium auf Benzol einwirken, dasselbe Propylbenzol erzeugen. Er hat also nachgewiesen, dass jedenfalls bei der einen oder bei der anderen Synthese eine Umlagerung stattfindet.

Der Gedanke lag nahe, dass das Aluminiumbromid, auch ohne Anwesenheit von Benzol, die Umwandlung der einen Modification des Propylbromids in die andere bewirken könne, und es musste, weil bei zahlreichen, ähnlichen Reactionen stets diejenigen Derivate die grössere Beständigkeit zeigen, welche das Haloïd an einem mittelständigen Kohlenstoffatom enthalten, von vornherein wahrscheinlicher erscheinen, dass sich das Propylbromid in Isopropylbromid umwandeln werde, als umgekehrt. Eine derartige, an sich schon interessante Umwandlung würde um so wichtiger erscheinen, weil sie die viel discutirte Frage nach der Constitution des Cumols ihrer Lösung wesentlich näher brächte. Zur Ergänzung einiger Versuche, die dermalen im hiesigen Laboratorium über die Constitution einzelner Körper der Cumingruppe ausgeführt werden, haben wir es für geeignet gehalten, die erwähnte Frage auch von dieser Seite anzugreifen, und wir haben geglaubt,

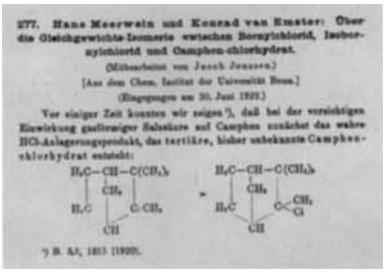
Fig. 1. Title page of publication by *Kekulé et al.* on the isomerization of *n*-propyl bromide [1].

[*] Prof. Dr. K. Hafner
Institut für Organische Chemie der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)

[**] Based on a Commemorative Lecture delivered at the Chemiedozententagung at Darmstadt, March 27, 1979.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0909-0641 $ 02.50/0*

already—hardly fifty years old—completed his major life's work. It was left to *Hans Meerwein* (1879—1965), born in the same year, to introduce the then revolutionary concept of ionic reactions into organic chemistry more than four decades later[2].



277. Hans Meerwein und Konrad van Emster: Über die Gleichgewichts-Isomerie zwischen Bornylchlorid, Isobornylchlorid und Camphen-chlorhydrat.

[Mitbearbeitet von Jacob Jonssen]

[Aus dem Chem. Institut der Universität Bonn.]

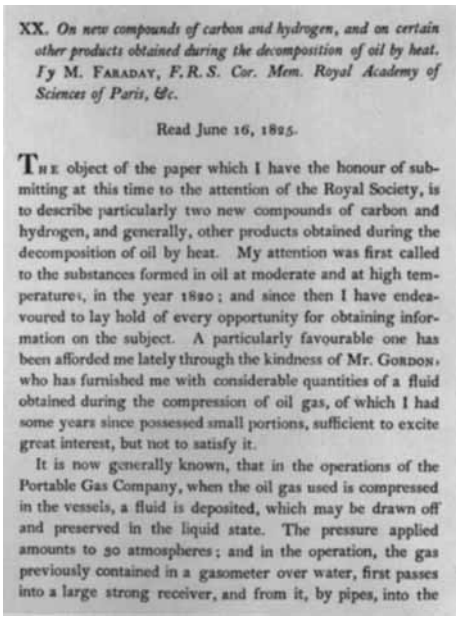
(Eingegangen am 30. Juni 1922.)

Vor einiger Zeit konnten wir zeigen[1], daß bei der vereinigten Einwirkung gasförmiger Salzsäure auf Camphen zunächst das wahre HCl-Anlagerungsprodukt, das tertiäre, bisher unbekannte Camphen-chlorhydrat entsteht:

Fig. 2. Title page of the first publication, by *H. Meerwein*, on ionic reactions in organic chemistry [2].

August Kekulé lived in a century between the world-shaking events of Napoleon's Hundred Days and the First World War. This was an age of scientific revolutions, ranging from the disproof of spontaneous generation and the discovery of microorganisms to the description of viruses and enzymes, from *Faraday*'s laws of electrolysis to the discovery of X-rays and that of the radioactivity of uranium compounds. It was also an age of engineering, ranging from the first railway to the discovery of the Diesel engine, and from the first electromagnetic telegraph to wireless telegraphy.

Kekulé's birth—on September 7, 1829—coincided with the actual beginning of organic chemistry. Just one year earlier, *Friedrich Wöhler* (1800—1882) had disproved the concept of vitalism[4] by synthesizing urea from ammonium cyanate[3]. Thus was initiated an incredibly productive and lively development of organic chemistry. *Michael Faraday* (1791—1867) obtained "bicarburetted hydrogen"[5] from compressed illuminating gas; shortly afterwards the same compound was obtained by *Eilhard Mitscherlich* (1794—1863) when benzoic acid was heated with quicklime[6], and was called benzene in accord with its mode of formation. 30 years later, its structural elucidation was destined to crown *Kekulé*'s life's work and also to initiate a tremendous upswing of the chemical industry. During the first years of *Kekulé*'s life, *Friedlieb Ferdinand Runge* (1795—1867) discovered aniline and phenol in coal tar[7], and *Jöns Jacob Berzelius* (1779—1848) introduced the concepts of catalysis[8] and of isomerism[9]. *Justus Liebig*'s (1803—1873) and *Wöhler*'s studies on benzoyl compounds[10] laid the foundations of the radical theory of carbon com-



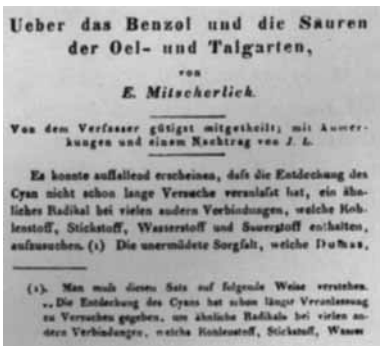
XX. *On new compounds of carbon and hydrogen, and on certain other products obtained during the decomposition of oil by heat.* By M. Faraday, *F.R.S. Cor. Mem. Royal Academy of Sciences of Paris, &c.*

Read June 16, 1825.

The object of the paper which I have the honour of submitting at this time to the attention of the Royal Society, is to describe particularly two new compounds of carbon and hydrogen, and generally, other products obtained during the decomposition of oil by heat. My attention was first called to the substances formed in oil at moderate and at high temperatures, in the year 1820; and since then I have endeavoured to lay hold of every opportunity for obtaining information on the subject. A particularly favourable one has been afforded me lately through the kindness of Mr. Gordon, who has furnished me with considerable quantities of a fluid obtained during the compression of oil gas, of which I had some years since possessed small portions, sufficient to excite great interest, but not to satisfy it.

It is now generally known, that in the operations of the Portable Gas Company, when the oil gas used is compressed in the vessels, a fluid is deposited, which may be drawn off and preserved in the liquid state. The pressure applied amounts to 50 atmospheres; and in the operation, the gas previously contained in a gasometer over water, first passes into a large strong receiver, and from it, by pipes, into the

Fig. 3. *Faraday*'s publication [5a] on the first isolation of benzene from illuminating gas (1825).



Ueber das Benzol und die Säuren der Oel- und Talgarten,

von

E. Mitscherlich.

Von dem Verfasser gütigst mitgetheilt; mit Anmerkungen und einem Nachtrag von J. L.

Es konnte auffallend erscheinen, daß die Entdeckung des Cyan nicht schon lange Versuche veranlaßt hat, ein ähnliches Radikal bei vielen andern Verbindungen, welche Kohlenstoff, Stickstoff, Wasserstoff und Sauerstoff enthalten, aufzusuchen. (1) Die unermüdete Sorgfalt, welche Dulong,

(1). Man muß diesen Satz auf folgende Weise verstehen. „Die Entdeckung des Cyans hat schon längst Veranlassung zu Versuchen gegeben, um ähnliche Radikale bei vielen andern Verbindungen, welche Kohlenstoff, Stickstoff, Wasser

Fig. 4. *Mitscherlich*'s publication [6] on the production of benzene from benzoic acid (1834).

Life of *August Kekulé*

1829	Born at Darmstadt, Neckarstrasse 19, on September 7
1835 to 1847	Pupil at the private school run by *Heinrich Schmitz* and at the Ludwig-Georgs-Gymnasium, Darmstadt
1847 to 1848	Study of architecture at Giessen
1848 to 1849	Semester at Darmstadt Polytechnic
1849 to 1851	Study of chemistry at Giessen
1851 to 1852	Period of study at Paris
1852	Awarded degree of Dr. phil.
1852 to 1853	Private assistant to *A. von Planta* at Reichenau Castle, Chur
1854 to 1855	Private assistant to Professor *J. Stenhouse* at St. Bartholomew's Hospital, London
1855 to 1858	*Privatdozent* at Heidelberg University
1856	Habilitation for chemistry, physics, and geognosy
1857 to 1858	Publication of fundamental papers on the theory of valency
1858 to 1867	Professor of chemistry at the State University of Ghent, Belgium
1859	Publication of the first instalment of *Kekulé*'s textbook of organic chemistry
1860	Participation in the first international congress on chemistry at Karlsruhe September 3 to 5, 1860
1862	Marriage to *Stephanie Drory*
1863	Birth of son *Stephan*; death of *Stephanie Kekulé, née Drory*
1865	Proposal of formula of benzene
1867	Call to Bonn University
1868	Award of honorary degree of Dr. med. at 50th anniversary of the foundation of Bonn University
1875	Call to Munich University as successor to *J. von Liebig*—not accepted
1876	Marriage to *Luise Högel*
1877 to 1878	Chancellor of Bonn University
1878	Birth of son *Fritz*
1878, 1886, 1891	President of German Chemical Society
1882	Birth of daughter *Louise*
1885	Birth of daughter *Auguste*
	Award of Copley medal
1889	Award of Huyghens medal
1890	Benzene festival of German Chemical Society held in the City Hall of Berlin
	Award of the "Kronenorden II. Klasse" and election to "Ritter des Maximilian-Ordens für Wissenschaft und Kunst in Bayern"
1893	Nomination as "Ritter des Ordens pour le mérite für Wissenschaften und Künste"
1895	Prussian title of nobility *(Kekulé von Stradonitz)*
1896	Died at Bonn on July 13

pounds which was welcomed by *Berzelius*, the father of the then generally accepted electrochemical-dualistic concepts which were so very fruitful for inorganic chemistry, as the "dawn of a new day in vegetable chemistry"[11].



Fig. 5. From left to right: *J. J. Berzelius, M. Faraday, E. Mitscherlich, F. Wöhler.*

At this time, *Friedrich August Kekulé* grew up as the youngest child of the "Grossherzoglicher Oberkriegsrat" *Ludwig Karl Emil Kekulé* (1773—1847)[12] in Darmstadt. Although highly gifted and very interested in all scientific phenomena, the schoolboy showed no pronounced interest in chemistry. Like *Georg Christian Lichtenberg* (1742—1799), *Johann Heinrich Merck* (1741—1791), and *Georg Büchner* (1813—1837) before him, and like *Stefan George* (1868—1933) and *Friedrich Gundolf* (1880—1931) after him, he was a pupil of the Grossherzogliches Gymnasium[13] of his home town which he left in 1847 with a distinguished leaving certificate[14].

A gift of rapid comprehension coupled with an exceptionally good memory guaranteed his success, as did a vivid imagination which became almost visionary in later life. "His thoughts turned into pictures and at times he could visually observe his thoughts"[15]. Remarkable graphic and mathematical ability and several designs for houses in the old part of Darmstadt drawn while he was still at school predestined him for the study of architecture at the Hessian University at Giessen. At that seat of learning, it was his fellow Hessian *Liebig*, then at the zenith of his scientific career, who inspired him by his lectures and persuaded him to change over to chemistry in which he was soon to develop his constructive bent in such magnificent manner. Philology and classics were then, and later, the main props of German education and it is hardly surprising that *Kekulé*'s family, strongly influenced by such ideals, were reluctant to condone this change. Instead, a time of deliberation was prescribed at the Darmstadt Polytechnic, the forerunner of the Technical University[16]. He spent that winter-semester of 1848/49—far away from the political unrest of the time—performing analytical work in the laboratory of *Friedrich Moldenhauer* (1797—1866). He did not return to architecture, but instead to *Liebig*'s laboratory at Giessen, where he pursued analytical studies with enthusiasm, carefulness, and persistence, a dedication without haste, which was to characterize him throughout his life. "It was not practical chemistry which attracted him, but the philosophy of chemistry"[17]. He participated briefly in *Liebig*'s physiological work on plants and animals with an analytical study on gluten and wheat bran[18]; *Liebig* had already turned his attention away from pure organic chemistry. *Kekulé* was awarded his doctorate for an experimental thesis "Über die Amyloxydschwefelsäure und einige ihrer Salze"[19] completed under the supervision of *Heinrich Will* (1812—1890)[20], one of *Liebig*'s students.

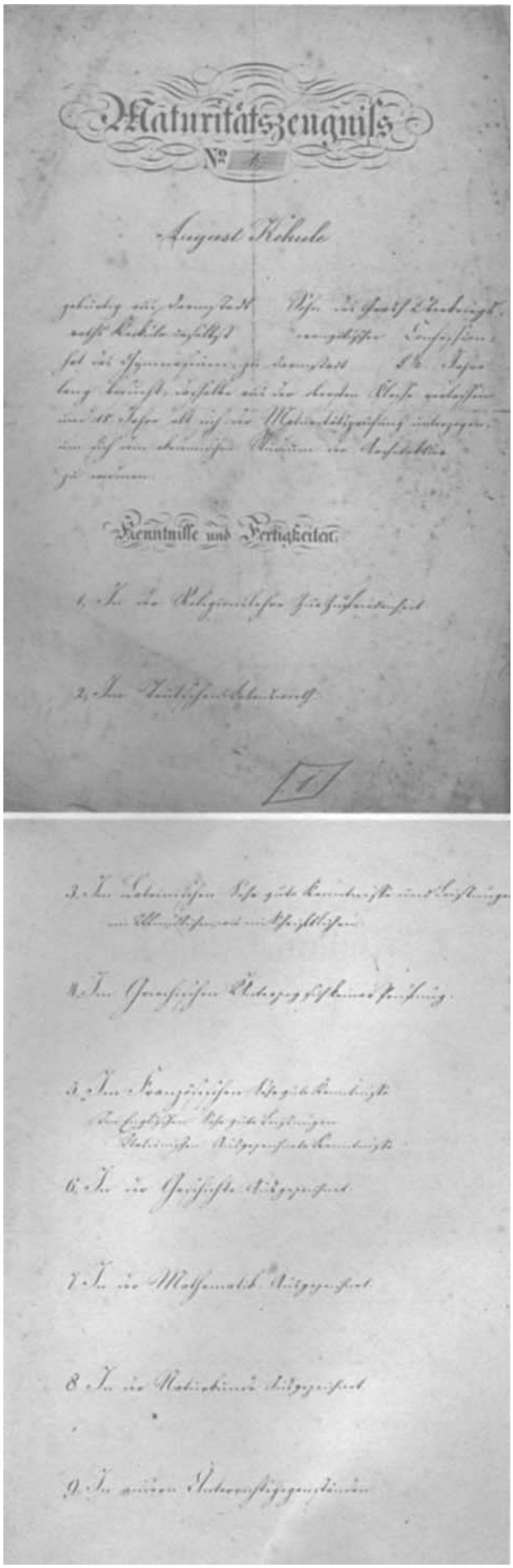


Fig. 6. *Kekulé*'s school leaving certificate.



Fig. 7. Drawing by *Kekulé* at age 13.



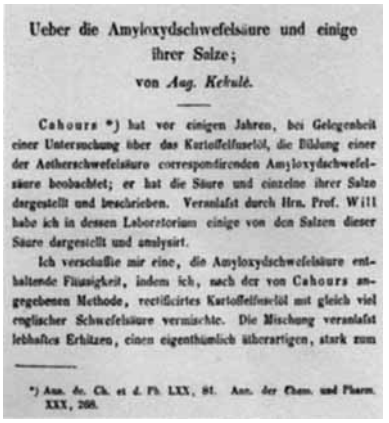
Fig. 8. Drawing by *Kekulé* at age 18.

It was an ingenious turn of history which took the young *Kekulé* from his studies at Giessen to meet *Charles Gerhardt* (1816—1856) in Paris and *Alexander William Williamson* (1824—1904) in London. Both of these contacts were to prove crucial for his intellectual work.



Fig. 9. Left: *Justus von Liebig ca.* 1850. Right: *H. Will.*

When *Kekulé* entered the scientific arena the first steps had just been taken towards a clearer understanding of the linkage between atoms of the simplest nitrogen and oxygen compounds. The nature of hydrocarbon "radicals" was still shrouded in mystery. They appeared, as aptly stated by *Jean Baptiste Dumas* (1800—1884), "as planetary systems, held together by a force resembling gravitation but acting in accord with much more complicated laws"[21]. Even concepts such as atom, molecule, and equivalent were used in different ways. Confusion surrounded both the significance and the magnitude of atomic weights, and molecular weights were not employed, although *Amedeo Avogadro* (1776—1856) and *John Dalton* (1766—1844) had already prepared the ground



Ueber die Amyloxydschwefelsäure und einige ihrer Salze;

von *Aug. Kekulé.*

Cahours *) hat vor einigen Jahren, bei Gelegenheit einer Untersuchung über das Kartoffelfuselöl, die Bildung einer der Aetherschwefelsäure correspondirenden Amyloxydschwefelsäure beobachtet; er hat die Säure und einzelne ihrer Salze dargestellt und beschrieben. Veranlafst durch Hrn. Prof. Will habe ich in dessen Laboratorium einige von den Salzen dieser Säure dargestellt und analysirt.

Ich verschaffte mir eine, die Amyloxydschwefelsäure enthaltende Flüssigkeit, indem ich, nach der von Cahours angegebenen Methode, rectificirtes Kartoffelfuselöl mit gleich viel englischer Schwefelsäure vermischte. Die Mischung veranlafst lebhaftes Erhitzen, einen eigenthümlich ätherartigen, stark zum

*) Ann. de Ch. et d. Ph. LXX, 81. Ann. der Chem. und Pharm. XXX, 266.

Fig. 10. *Kekulé*'s first publication (doctoral dissertation).

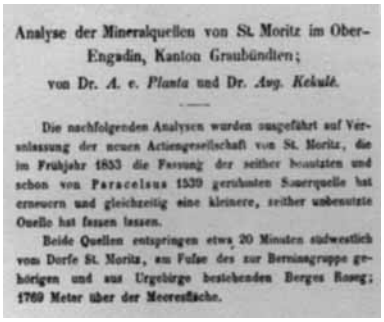
for their use at the beginning of the century. *Kekulé* later described the situation thus[22]: "At that time a general feeling of discouragement had just overcome the most influential chemists. Because whole categories of facts could be reconciled neither with one another nor with the general theoretical views of the time, it was believed that all speculations had to be banned from chemistry and all atomistic considerations relinquished."

A reasonable classification of the known organic compounds whose number had grown beyond comprehension was beyond the scope of the dualistic radical theory. The concept of building up chemical compounds from an electropositive and an electronegative partner was incompatible, in the realm of carbon compounds, with the feasibility of replacing electropositive elements such as hydrogen by electronegative ones such as chlorine without any great change in chemical character of a compound. *Dumas* and *Auguste Laurent* (1807—1853) attempted to explain these findings in terms of their unitary substitution theory, freed from the constraints of "dipolarity"; this theory provided preparative chemistry with fruitful stimulation but failed to supply a key to the understanding of the structure of carbon compounds. The "radicals" associated with an electric charge were replaced by "types" or "nuclei" susceptible to both substitution and addition. The desire for some kind of understanding of the complex phenomena, even if only in formal terms, prompted *Gerhardt* to propose his theory of types, which was a comprehensive classification destined to assume an intermediary role between the radical and substitution theory and the theory of valency soon to be developed by *Kekulé*. From a formal point of view, a satisfactory relationship was seen to exist in the case of simple substances by assigning a key role to simple parent compounds, *i.e.* "types" such as water or ammonia, in which hydrogen is replaced by various groups, *e.g.* of carbon compounds. However, an understanding of more complicated substances required the assumption of complex units, called "paired types", which were confusing and did not further the understanding of the mode of reaction. The sheer wealth of experimental data stood in the way of their correlation, and of a systematic overall classification.



Fig. 11. From left to right: *J. B. Dumas, A. Wurtz, C. Gerhardt.*

This was the time of *Kekulé*'s sojourn in Paris, then the stronghold of chemistry, and his meeting with *Dumas* and *Adolphe Wurtz* (1817—1884), the discoverer of the amines[23], which were so important for further development of theoretical concepts. Above all, however, a bond of friendship grew out of the innumerable discussions he had with the highly intellectual and quickwitted theoretician *Gerhardt*. The combination of *Gerhardt*'s principle of classification with the results of chemical reactions, paying due attention to *Avogadro*'s law and the concepts of equivalent and atomic and molecular weight, paved *Kekulé*'s way to his structural theory. Gifted with a vivid imagination which strove for visualization, with a critical intellect, and with an unusual memory, *Kekulé* could not have been better equipped to absorb all the available facts of his science and to collate them from a fresh angle. An interlude lasting one and a half years as private assistant to *Adolf von Planta* (1820—1895), another former student of *Liebig*, at Reichenau Castle near Chur gave him sufficient opportunity for contemplation to digest the multitude of impressions and stimulation gained in Paris[24].



Analyse der Mineralquellen von St. Moritz im Ober-Engadin, Kanton Graubündten;

von Dr. *A. v. Planta* und Dr. *Aug. Kekulé.*

Die nachfolgenden Analysen wurden ausgeführt auf Veranlassung der neuen Actiengesellschaft von St. Moritz, die im Frühjahr 1853 die Fassung der seither benutzten und schon von Paracelsus 1539 gerühmten Sauerquelle hat erneuern und gleichzeitig eine kleinere, seither unbenutzte Quelle hat fassen lassen.

Beide Quellen entspringen etwa 20 Minuten südwestlich vom Dorfe St. Moritz, am Fuße des zur Berninagruppe gehörigen und aus Urgebirge bestehenden Berges Rosatsch; 1769 Meter über der Meeresfläche.

Fig. 12. One of *Kekulé*'s publications on work performed in Switzerland [24].

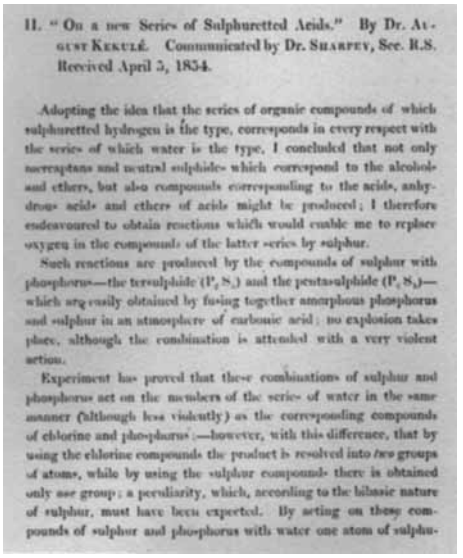
During a subsequent year of comparable importance for his life's work spent with *John Stenhouse* (1809—1880) in London he made the acquaintance of *Williamson*, who had just obtained further confirmation of the theory of types with his synthesis of ether[25]; he modified the theory by placing greater emphasis on atomic weights. While in London, *Kekulé* also met *Edward Frankland* (1825—1899), the discoverer of the first organometallic compounds[26] which underscored the significance of the concept of valency, and *William Odling* (1829—1921), a gifted young theoretician.

"Originally a scholar of *Liebig*", remarked *Kekulé* not without pride on a later occasion, "I became a scholar of *Dumas, Gerhardt,* and *Williamson*; I no longer belonged to any one school"[27]. In the course of his own experimental work "on a series of sulfur-containing organic acids"[28] and joint intellectual studies with *Williamson* the concept of the theory of valency took on shape. The parent "types" water and ammonia were supplemented by hydrogen sulfide[29] and ultimately by marsh gas[30], *i.e.* methane.



Fig. 13. From left to right: *A. W. Williamson, E. Frankland, W. Odling.*

In the winter of 1856, the 27-year-old *Kekulé* went to Heidelberg to work under *Robert Wilhelm Bunsen* (1811—1899) as Privatdozent. A confined appartment which he had to rent for himself became his work-place, with the kitchen serving as laboratory for experiments on mercury fulminate[30] and



II. "On a new Series of Sulphuretted Acids." By Dr. August Kekulé. Communicated by Dr. Sharpey, Sec. R.S. Received April 5, 1854.

Adopting the idea that the series of organic compounds of which sulphuretted hydrogen is the type, corresponds in every respect with the series of which water is the type, I concluded that not only mercaptans and neutral sulphides which correspond to the alcohols and ethers, but also compounds corresponding to the acids, anhydrous acids and ethers of acids might be produced; I therefore endeavoured to obtain reactions which would enable me to replace oxygen in the compounds of the latter series by sulphur.

Such reactions are produced by the compounds of sulphur with phosphorus—the tersulphide (P_2S_3) and the pentasulphide (P_2S_5)—which are easily obtained by fusing together amorphous phosphorus and sulphur in an atmosphere of carbonic acid; no explosion takes place, although the combination is attended with a very violent action.

Experiment has proved that these combinations of sulphur and phosphorus act on the members of the series of water in the same manner (although less violently) as the corresponding compounds of chlorine and phosphorus;—however, with this difference, that by using the chlorine compounds the product is resolved into *two* groups of atoms, while by using the sulphur compounds there is obtained only *one* group; a peculiarity, which, according to the basic nature of sulphur, must have been expected. By acting on these compounds of sulphur and phosphorus with water one atom of sulphu-

Fig. 14. Publication of *Kekulé* at the age of 25 during his sojourn in England [28].

cacodyl compounds[31]; cleaning of the room used as lecture hall was the duty of the young Privatdozent. He soon gathered a large following of enthusiastic friends and students,



Fig. 15. Left: *August Kekulé* 1857. Right: *R. W. Bunsen.*

including *Emil Erlenmeyer* (1825—1909), *Hans Landolt* (1831—1910), *Lothar Meyer* (1830—1895), as well as *Friedrich Conrad Beilstein* (1838—1906) and *Adolf Baeyer* (1835—1917), who later reported: "In a theoretical context, a



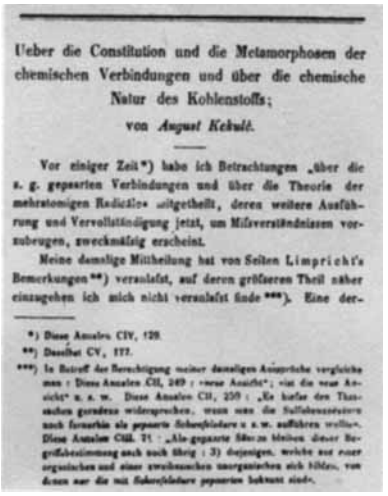
Ueber die Constitution des Knallquecksilbers;

von *Aug. Kekulé*,

Im Nachstehenden theile ich die Resultate einiger Versuche mit, die in der Absicht angestellt wurden, eine Ansicht über die Constitution des Knallquecksilbers experimentell zu begründen. Obgleich diese Versuche noch nicht zu vollständigem Abschluß gekommen sind, scheint es doch geeignet, sie einstweilen mitzutheilen, da ich voraussichtlich in der nächsten Zeit diese Untersuchung nur langsam werde fördern können.

Die verschiedenen Ansichten über die Constitution des Knallsäure und Knallquecksilbers sind so oft zusammengestellt und beleuchtet worden, daß eine Wiederholung hier überflüssig erscheint, zumal da von den meisten Chemikern die von Gay-Lussac und Liebig*) zuerst vorgeschlagene rationelle Formel beibehalten worden ist. Diese Chemiker,

Fig. 16. *Kekulé*'s studies on mercury(II) fulminate $Hg(OCN)_2$ [30].



Ueber die Constitution und die Metamorphosen der chemischen Verbindungen und über die chemische Natur des Kohlenstoffs;

von *August Kekulé*.

Vor einiger Zeit*) habe ich Betrachtungen „über die s. g. gepaarten Verbindungen und über die Theorie der mehratomigen Radicale" mitgetheilt, deren weitere Ausführung und Vervollständigung jetzt, um Mißverständnissen vorzubeugen, zweckmäßig erscheint.

Meine damalige Mittheilung hat von Seiten Limpricht's Bemerkungen**) veranlaßt, auf deren größeren Theil näher einzugehen ich mich nicht veranlaßt finde***). Eine der-

*) Diese Annalen CIV, 129.

**) Daselbst CV, 177.

***) In Betreff der Berechtigung meiner damaligen Ansprüche vergleiche man: Diese Annalen CII, 249: „neue Ansicht"; ein die neue Ansicht" u. s. w. Diese Annalen CII, 259: „Es hatte den Thatsachen geradezu widersprochen, wenn man die Sulfobenzoësäure auch fernerhin als gepaarte Schwefelsäure u. s. w. aufführen wollte". Diese Annalen CIII, 71: „Als gepaarte Säuren blieben dieser Begriffsbestimmung auch noch übrig: 3) diejenigen, welche aus einer organischen und einer zweibasischen unorganischen sich bilden, von denen nur die mit Schwefelsäure gepaarten bekannt sind".

Fig. 18. Title page of *Kekulé*'s famous publication on the theory of valency [34].

new world opened up to me in his lectures and in personal contact with him. Young chemists cannot gain an adequate idea from the literature of the influence exerted by the young *Kekulé* on his contemporaries. His textbook, in which he was frequently unfaithful to his own views, gives but an incomplete picture. His lectures were completely different. Captivated by the logical consistency of the new theory which was later known as structural theory, he constructed, before his enthusiastic listeners, the edifice of theoretical chemistry in which we still reside today"[32].



Fig. 17. From left to right: *E. Erlenmeyer, H. Landolt, F. C. Beilstein, A. Baeyer.*

For *Kekulé* the years spent in Heidelberg were a time of scientific maturation and the acquisition of complete independence. He developed his creative activity from the interaction between intuition and critical intellect. After the discovery of the methane type and of numerous other "radicals" derived therefrom, as well as the further development of the "mixed and double types" suggested by *Williamson* on the basis of the existence of dibasic acids, and the recognition of the significance of "atomicity", *i.e.* the valency of the elements themselves, the final step was taken with the discovery of the tetravalency of carbon and of its ability to join to itself. After years of hesitation, reconsideration, and repeated critical examination, he reported, in two papers published in 1857 and 1858[33,34], his brilliant and at the time daring ideas which were to bring about such a dramatic turn of events, perhaps the most decisive in the whole history of chemistry. The break with the old classification of chemical compounds was complete.

Kekulé wrote[34]: "I consider it necessary and, at the present state of chemical knowledge, feasible in many cases to go back to the elements themselves which make up a compound in explaining the properties of chemical compounds. I no longer consider it the primary task of our time to detect groups of atoms which can be regarded as radicals owing to certain properties and thus to ascribe the compounds to various types which have hardly any significance other than that of a typical formula. I rather believe that one should also extend the consideration to include the constitution of the radicals themselves, determine the relationship of the radicals with one another, and derive the nature of the radicals and that of their compounds from the nature of the elements. The considerations of the nature of the elements and of the basicity of atoms formerly compiled by myself are the starting point. The simplest combinations of the elements, as they are caused by the unequal basicity, are the simplest types. The compounds can be ascribed to certain types so long as the compound is attacked, during the reaction under consideration, in such a way that it shows the reaction characteristic of the type. I call that group a radical which is not attacked in the reaction concerned, and about whose composition one therefore need not concern oneself for the moment."

No sooner had *Baeyer*—still under the influence of *Bunsen*—attempted to establish the difference between methyl chloride and chloromethane[35], than *Kekulé* postulated the equivalence of the four hydrogen atoms of methane. He recognized that the endless variety of the carbon compounds is attributable to the ability of carbon to form single and multiple bonds with itself and other elements. He was the first to propose "rational formulae" for many of the more simple organic compounds. The theory of valency became the first classifying principle of far-reaching validity for the whole of chemistry. Time was ripe for publication of the new theory; the basic ideas were, so to speak, in the air after years of public discussion. Only a few months later, a treatise was published by the Scotsman *Archibald Scott Couper* (1831—1892) who was working with *Wurtz* at Paris but who was condemned all too soon to inactivity by illness, which likewise recognized the tetravalency of carbon and assumed the existence of carbon chains[36]. *Couper* was the first to symbolize

bonds in a manner resembling subsequent convention, *viz.* by dotted lines. In contrast, Kekulé initially continued to use "rational formulae", which—as he said—were intended only as "reaction but not constitutional formulae"[37] and in which the symbol for the element merely expressed the magnitude of the valency. They were jokingly called "sausages" by *Otto Nikolaus Witt* (1853—1915)[38], and "bread rolls" by the everbellicose *Hermann Kolbe* (1818—1884)[39]. *Alexander Michailowitsch Butlerow* (1846—1886), on the other hand, already considered it feasible to describe unequivocally the structure of a molecule[40].



Fig. 19. Left: *A. S. Couper.* Right: *A. M. Butlerow.*

This idea was also to gain *Kekulé*'s acceptance; he ultimately adopted the simpler formula notation of *Alexander Crum Brown* (1838—1922)[41], *Wurtz*[42], and *Hofmann*[43]. Meanwhile appointed professor of chemistry at the University of Ghent[44], he devoted his energy to the extension of structural theory, as is impressively documented in his four-volume textbook[45], which remained unfinished, and continued to exert a strong influence on his contemporaries.

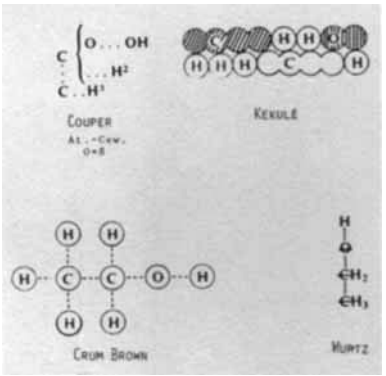


Fig. 20. Development of the notation of chemical formulae as illustrated for ethanol.

Various passages in *Kekulé*'s publications and particularly his lecture "Über die Constitution der Salze"[46] presented to the "Naturforschertagung" held at Innsbruck in 1869 bear witness to his early concepts of the three-dimensional arrangement of atoms. In 1867 he wrote in his important treatise "Über die Constitution des Mesitylens"[47]: "This imperfection"—of the older models—"can be avoided if the four relationship units of carbon instead of being located in a plane are allowed to project from the sphere of the atom in the direction of hexahedral axes such that they terminate in tetrahedral planes." He thus transferred the realm of the chemical bond out of the plane into three-dimensional space.

All that his student *Jacobus Henricus van't Hoff* (1852—1911) was to add to this idea seven years later was actually already present in *Kekulé*'s models. The 22-year-old *van't Hoff*[48] and the 27-year-old *Joseph Achille LeBel* (1847—1930)[49] however drew the ultimate consequences from the discoveries of *Jean-Baptiste Biot* (1774—1862)[50] and *Louis Pasteur* (1822—1895)[51] and thus laid the foundation of stereochemistry which has lost none of its topicality to this day[52]. A logical development took place from *Kekulé*'s structural chemistry and *van't Hoff* and *LeBel*'s hypothesis *via Baeyer*'s strain theory[53] and the geometrical isomerism of *Johannes Wislicenus* (1835—1902)[54] to *Emil Fischer*'s (1852—1919) studies on relative configuration[55], and thence *via* the isomerism of nitrogen compounds observed by *Arthur Hantzsch* (1857—1935)[56] and the coordination chemistry of *Alfred Werner* (1866—1919)[57], the steric hindrance of chemical reactions[58] discovered by *Victor Meyer*[59] (1848—1897), the Walden inversion [*Paul Walden* (1863—1957)], and the Sachse-Mohr theory[60] [*H. Sachse, Ernst Mohr* (1873—1926)] up to the study of conformation as introduced by *Kenneth S. Pitzer* (born 1914)[61], *Odd Hassel* (born 1897)[62], and



Fig. 21. From left to right: *J. H. van't Hoff, J. A. LeBel, J. Wislicenus, E. Fischer.*

above all *Sir Derek H. R. Barton* (born 1918)[63]. Experimental proof of the validity of the tetrahedral model was provided by X-ray structure analysis as performed by *Sir William Henry Bragg* (1862—1942) and *Sir William Lawrence Bragg* (1890—1971)[64]; the theoretical foundation was laid by *Linus Pauling* (born 1901)[65] and *Erich Hückel* (born 1896)[66] with the aid of quantum chemistry.

Structural chemistry provided a basis for the explanation of the composition and mode of reaction of aliphatic compounds, not least after clear conventions had been agreed upon concerning the terms atom, molecule, equivalent, *etc.*, at the first international congress on chemistry at Karlsruhe in 1860[67] instigated by *Kekulé*, and thanks mainly to *Stanislao Cannizzaro*'s (1826—1910) convincing statements concerning *Avogadro*'s law and the significance of atomic weights for chemical formulae. However, the large class of aromatic compounds still defied understanding, in spite of *Peter Griess*' (1829—1888) discovery of diazonium salts[68] and *Kolbe*'s synthesis of salicylic acid[69], as well as that of the first organic dyestuff mauvine[70], whose color resembles that of the mallow flower, by *William Henry Perkins* (1838—1907) in 1856.

Once more *Kekulé*'s efforts were crowned with success. His irrepressible striving for visual clarity and his exceptionally powerful imagination were again instrumental in this achievement. Derivation of the formula of benzene is basically a logical consequence of his structural theory—an ob-

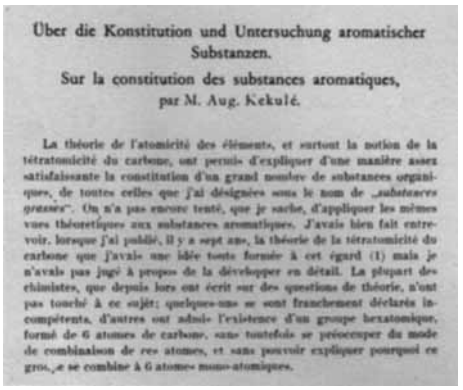
vious step when viewed from the vantage point of present-day knowledge but a great leap more than a century ago, comparable perhaps with the intellectual effort once required for man to replace the sled by the wheel. Appreciation of the fact that carbon compounds could have cyclic



Fig. 22. Left: *S. Cannizzaro.* Right: *A. W. von Hofmann.*

structures was withheld from the chemists of that epoch. The circle was the symbol for the indivisible, the atom. *August Wilhelm von Hofmann* (1818—1892) remarked on a later occasion "I would forfeit all my discoveries for that thought of *Kekulé*'s"[71].

In his paper "Sur la Constitution des Substances Aromatiques"[72] submitted to the Paris Academy in 1865, once again after several years of deliberation and examination, and in the following contribution to Liebigs Annalen entitled "Untersuchungen über aromatische Verbindungen"[73] he refined his theory of the structure of benzene, *inter alia,* with the



Über die Konstitution und Untersuchung aromatischer Substanzen.

Sur la constitution des substances aromatiques,

par M. Aug. Kekulé.

La théorie de l'atomicité des éléments, et surtout la notion de la tétratomicité du carbone, ont permis d'expliquer d'une manière assez satisfaisante la constitution d'un grand nombre de substances organiques, de toutes celles que j'ai désignées sous le nom de „substances grasses". On n'a pas encore tenté, que je sache, d'appliquer les mêmes vues théoriques aux substances aromatiques. J'avais bien fait entrevoir, lorsque j'ai publié, il y a sept ans, la théorie de la tétratomicité du carbone que j'avais une idée toute formée à cet égard (1) mais je n'avais pas jugé à propos de la développer en détail. La plupart des chimistes, que depuis lors ont écrit sur des questions de théorie, n'ont pas touché à ce sujet; quelques-uns se sont franchement déclarés incompétents, d'autres ont admis l'existence d'un groupe hexatomique, formé de 6 atomes de carbone, sans toutefois se préoccuper du mode de combinaison de ces atomes, et sans pouvoir expliquer pourquoi ce groupe se combine à 6 atomes mono-atomiques.

Fig. 23. Titel page of *Kekulé*'s first publication on the structure of benzene [72].

striking sentence "These facts apparently justify the conclusion that in all aromatic substances one and the same atomic group, or, if one will, a common nucleus is present which is made up of six carbon atoms." This idea was also present in considerations of *Joseph Loschmidt* (1821—1895)[74] although he had no clear idea of the structure of this nucleus.

Even *Kekulé*'s first publications on benzene contain the symmetrical hexagonal formula and mention the equivalence of the six hydrogen atoms. Not long afterwards he and his students *Wilhelm Körner* (1839—1925)[75] and *Albert Ladenburg* (1842—1911)[76] were able to substantiate this idea experimentally. *Kekulé* supplemented his static concept of bonding by introduction of the hypothesis of oscillation[77].

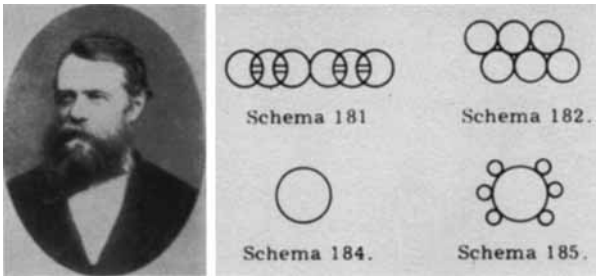


Fig. 24. Left: *J. Loschmidt.* Right: *Loschmidt*'s benzene formulae.

The discovery of the benzene formula was recounted in all developed countries 100 years later—14 years ago—and the significance of a theory which has retained its full validity for more than a century and the consequences of this theory were emphasized by qualified commentators[15]. *Kekulé*'s proposed structure of benzene also initiated a development



Fig. 25. Left: *W. Körner.* Right: *A. Ladenburg.*

that has continued to this day, and which has been especially promoted by quantum mechanics which provides all the necessary requirements for a "mechanical approach"[78] to

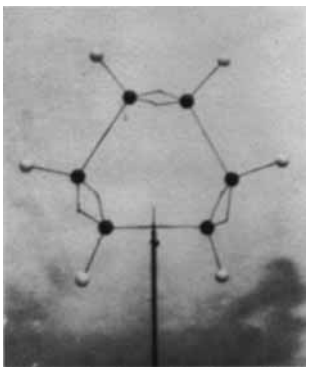


Fig. 26. Kekulé's benzene model of 1866 (original).

chemistry as already demanded by *Kekulé.* It acquired a new dimension in *Erich Hückel*'s theory of cyclic π-electron systems[79].



Fig. 27. Left: *E. Hückel.* Right: *August Kekulé* 1867.

After nine years of restless activity at Ghent, which made *Kekulé* the reformer of organic chemistry, he accepted a call to Bonn[80] in 1867. This was the last stage in the career of this truly European scholar and teacher whose years of international travel as apprentice and scientist call for emulation on the part of the younger generation, more urgently than ever before!



Fig. 28. *Kekulé*'s certificate of appointment at Bonn (bearing the signature of *Wilhelm I*) [80].

The three decades left to him were mainly devoted to further testing and confirmation of the benzene theory. Together with numerous students, including *Theodor Zincke* (1843—1928), *Ludwig Claisen* (1851—1930), and *Julius Bredt* (1855—1937), as well as *Richard Anschütz* (1847—1937) and *Otto Wallach* (1847—1931), many of whom were to become pioneers of chemistry in the closing 19th and early 20th century, he refuted other views and structural proposals of his colleagues by pointing out errors and false conclusions[81]. His sole motivation was the quest for knowledge of the true scientist, far removed from all striving after technical perfection and immediate utility. Views such as that propounded by his adversary *Kolbe*, "It is not so much a matter of explaining everything but of how things are interpreted"[82] contradicted the critical intellect of the seeker after truth[83].

During the years spent at Bonn, *Kekulé* saw the dramatic effect of his ideas on the expanding chemical industry. He was awarded the highest honors[84]. His benzene theory had made possible the directed synthesis of dyestuffs, initiated



Fig. 29. Above, from left to right: *H. Kolbe, Th. Zincke, L. Claisen.* Below: *J. Bredt, R. Anschütz, O. Wallach.*

the rise of the entire organic chemical industry—especially coal tar chemistry—and had an enduring stimulating effect on the imagination of chemists. Industry and chemical science drew closer together and adopted a symbiotic relationship[85]. This is compelling confirmation of the known fact that fundamental research, however abstract or "unpractical" its aims may appear, is indispensable and can crucially influence the development of technology sooner or later. "The depths of knowledge are never explored by him who seeks profit but by him who, motivated by a vital urge for inquiry, deploys his entire personality". Research is not just a matter for civil servants, neither does it thrive under the direction of burocracy and ideologies or the requirement of "relevance" of science. *Kekulé*'s fruitful work demonstrates convincingly that highly qualified fundamental research can be neither planned nor forced and can only rarely be assessed according to its immediate utility. This is a timely warning for the state and university administrations to reinstate research to its central position in universities and to give preferential consideration to conditions necessary for the development of the personalities required for such work rather than to formal aspects and matters of university politics.

In his famous, psychologically interesting address to the "Benzene Festival" of the German Chemical Society at Berlin in 1890[86] celebrated on the 25th anniversary of the benzene formula—probably one of the most ostentatious conferences ever held by a learned society—*Kekulé* himself contributed to the legends associated with his person. His great achievements will hardly have come to him merely in a dream on a London bus[87] or by his fireplace in Ghent[88]. Rather, they were the fruit of decades of hard work by day and often by night, loyal to the advice of his teacher *Liebig* "... whoever fails to ruin his health by study will not make his way in chemistry today"[89], or as expressed by *Max von Pettenkofer* (1818—1901): "The man who wishes to be superior to an animal must be prepared to sacrifice life and health for higher things"[90]. This condition is certainly not so rigorous in today's laboratories, but utter commitment and renunciation for the sake of increasing knowledge are still

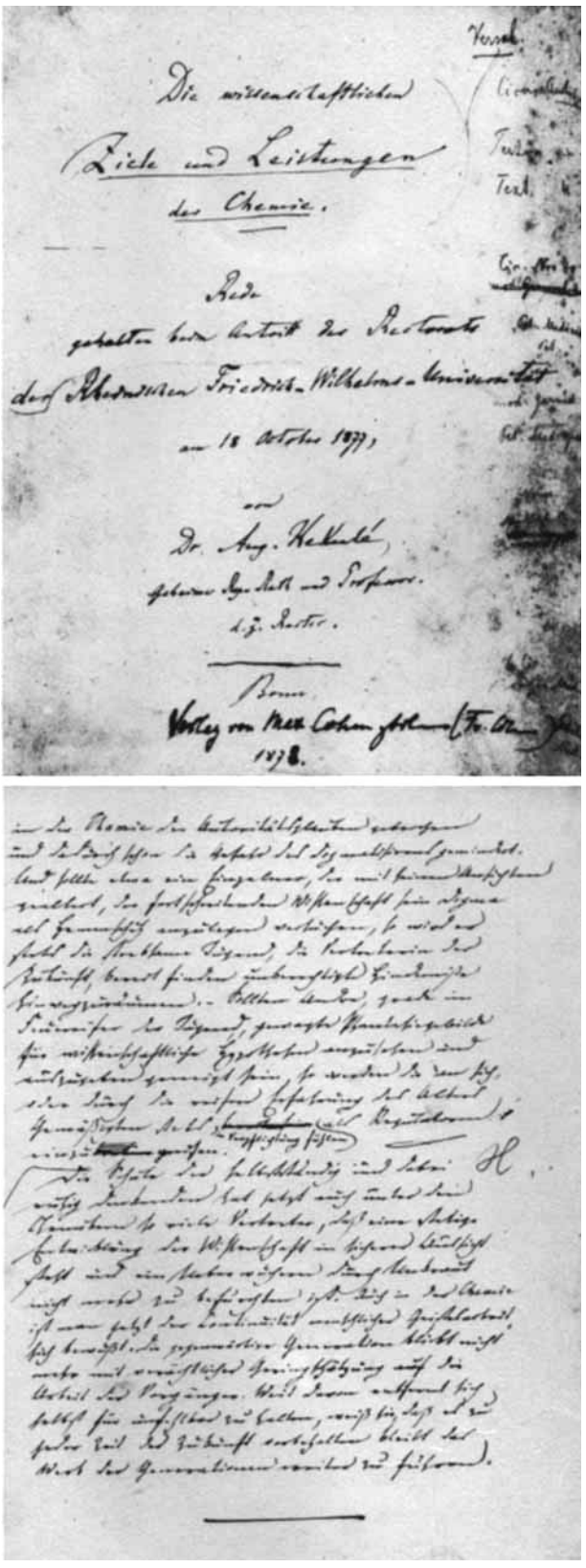


Fig. 30. Handwritten title page and last page of manuscript of *Kekulé*'s speech as University Chancellor in 1877 [14].

just as essential. Above all, however, we see *Kekulé*, the architect of chemistry, as an ideal researcher by virtue of his rare combination of daring and caution, his pronounced critical powers (also with regard to himself), his polite reservedness, always avoiding aggressive irony, conflicts, and polemics, in particular his great modesty which grew out of the recognition that all his ideas and practical work were only the extension of the achievements of his predecessors and teachers. That inner greatness which creates modesty moved him to say: "Something completely new has never been thought of, certainly not in chemistry"[91]. The warning and encouragement of the closing lines of his important speech as University Chancellor in 1877[92] still appear valid a century later: "As in all areas of knowledge in chemistry, too, faith in authority has been broken and the danger of dogmatization thus reduced. Should an individual who has aged with his ideas attempt to apply his dogma as a brake to an advancing science, he will always find zealous youth, as representative of the future, ready to clear away unjustified obstacles. Should others, in the ardor of youth, be inclined to regard and propound bold flights of fancy as scientific hypotheses, then those who are more moderate by nature or through the maturing experience of age will always feel obliged to intervene as regulators.

The school of independently and calmly reasoning people has now gained so many representatives among chemists that a constant development of this science is ensured and a takeover by weeds need no longer be feared. In chemistry too, the continuity of human intellectual work is recognized; the present generation no longer looks upon the work of its predecessors with scornful contempt; far removed from considering itself infallible, it knows that at any time it is the prerogative of the future to continue the work of generations."

July 13, 1896, was the last day in the life of this giant among men, who was privileged to know that his theories never led anybody astray but instead opened the way for innumerable discoveries.

I am indebted to my co-workers Dr. M. Gold and Dipl.-Ing. H. G. Kläs for extensive photographic work in the reproduction of original documents and portraits.

Received: May 3, 1979 [A 286 IE]
German version: Angew. Chem. *81*, 685 (1979)

[1] *A. Kekulé, H. Schrötter,* Ber. Dtsch. Chem. Ges. *12*, 2279 (1879).
[2] *H. Meerwein, K. van Emster,* Ber. Dtsch. Chem. Ges. *55*, 2500 (1922).
[3] *F. Wöhler,* Poggendorffs Ann. Phys. Chem. *12*, 253 (1828).
[4] *Georg Ernst Stahl* (1660—1734), father of the phlogiston theory.
[5] a) *M. Faraday,* Philos. Trans. R. Soc. London *1825*, 440; b) Ann. Chim. Phys. [2] *30*, 269 (1825).
[6] *E. Mitscherlich,* Ann. Pharm. (Lemgo, Ger.) *IX*, 39 (1834).
[7] *F. F. Runge,* Poggendorffs Ann. Phys. Chem. *32*, 308 (1834).
[8] *J. J. Berzelius,* Berz. Jahresber. *15*, 237 (1834/36).
[9] *J. J. Berzelius,* Poggendorffs Ann. Phys. Chem. *19*, 305 (1832).
[10] *F. Wöhler, J. Liebig,* Ann. Pharm. (Lemgo, Ger.) *III*, 249 (1832).
[11] *J. J. Berzelius,* Ann. Pharm. (Lemgo, Ger.) *III*, 282 (1832), p. 285.
[12] *R. Schäfer* in: Ahnentafel berühmter Deutscher, publ. by Zentralstelle für Personen- und Familiengeschichte, Vol. 5, Part 7, p. 137, Leipzig 1939.
[13] Festschrift "325 Jahre Ludwig-Georgs-Gymnasium Darmstadt" (1629—1954), Darmstadt 1954.
[14] The original document is in the *Kekulé* archives of the Institute of Organic Chemistry of the Technical University of Darmstadt.
[15] *R. Witzinger-Aust* "August Kekulé, Leben und Werk" in: Kekulé und seine Benzolformel. Verlag Chemie, Weinheim 1966, p. 8.
[16] *W. Schlink:* Die Technische Hochschule Darmstadt 1836—1936. Verlag E. Roether, Darmstadt 1936.
[17] *R. Anschütz:* August Kekulé, Vol. I (Leben und Wirken). Verlag Chemie, Berlin 1929, p. 11.
[18] *J. v. Liebig:* Chemische Briefe, 3rd Edit. Heidelberg 1851, pp. VIII and 27. Brief pp. 592, 595.
[19] *A. Kekulé,* Ann. Chem. Pharm. *LXXV*, 275 (1850).

[20] Degree of Giessen University of June 25, 1852.

[21] *J. B. Dumas*, Ann. Chim. Phys. [2] *73*, 205 (1840); cf. also *C. Graebe:* Geschichte der Organischen Chemie. J. Springer, Berlin 1920, p. 92.

[22] Chancellor's address on October 18, 1877, Bonn University. M. Cohen & Sohn, Bonn 1878, p. 7.

[23] *A. Wurtz*, C. R. Acad. Sci. *28*, 233 (1849); *29*, 169 (1849).

[24] With *A. von Planta*, *A. Kekulé* conducted investigations on nicotine [Ann. Chem. Pharm. *LXXXVII*, 1 (1853)] and coniine [*ibid LXXXIX*, 129 (1854)], as well as analyses of limestones, gall stones, and mineral springs [*ibid. LXXXVII*, 364 (1853); *XC*, 316 (1854)].

[25] *A. W. Williamson*, Philos. Mag. *37*, 350 (1850); Ann. Chem. Pharm. *LXXVII*, 37 (1851); J. Chem. Soc. *4*, 229 (1851).

[26] *E. Frankland*, Ann. Chem. Pharm. *LXXI*, 171, 213 (1849).

[27] *A. Kekulé*, address delivered at the "Benzene festival" of the German Chemical Society at Berlin on March 11, 1890; cf. [86], p. 1308.

[28] *A. Kekulé*, Proc. R. Soc. London *VII*, 37 (1854).

[29] *A. Kekulé*, Ann. Chem. Pharm. *XC*, 309 (1854).

[30] *A. Kekulé*, Ann. Chem. Pharm. *CI*, 200 (1857); *CV*, 279 (1858).

[31] *A. Baeyer*, Ann. Chem. Pharm. *CVII*, 257 (1858).

[32] *A. v. Baeyer:* Gesammelte Werke, Vol. I, p. XV. F. Vieweg & Sohn, Braunschweig 1905.

[33] *A. Kekulé*, Ann. Chem. Pharm. *CIV*, 129 (1857).

[34] *A. Kekulé*, Ann. Chem. Pharm. *CVI*, 129 (1858).

[35] *A. Baeyer*, Ann. Chem. Pharm. *CIII*, 181 (1857).

[36] *A. S. Couper*, C. R. Acad. Sci. *46*, 1157 (1858); cf. also comment by *A. Kekulé*: *ibid. 47*, 378 (1858).

[37] *A. Kekulé:* Lehrbuch der Organischen Chemie, Vol. I. F. Enke, Erlangen 1861, p. 157.

[38] *O. N. Witt* at the Naturforscherversammlung held at Berlin on September 20, 1886 ("Berichte der Durstigen Chemischen Gesellschaft—Unerhörter Jahrgang No. 20", Disputation, R. Friedländer und Sohn, Berlin 1886); cf. also *W. Ruske:* 100 Jahre Deutsche Chemische Gesellschaft. Verlag Chemie, Weinheim 1967, p. 82.

[39] *H. Kolbe*, J. Prakt. Chem. [2] *23*, 305, 353, 489 (1881).

[40] *A. M. Butlerow*, Z. Chem. *4*, 549 (1861); *5*, 297 (1862).

[41] *A. Crum Brown*, Proc. R. Soc. Edinburgh *23*, 428 (1865).

[42] *A. Wurtz:* Lecons de philosophie chimique. Librairie de L. Hachette et Cie., Paris 1864, pp. 133 ff.

[43] *A. W. Hofmann*, Chem. News *12*, 166, 175, 187 (1865).

[44] At the instigation of *Jean Servars Stas* (Brussels), *A. Kekulé* is called to the State University of Ghent, Belgium, in *1858*, as successor of *Joseph Mareska* (cf. *J. B. Gillis:* "Leben und Wirken von Kekulé in Gent" in [15]; also [17]).

[45] *A. Kekulé:* Lehrbuch der Organischen Chemie, Bd. I (1861), II (1866), III (1882), IV (first instalment) (1887). F. Enke, Erlangen.

[46] *A. Kekulé*, Ber. Dtsch. Chem. Ges. *2*, 650 (1869).

[47] *A. Kekulé*, Z. Chem. [2] N. F. *3*, 214 (1867).

[48] *J. H. van't Hoff:* Voorstel tot uitbreiding der tegenwoordig in de scheikunde gebruikte structuur-formules in de ruimte. Greven, Utrecht 1874; Bull. Soc. Chim. Fr. [2] *23*, 295 (1875).

[49] *J. A. LeBel*, Bull. Soc. Chim. Fr. [2] *22*, 337 (1874).

[50] *J. B. Biot*, Mem. Acad. Sci. Inst. Fr. *2*, 41 (1817); *13*, 39 (1835).

[51] *L. Pasteur*, Ann. Chim. Phys. [3] *24*, 442 (1848).

[52] *J. Weyer*, Angew. Chem. *86*, 604 (1974); Angew. Chem. Int. Ed. Engl. *13*, 591 (1974).

[53] *A. Baeyer*, Ber. Dtsch. Chem. Ges. *18*, 2269 (1885).

[54] *J. Wislicenus*, Abh. Math.-Phys. Kl. Kgl. Saechs. Ges. Wiss. *14*, 1 (1887).

[55] *E. Fischer*, Ber. Dtsch. Chem. Ges. *24*, 2683 (1891); *29*, 1377 (1896).

[56] *A. Hantzsch*, *A. Werner*, Ber. Dtsch. Chem. Ges. *23*, 11 (1890).

[57] *A. Werner*, Z. Anorg. Chem. *3*, 267 (1893).

[58] *J. van Loon*, *V. Meyer*, Ber. Dtsch. Chem. Ges. *29*, 839 (1896).

[59] *P. Walden*, Ber. Dtsch. Chem. Ges. *29*, 133 (1896).

[60] *H. Sachse*, Ber. Dtsch. Chem. Ges. *23*, 1363 (1890); Z. Phys. Chem. Stöchiom. Verwandtschaftsl. *10*, 203 (1892); *E. Mohr*, J. Prakt. Chem. [2] *98*, 315 (1918).

[61] *J. D. Kemp*, *K. S. Pitzer*, J. Chem. Phys. *4*, 749 (1936); *Ch. W. Beckett*, *K. S. Pitzer*, *R. Spitzer*, J. Am. Chem. Soc. *69*, 2488 (1947).

[62] *O. Hassel*, Quart. Rev. Chem. Soc. *7*, 221 (1953).

[63] *D. H. R. Barton*, Experientia *6*, 316 (1950).

[64] *W. H. Bragg*, *W. L. Bragg*, Proc. R. Soc. London *A 89*, 277 (1913).

[65] *L. Pauling*, J. Am. Chem. Soc. *53*, 1367 (1931).

[66] *E. Hückel*, Z. Elektrochem. Angew. Phys. Chem. *36*, 641 (1930); Z. Phys. *60*, 423 (1930).

[67] The events leading up to this congress and the course it took are described by *Carl Engler* in his paper; "Vier Jahrzehnte chemischer Forschung unter besonderer Rücksicht auf Baden als Heimstätte der Chemie", Karlsruhe 1892; cf. also [17].

[68] *P. Griess*, Ann. Chem. Pharm. *CVI*, 123 (1858); *CXIII*, 201 (1860); *CXVII*, 1 (1861); *CXXI*, 257 (1862); *CXXXVII*, 39 (1866).

[69] *H. Kolbe*, Ann. Chem. Pharm. *CXIII*, 125 (1860).

[70] Cf. *R. Meldola*, Ber. Dtsch. Chem. Ges. *44*, 911 (1911). British Patent No. 1984 was granted for the dyestuff mauveine on August 26, 1856.

[71] *J. Volhard*, Ber. Dtsch. Chem. Ges. *35*, III. Sonderheft, p. 165 (1902).

[72] *A. Kekulé*, Bull. Soc. Chim. Fr. [2] *3*, 98 (1865).

[73] *A. Kekulé*, Ann. Chem. Pharm. *CXXXVII*, 129 (1866).

[74] *J. Loschmidt:* Chemische Studien. Wien 1861; cf. also *R. Anschütz*, Ber. Dtsch. Chem. Ges. *45*, 539 (1912); Ostwalds Klassiker der exakten Naturwissenschaften Nr. 190, Leipzig 1913.

[75] *W. Körner*, Bull. Acad. R. Belg. [2] *24*, 166 (1867); Gazz. Chim. Ital. *4*, 305 (1874); cf. also Jahresber. Chem. *28*, 299 (1875).

[76] *A. Ladenburg*, Ber. Dtsch. Chem. Ges. *2*, 140, 272 (1869); *7*, 1133 (1874).

[77] *A. Kekulé*, Ann. Chem. Pharm. *CLXII*, 77 (1872).

[78] See [77]; cf. also *H. Hartmann*, Angew. Chem. *77*, 750 (1965); Angew. Chem. Int. Ed. Engl. *4*, 729 (1965).

[79] *E. Hückel*, Z. Phys. *70*, 204 (1931).

[80] The "certificate of appointment" signed by *Wilhelm I* of Prussia was issued on June 1, 1862 [14]. In 1875 *Kekulé* refused a call to Munich University as *Liebig*'s successor.

[81] Cf. [17], pp. 496 ff.

[82] *H. Kolbe* in: Das chemische Laboratorium der Universität Leipzig. F. Vieweg & Sohn, Braunschweig 1872, p. 163.

[83] See "Cassirte Kapitel aus der Abhandlung: Ueber die Carboxytartronsäure und die Constitution des Benzols". At the advice of *Volhard*, *Kekulé* did not publish them. A facsimile reprint of the unpublished manuscript [14] of August 12, 1883, was published by Verlag Chemie, Weinheim, in 1965.

[84] *A. Kekulé* was a member of most of the European Academies. In addition to other honors, he was awarded the Copley medal in 1885, the Huyghens medal in 1889, and the "Kronenorden II. Klasse" and the Bavarian "Maximilian-Orden für Kunst und Wissenschaft" in 1890. He was nominated as voting "Ritter des Ordens pour le mérite für Wissenschaft und Künste" in 1893 by *Wilhelm II* of Prussia.

[85] *A. von Weinberg*, Z. Angew. Chem. *43*, 167 (1930); *C. Wurster* "Die heutige Bedeutung der Benzolchemie" in [15].

[86] Report by *G. Schultz*, Ber. Dtsch. Chem. Ges. *23*, 1265 (1890).

[87] In his address at the "Benzene festival", *A. Kekulé* recounted his discovery of the theory of valency: "During my stay in London I lived for some time in Clapham Road, near the Common. However, I often spent the evenings with my friend *Hugo Müller* in Islington, at the other end of the great city. We talked about diverse matters, but mostly about our beloved chemistry. One fine summer day I was traveling once again on the last omnibus through the empty streets of the otherwise so bustling metropole; 'outside', on the roof of the omnibus, as always, I began to dream. Atoms danced before my eyes. I had always seen them in motion, those little entities, but I had never succeeded in detecting the nature of their motion. Today I saw how two of them frequently joined to form pairs; how larger ones surrounded two smaller ones, yet larger ones held three and even four of the small ones, and how everything turned in whirling dance. I saw how larger ones formed a row, drawing along smaller ones only at the ends of the chain. I saw what past-master *Kopp*, my venerable teacher and friend, has described in such a charming way in his "molecular world": but I saw it long before him. The conductor's call: "Clapham Road" wakened me out of my reverie, but I spent part of the night committing at least sketches of that dream to paper. Thus arose the theory of structure (cf. [86], p. 1306).

[88] Concerning the enunciation of the benzene formula, *Kekulé* said, in the same speech (cf. [86], p. 1306): "It was a similar matter with the benzene theory. During my time at Ghent in Belgium, I lived in elegant bachelors' rooms in the main street. However, my study looked onto a dark side-alley and was without light during the day. That was no disadvantage for a chemist who spends the daylight hours in the laboratory. There I sat and wrote for my textbook; but things did not go well; my mind was occupied with other matters. I turned the chair towards the fireplace and began to doze. Once again the atoms danced before my eyes. This time smaller groups modestly remained in the background. My mental eye, sharpened by repeated apparitions of similar kind, now distinguished larger units of various shapes. Long rows, frequently joined more densely; everything in motion, twisting and turning like snakes. And behold, what was that? One of the snakes caught hold of its own tail and mockingly whirled round before my eyes. I awoke, as if by lightening; this time, too, I spent the rest of the night working out the consequences of this hypothesis".

[89] Cf. [86], p. 1306.

[90] *K. Kisskalt:* Max von Pettenkofer, Gedächtnisrede zur Feier seines 125. Geburtstages gehalten in der öffentlichen Sitzung der Bayerischen Akademie der Wissenschaften am 19. Januar 1944. Verlag der Bayerischen Akademie der Wissenschaften, München 1944.

[91] Cf. [86], p. 1304.

[92] Cf. [22], p. 28.

Criteria for the Efficiency, Stability, and Capacity of Abiotic Photochemical Solar Energy Storage Systems[**]

By Hans-Dieter Scharf, Jörg Fleischhauer, Hans Leismann, Ingrid Ressler, Wolfgang Schleker, and Robert Weitz[*]

The utilization of simple photochemical reactions for the storage of solar energy in the form of chemical energy in energy-rich products has often been considered in the further development and improvement of *e.g.* simple thermosolar techniques. The hitherto proposed criteria for the qualification of an abiotic photochemical system are, however, mostly of a qualitative nature, so a mutal comparison of the systems is not precise enough. In this article it is shown how a useful correlation on the basis of time-independent experimental data can be achieved and how, from the viewpoint of photochemistry, a comparative classification of known reactions is possible. The following reactions are compared: the [2+2]-photocycloadditions of norbornadiene, dimethyl 2,3-norbornadienedicarboxylate, and dicyclopentadienone, the photoisomerization of *trans*- to *cis*-diacetylindigo, the photodissociation of nitrosyl chloride as well as a photocatalytic redox reaction. The quantity of material required and storage efficiency are by far the most favorable in the case of *trans*-diacetylindigo. The main disadvantage of the latter however, is that the energy-rich *cis*-form rapidly reverts to the stable *trans*-form at elevated temperatures.

1. Introduction

The utilization of solar energy for domestic and industrial purposes has acquired paramount importance in the research efforts of all industrialized nations. The principal aim of the investigations undertaken is the conversion of the sun's radiant energy into

1) low-temperature heat (thermosolar technique),
2) mechanical energy (thermomechanical solar power stations),
3) electrical energy (solar cells, photovoltaic processes, *etc.*),
4) chemical energy (production of "fuel").

The techniques involved in the conversions 1 and 2 as well as the solar cell technique have already been developed to the points of industrial application; however, their application is rendered difficult by the following facts:

a) solar radiation has a low energy density[1], so suitable collector systems require a lot of space and are costly,
b) the energy supply is not constant with time,
c) places enjoying high solar radiation density are often geographically unfavorable.

Therefore, in order to utilize solar energy independently of time and geographic position it is essential to generate "fuel" (free chemical energy) with the aid of sunlight. Worldwide research activities in this sector are at present primarily concerned with the fundamental principles of the following interdisciplinary topics:

4.1. the thermochemical decomposition of water[2], NH_3[3], SO_3[4] at high temperatures (>500 °C)
4.2. model systems for photosynthesis[5–7] (artificial membranes[8], micelles[9], synthetic molecular organizates[10])
4.3. photoelectrochemistry of semiconductors[11] (production of electrical and/or chemical energy)
4.4. photogalvanic cells[12]
4.5. photochemical redox systems (*e.g.* photolysis of water[13])
4.6. photochemical unimolecular solar energy storage in energy-rich inorganic or organic molecules

Some excellent reviews of the topics outlined under point 4 are to be found in the American[14], British[15], and Swedish[16] literature.

Obviously, the abiotic conversion of solar energy into a form of energy useful for domestic and industrial purposes is difficult. First of all, suitable storage processes are lacking, to bridge the time when the sun is not shining. The only example of long-term storage of solar energy (photosynthesis) is provided by nature. Disregarding the utilization of fossil fuels, the green plant is not an ideal energy-storage system for man, except from the point of view of its nutritional value, because its cultivation requires large amounts of water, fertilizers and entails a lot of work.

Whereas the efficiency of solar energy storage in photosynthesis is about 6—8%[17,18], the thermodynamic limitation for photochemical energy storage is 15—20%[17,19], so chemists are searching for synthetic compounds, which form energy-rich products by absorption of the sun's radiation. The energy thus stored must be regainable at a later date, with simultaneous recovery of the starting material.

In general the following advantages over the storage of solar energy in molecular movement in condensed phases or in latent heat (called simple thermosolar techniques) are well acknowledged: no elaborate heat insulation is required, energy "harvesting" is even possible in winter and from diffuse daylight and the storable energy can reach up to five times the heat storage value of water (209 J/g; 20—70 °C). This would favor especially the production of low temperature heat for everyday purposes.

A number of photochemical systems (topics 4.5 and 4.6) able to store solar energy have been proposed[20–30] in the

[*] Prof. Dr. H.-D. Scharf, Prof. Dr. J. Fleischhauer, Dr. H. Leismann, Dipl.-Chem. I. Ressler, Dipl.-Chem. W. Schleker, Dipl.-Chem. R. Weitz
Institut für Organische Chemie der Technischen Hochschule
Prof.-Pirlet-Strasse 1, D-5100 Aachen (Germany)

[**] Presented in part at the meeting of the GdCh-Fachgruppe "Photochemie" in Mülheim/Ruhr, November 23, 1978, under the title "Utilization of solar energy—a challenge to photochemistry?"

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0909-0652 $ 02.50/0

past, but no great effort has been made to consistently and quantitatively compare the storage efficiencies, material requirements, and stabilities of the cited systems. Such criteria, however, are desirable in order to validate sometimes optimistically represented empirical data and to be able to evaluate known as well as new systems with regard to the above mentioned properties.

Therefore, in this paper we shall establish criteria based on quantum yields, reaction enthalpies, absorption spectra, and the extent of side reactions, and apply them, for purpose of comparison, to photochemical storage systems (topics 4.5 and 4.6), wherever the necessary experimental data are available.

2. Principles of Photochemical Storage Systems in Homogeneous Phases

Starting from a compound A the storage of photon energy as chemical energy in a product B requires a photon absorber, whose energy level (Jablonski) diagram is shown in Figure 1. This light absorber can be either compound A itself or a sensitizer (Sens), or a photocatalyst (Cat).

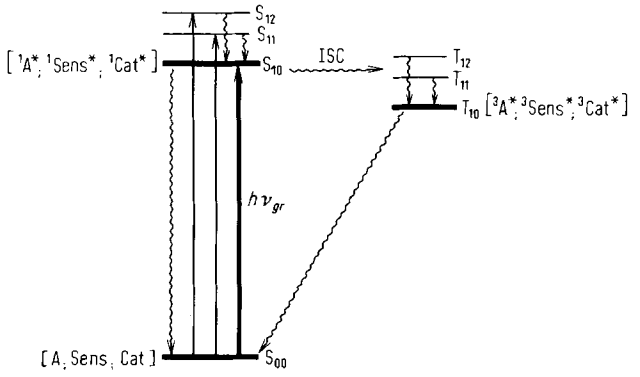


Fig. 1. Photophysical activation and deactivation processes of the photon absorbers A, Sens, and Cat respectively. A = starting material; Sens = sensitizer; Cat = photocatalyst; S_{00} = singlet ground state of A, Sens, or Cat; S_{10} = first excited singlet state: $^1A^*$, $^1Sens^*$, or $^1Cat^*$; S_{11}, S_{12} = higher vibrational levels of S_1; T_{10} = first excited triplet state: $^3A^*$, $^3Sens^*$, or $^3Cat^*$; T_{11}, T_{12} = higher vibrational levels of T_1; ISC = intersystem crossing; $h\nu_{gr}$ = energy of a photon capable of the excitation $S_{00} \rightarrow S_{10}$ (threshold energy); $\rightarrow \hat{=}$ optical transitions; $\rightsquigarrow \hat{=}$ radiationless transitions.

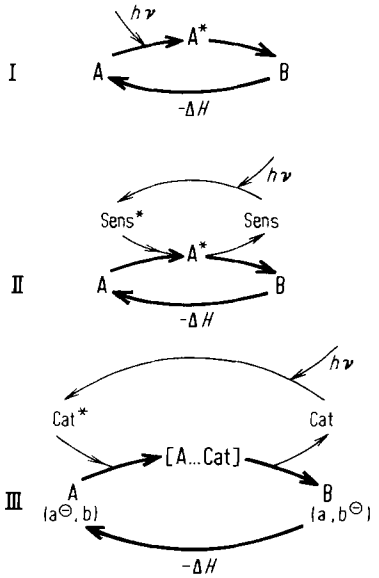


Fig. 2. Simple schemes of thermoreversible photoreactions (type I, II, and III). B = energy-rich photochemical product in ground state; A* = excited singlet or triplet state of starting material A; Sens* = singlet or triplet excited sensitizer; Cat* = singlet or triplet excited photocatalyst; $(a^{\ominus}, b)$, $(a, b^{\ominus})$ = A and B, respectively, as redox couples; {A.....Cat} = electron transfer complex; ΔH = enthalpy difference of the ground states of B and A.

According to this energy level diagram most of the thermoreversible photoreactions proposed in the literature[20-30] can be reduced to three simple types of reactions (see Fig. 2).

In cases I and II the starting material A is excited to A* by a photon or Sens* and then forms the energy rich product B. In case III, A and B are complementary redox couples. The couple A $(a^{\ominus}, b)$ reacts with the excited photocatalyst (Cat*) *via* an electron-transfer complex to form the redox couple B $(a, b^{\ominus})$. In all three cases the fuel B must be re-convertible into A, when the stored energy is subsequently required.

3. Efficiency of Abiotic Photochemical Solar Energy Storage Systems

Figure 3 shows the spectral energy distribution of the sun's radiation[31] for different angles of incidence on a collector.

For the storage of photochemical energy, as opposed to purely thermal energy, only the range b) of wavelengths up to about 700 nm is available, since this latter wavelength is the maximum threshold wavelength of all photochemical reactions known so far.

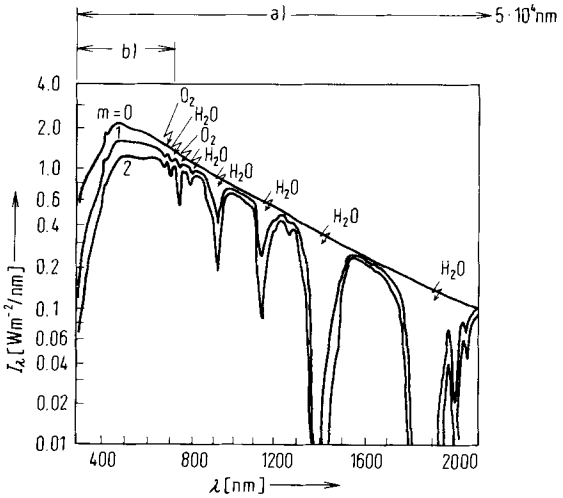


Fig. 3. Spectrum of the sun [31] for various angles of incidence δ to the normal of the earth. m = 0: irradiation of the sun outside the atmosphere (AM0-spectrum); $m = 1 \hat{=} \delta = 0°$ (AM1 spectrum); $m = 2 \hat{=} \delta = 60°$ (AM2 spectrum). a) thermally useful range of the spectrum of the sun [29]; b) photochemically useful range of the spectrum of the sun. I_λ = irradiation power per unit area and interval of wavelength at the wavelength λ of the terrestrial solar spectrum.

This range b) covers about 50%[29] of the incident radiation energy. For a quantitative assessment of the efficiency of photoreactions we can use an efficiency factor η_w, defined as follows:

$$\eta_w = \frac{n \cdot \Delta \bar{H}}{t_B \cdot F \int_0^\infty I_\lambda \, d\lambda} \qquad (1)$$

where n is the amount of substance B (in moles), which is formed in the photoreaction A→B during the irradiation time t_B. $\Delta \bar{H}$ is the difference in the molar standard enthalpies of the ground states of A and B ($\Delta \bar{H} = \bar{H}_B - \bar{H}_A$)[32]. I_λ is the sun's energy incident on a unit surface area in unit time per unit of wavelength at the wavelength λ (cf. Fig. 3). F is the collector area of the reaction cell. Hence, η_w is the ratio of

the stored enthalpy to the incident energy. Starting from the work of *Porter* and *Archer*[33,34] and *Bolton*[35], who, on the basis of earlier work [36–39], have formulated an efficiency for photochemical systems, η_w [eq. (1)] may be represented by a product of four factors (see Section 11):

$$\eta_w = \eta_E \cdot \phi_B^A \cdot \eta_a \cdot \eta_{abs} \tag{2}$$

In formulating such an expression certain assumptions have to be made, *e. g.* homogeneous concentrations in the cell (this can always be realized by stirring) and nearly time-independent concentrations (this may be achieved by short irradiation times). These four factors are discussed in detail in the following Sections.

3.1. Energy Conversion Factor η_E and Quantum Yield ϕ_B^A

The energy conversion factor η_E represents the ratio of the stored molar enthalpy ($\Delta\bar{H}$) to the energy of one mole of photons having the threshold wavelength λ_{gr}:

$$\eta_E = \frac{\Delta\bar{H}}{h \cdot c \cdot N_A/\lambda_{gr}} \leq 1 \tag{3}$$

where h is Planck's constant, c is the velocity of light, N_A is Avogadro's number and λ_{gr} is the wavelength for the 0-0-transition of A or Sens or Cat (threshold wavelength, cf. Fig. 1). The second factor in equation (2), ϕ_B^A, is the quantum yield[40] of the photoreaction, which is assumed to be independent of the wavelength λ for $\lambda \leq \lambda_{gr}$. (For sensitized processes the efficiency of energy transfer has to be taken into account in ϕ_B^A[41].) $\phi_B^A \cdot \eta_E$ corresponds to *Calvert*'s "Q-factor"[42].

3.2. Useful Fraction η_a of Incident Energy

In equation (2) η_a is the factor which has been carefully studied by *Archer*[34] for an ideal converter (*i. e.* complete absorption). η_a is referred to as "available energy" by *Archer*[34] and as "useful energy" by *Flynn* and *Trivich*[36]:

$$\eta_a = \frac{\int_0^{\lambda_{gr}} I_\lambda \cdot (\lambda/\lambda_{gr}) \cdot d\lambda}{\int_0^{\infty} I_\lambda \, d\lambda} < 1 \tag{4}$$

η_a is the ratio of the energy of one Einstein (1 Einstein = 1 mole photons) of the wavelength λ_{gr} multiplied by the number of Einstein available for $\lambda \leq \lambda_{gr}$ to the total incident solar energy of a special sunlight spectrum I_λ (cf. Fig. 3). The product $\eta_E \cdot \phi_B^A \cdot \eta_a$ was used by *Porter* and *Archer*[33,34] as a measure of the solar energy storage efficiency.

To illustrate more clearly the significance of the factor η_a the "used" energy (dark area) and the "wasted" energy (hatched + checkered areas) are show in Figures 4a—4d for four typical threshold wavelengths λ_{gr}. The photons whose energy is depicted by the hatched area will not be absorbed. The energy represented by the checkered area gets lost because the excited molecule relaxes into the S_{10}-state (cf. Fig. 1). It can be seen that η_a (dark area/total area) will always be smaller than unity and will have its highest value at $\lambda_{gr} \approx 1500$ nm (cf. Fig. 4c and 5).

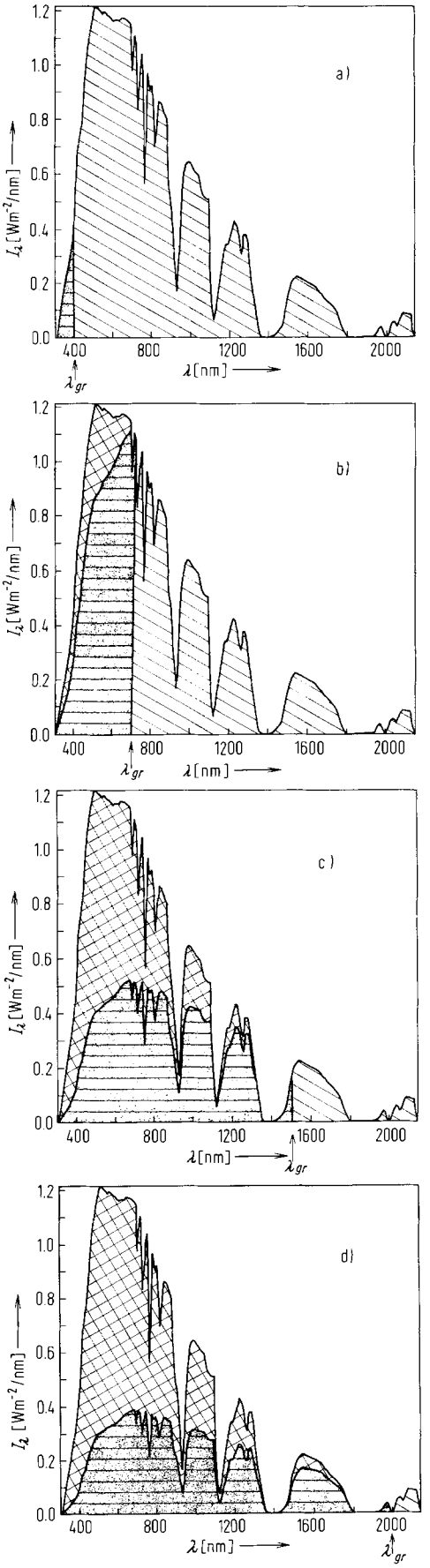


Fig. 4. Representation of the utilizable energy (▨), the unabsorbed energy (▨), and the energy "wasted" through relaxation into the S_{10} state (▨) of the AM2 solar spectrum for four sample threshold wavelengths [a) $\lambda_{gr} = 400$ nm; b) $\lambda_{gr} = 700$ nm; c) $\lambda_{gr} = 1500$ nm; d) $\lambda_{gr} = 2000$ nm]. The dark area is limited by the curve $I_\lambda \cdot \lambda/\lambda_{gr}$ [cf. eq. (4)]. Definition of the parameters, see Fig. 3.

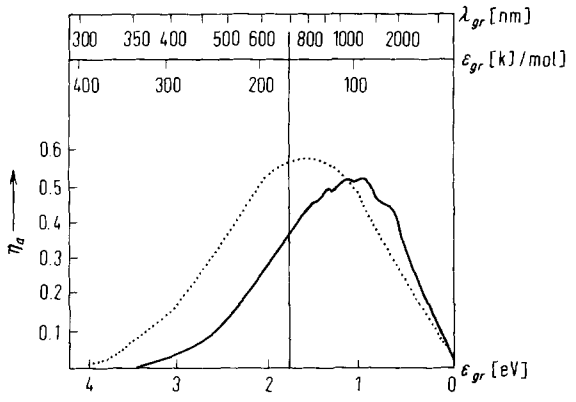


Fig. 5. Useful fraction η_a of the AM2 radiation of the sun [31] (—) and the diffuse component of daylight [34] (...) as a function of the threshold energy ε_{gr} corresponding to the wavelength λ_{gr}. 700 nm is the maximum threshold wavelength of photochemical reactions known up to now.—It is not expressed here that the intensity of the diffuse daylight is only 1% of the intensity of the direct irradiation of the sun.

This may be explained in the following way: In passing from small values of λ_{gr} to larger values of λ_{gr} the number of photons radiated below λ_{gr} increases with wavelength whereas the threshold energy ε_{gr} corresponding to λ_{gr} decreases. Up to λ_{gr}^{max} the first factor is greater than the second one. At $\lambda_{gr} > 1500$ nm, however, the increase in the radiated photons is less than the decrease in the threshold energy ε_{gr} and η_a decreases again. Photochemical reactions above 700 nm with a significant value of $\Delta\bar{H}$ are as yet unknown, *i.e.* the η_a value given at 700 nm in Figure 5 has not yet been exceeded.

3.3. Absorption Yield η_{abs}

η_{abs} [cf. eq. (2)] is the ratio of photons absorbed by A (or Sens or Cat) to all the photons of wavelength $\lambda \leq \lambda_{gr}$:

$$\eta_{abs} = \frac{\int_0^{\lambda_{gr}} I_\lambda \cdot \lambda \cdot (E_{A\lambda}/E_\lambda)(1-10^{-E_\lambda})\,d\lambda}{\int_0^{\lambda_{gr}} I_\lambda \cdot \lambda \cdot d\lambda} \leq 1 \qquad (5)$$

Here $E_{A\lambda}$ is the wavelength-dependent extinction of A (or Sens or Cat) and E_λ the analogous value for the total system. η_{abs} will have its optimal value 1 if all the sunlight is absorbed by A (or Sens or Cat) alone ($E_{A\lambda} = E_\lambda$) and if the sunlight is completely absorbed ($10^{-E_\lambda} = 0$).

Figures 6a and 6b show for the systems norbornadiene *(1a)*/acetophenone and *trans*-diacetylindigo *(5a)* the photons of wavelength between $\lambda = 300$ nm and λ_{gr} radiated by the sun (dark + checkered area) compared to those actually absorbed (dark area).

η_{abs} is the ratio of the dark area to the sum of the dark and checkered area. Though *trans*-diacetylindigo *(5a)* absorbs many more photons from the solar spectrum (50%) then norbornadiene *(1a)*/acetophenone (0.8%), the η_{abs}-values of both systems are nevertheless comparable (0.7 and 0.8), for by definition only the range up to λ_{gr} has to be taken into account in the evaluation of η_{abs}.

Thus the factors necessary for evaluating the efficiency of an abiotic photochemical solar energy storage system are defined and it is now possible to compare various systems.

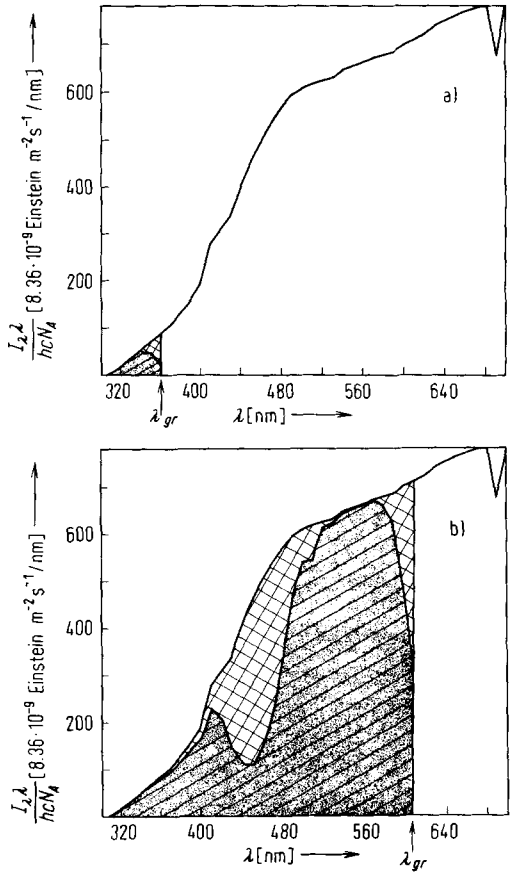


Fig. 6. Photons aborbed (▨) between $\lambda = 300$ nm and λ_{gr}, and the total amount of photons (▨ + ⊠) available in this wavelength range of AM2 solar radiation, for (a) norbornadiene *(1a)*/acetophenone ($\lambda_{gr} = 366$ nm) and (b) *trans*-diacetylindigo *(5a)* ($\lambda_{gr} = 610$ nm) for a maximum extinction of 3. The dark area is bounded by the curve $\frac{I_\lambda \cdot \lambda}{h \cdot c \cdot N_A} \cdot (1 - 10^{-E_\lambda})$ [cf. eq. (5) for $E_{A\lambda} = E_\lambda$].

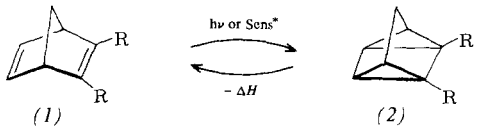
4. Examples of Photochemical Solar Energy Storage Systems

In the following a selection of those photochemical systems has been complied, which are mentioned in the literature as being "particularly promising". The efficiency factors η_w of these systems (see Tables 2 and 3 and Fig. 8) have been calculated according to equation (2) using what we consider are the most reliable data in the literature.

4.1. Intramolecular [2+2]-Cycloadditions: Norbornadiene/Quadricyclane

The photochemical system *(1)/(2)*, R = H, CO_2R', has long been known[23,46–60] and has been very thoroughly investigated both under direct irradiation as well as under sensitized conditions[23,24,52–54]. The large enthalpy difference $\Delta\bar{H}$ between the valence isomers *(1a)* and *(2a)* is often referenced as an advantage for its suitability as a solar energy storage system; in the case of *(1b)* and *(2b)*, however, it is one third smaller (referred to 1 g of material).

The conversion of *(2a)* into *(1a)* at room temperature and below can be neglected, so far as traces of metals or their ions can be excluded. The halflife for this reaction in the con-



(1) (2)

(a), R = H; (b), R = CO_2CH_3

(a): $\Delta\bar{H} = -110$ kJ/mol ≙ −1.2 kJ/g [43]
(b): $\Delta\bar{H} = -77$ kJ/mol ≙ −0.39 kJ/g [44]

Phys. data \ Cpd.	(1a) [45]	(1b) [95]	(2a) [46]	(2b)
M.p. [°C]	−19.1	—	—	55—58
B.p. [°C/torr]	89.5/760	134—135/10	108/760	—
δ_4^{20}	0.9064	—	—	—
n_D^{20}	1.4702	—	1.4804	—

densed phase at 140 °C is about 14 h[46,61]. *(2b)* is completely stable up to its melting point. The rate constant of the thermal isomerization of *(2a)* in the gas phase is $K = 10^{12.8\pm1}\exp(-140.3\ \text{kJ mol}^{-1}/RT)\ \text{s}^{-1}$[62].

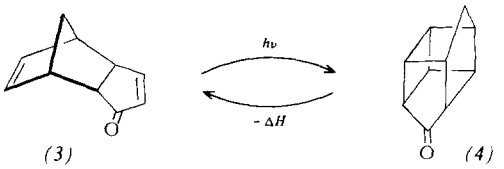
In the meantime tetraarylporphyrin-metal catalysts of high efficiency have been described which, as free[57] or polymer-bound[60] molecules, enable back-isomerization of *(2a)* to *(1a)* with liberation of the stored chemical energy as heat. This finding would at least serve as a model for a staggered "energy harvesting" (summer) and its effective utilization (winter). A number of disadvantages, however, should not be overlooked. Thus, the absorption data of the system *(1a)/(2a)* which are given in Table 1 show that the wavelengths necessary for excitation are not present in the sun's radiation reaching the earth (see Fig. 3). They lie in the UV-part of the spectrum. Even the free[46,50,52] or polymer bound[24] acetophenone sensitized reaction *(1a)*→*(1b)* requires light of very short wavelength (see Fig. 6a and 4a).

Other sensitizers[50,52] have proven to be inefficient[63]. The CuCl–CT complex of *(1a)*[23,53] and complexes with Cu^I-phosphane ligands[54] have a better chance of absorbing radiation from the short wavelength edge of the sun's spectrum (see Fig. 3).

Although *(1a)* is a commercially available product[64], the following disadvantages further restrict its utilization as a solar energy storage system. The compounds are combustible and are not miscible with water. *(1a)* reacts with oxygen irreversibly to give a copolymer[65] which does not further react photochemically. According to *Roquitte*[67] cyclopentadiene, acetylene, and toluene are formed during the gas-phase photolysis (and also to a smaller extent on photolysis in solution) of *(1a)*. According to *Hammond et al.*[50] arenes sensitize the reaction *(2)* $\xrightarrow{h\nu}$ *(1)*, but not, however, the reverse process. The cumulation of toluene for instance may decrease the quantum yields of the photochemical formation of *(2)* considerably—an effect which has hitherto not been checked.

4.2. Intramolecular [2 + 2]-Cycloadditions: *endo*-Dicyclopentadienone/Bishomocubanone

The *endo*-dicyclopentadienone *(3)* (*endo*-tricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one) has two advantages as a solar energy storage system over the well known parent hydrocarbon *endo*-dicyclopentadiene[69], which is photochemically cyclizable to 1,3-bishomocubane. 1. The nπ*-transition of *(3)*[22] is on the short wavelength edge of the sun's spectrum (Tab. 1, Fig. 3). 2. Whereas the excitation energy has to



(3) (4)

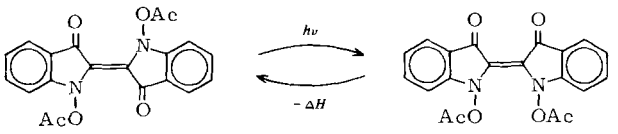
$\Delta\bar{H} = -68.6$ kJ/mol ≙ −0.5 kJ/g [22]

Phys. data \ Cpd.	(3) [68]	(4) [63]
M.p. [°C]	80	122—126

be transferred intermolecularly to dicyclopentadiene from a suitable sensitizer[69], *(3)* "possesses" an "intramolecular sensitizer", the carbonyl group. Thus the quantum yield of cycloaddition is larger in this case than in that of the parent hydrocarbon.

The quantum yield of bishomocubanone *(4)* (pentacyclo[5.3.0.$0^{2,5}$.$0^{3,10}$.$0^{4,8}$]deca-6-one) formation is wavelength-dependent. Consequently, the chemical yield which can be obtained at 330—380 nm is >99%; at 305 nm, however, it amounts to only 90%[22]. *(4)* is stable up to 295 °C[22]. Again this system exhibits considerable disadvantages. At higher concentrations of *(3)* intermolecular [2 + 2]-cycloaddition is observed. The catalytic back reaction *(4)*→*(3)* proceeds at 140 °C in only 95%[22] yield. *(3)* is not commercially available and, like *(4)*, is insoluble in water. 1,3-Bishomocubane is back-isomerized by the iridium complex $Ir(CO)_3Cl_2$ to *endo*-dicyclopentadiene without formation of byproducts[70]; similar catalytic investigations on *(4)* have not been reported.

4.3. *cis-trans*-Isomerization: *trans*-Diacetylindigo/*cis*-Diacetylindigo



trans-(5) cis-(5)

$\Delta\bar{H} = -34$ kJ/mol ≙ −0.1 kJ/g [28]
trans-(5), m.p. 245—250 °C [71]

N,N'-Disubstituted indigo derivatives have been proposed by *Schwerzel et al.*[28] as combined solar energy storage systems. A smaller part of the solar energy is stored as chemical energy in the *cis-(5)* isomer, the larger part, however, in the molecular motion in solution. The advantages of this system are the absorption spectrum, which matches very well with the photochemically active part of the solar spectrum (see Fig. 6b and 3), the well known light stability of the indigo dyes, and the catalytic back-reaction *cis-(5)*→*trans-(5)*, which proceeds quantitatively[28].

Considerable disadvantages should, however, not be overlooked. On the one hand, the quantum yield ϕ_B^A of the pho-

tochemical *trans-cis*-isomerization (see Table 2) is very low and on the other the photochemically storable energy does not exceed half of that which can be stored in hot water between 20—70 °C (*i.e.* 0.209 kJ/g), and the indigo dyes are only sparingly soluble in most solvents. A further disadvantage is the low stability of the energy rich *cis* form, which rapidly back-isomerizes to the stable *trans* form at higher temperatures[28].

4.4. Photodissociation: Nitrosyl Chloride

$$NOCl_{(g)} \underset{-\Delta H}{\overset{h\nu}{\rightleftharpoons}} NO_{(g)} + 1/2\ Cl_{2(g)}$$

$\Delta H = -37.6$ kJ/mol $\hat{=} -0.58$ kJ/g [21]

Phys. data [21] \ Cpd.	NOCl	NO	Cl_2
M.p. [°C]	−64.5	−136.6	−100.9
B.p. [°C/760 torr]	− 5.8	−151.9	− 36.4

The photodissociation of nitrosyl chloride is very well known[72], and has been proposed for photochemical syntheses[73] as well for the storage of solar energy[21,26]. The mechanism very likely involves the following chain reaction:

$$NOCl + h\nu \rightarrow NO + Cl\cdot$$
$$Cl\cdot + NOCl \rightarrow NO + Cl_2$$
$$2\,NOCl + h\nu \rightarrow 2\,NO + Cl_2$$

Both the quantum yield ϕ_B^A (Table 2) of the reaction as well as the position of the threshold wavelength (Tab. 1) are unusually favorable. The back-reaction proceeds spontaneously; hence the photoproducts have to be separated immediately to keep the photodissociation running[72]. The extremely corrosive substances necessitate employment of high quality flow devices.

4.5. Photocatalytic Redox Reactions: Oxidation of Chloride to Chlorine

Recently, photoredox reactions in homogenous solution for the catalytic cleavage of water or other small molecules have been the subject of detailed investigation[13].

One key problem is the photochemical stability of the catalysts, which in most cases are based on complex-bound noble metal ions, mainly of rhodium or ruthenium.

These reactions lead over to photoelectrochemical[74] and photogalvanic systems[12] as well as to membrane techniques for charge separation on the basis of synthetic molecule organizates[10].

For evaluation of the efficiency criteria according to equation (2) one photocatalytic redox system of Type III (see Fig. 2) has been chosen from the plethora of published examples. This system represents the photocatalytic oxidation of chloride to chlorine[75–77]. The value of this system lies in the storage of photon energy as chemical energy of chlorine and in addition in its being a potential chemical process with an alternative energy source: Hydrogen chloride is thermally oxidized by oxygen according to *Deacon*[78] in the gas phase with CuCl as a catalyst. As an alternative to this exothermal process, which so far has not been realized technically[79], hydrochloric acid can be oxidized photocatalytically to chlorine.

Deacon process:

$$2\,HCl_{(g)} + {}^1\!/_2 O_2 \underset{>350\,^\circ C}{\overset{CuCl}{\rightleftharpoons}} Cl_{2(g)} + H_2O_{(g)}$$

$\Delta H = -59$ kJ mol^{-1}

Photocatalytic process:

$$2\,HCl_{(aq)} + {}^1\!/_2 O_2 \xrightarrow[\Delta H]{{}^3(AQ)^*} Cl_{2(g)} + H_2O$$

$\Delta H = +49$ kJ/mol $\hat{=}$ 0.56 kJ/g

Potential photocatalysts are anthraquinone derivatives (AQ) such as *(6)* or *(7)*, which are soluble in aqueous hydrochloric acid and in the triplet excited state $^3(AQ)^*$ undergo a redox-reaction with chloride ions[75,76]. In the presence of oxygen the anthraquinone catalyst runs through a cycle (see Fig. 7) in which it is restored for further reaction sequences[77]. The chlorine which is formed is carried along with the air or oxygen stream which is bubbling through the reaction vessel.

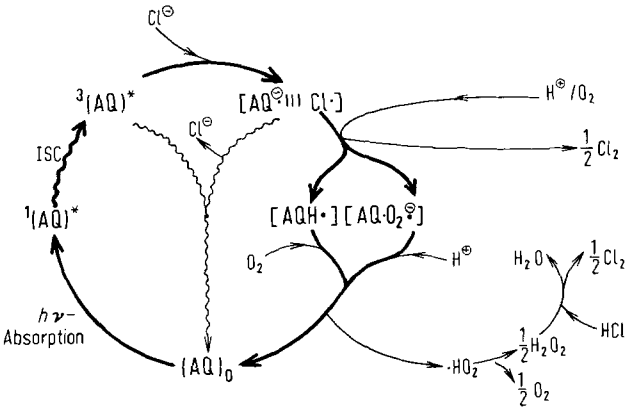
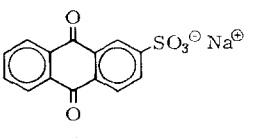
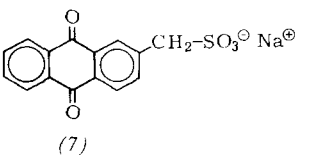


Fig. 7. Reaction cycle of anthraquinone derivatives (AQ) undergoing photocatalytic chloride oxidation in the presence of oxygen. $(AQ)_0$ = AQ in ground state; $^1(AQ)^*$ = AQ in the first excited singlet state; $^3(AQ)^*$ = AQ in the first excited triplet state; ISC = intersystem crossing; $[AQ^{\ominus} ||| Cl\cdot]$ = radical ion pair after electron transfer; [AQH·] = anthrasemiquinone radical of AQ; $[AQO_2^{\ominus}\cdot]$ = oxygen adduct of the AQ radical anion as an alternative intermediate.

The main problem in this photocatalytic chloride oxidation lies once again in the photochemical stability of the anthraquinone derivative, which is employed in concentrations of about 10^{-3} mol/l.



(6)



(7)

For example anthraquinonesulfonates such as *(6)* are very rapidly photosubstituted[76,80] in the excited singlet state to the corresponding chloroanthraquinones. Anthraquinone-2-methanesulfonate *(7)*[75] is slowly oxidized at the methylene

group under the reaction conditions. These degradation products cannot catalyze the reaction because of their insolubility in aqueous hydrochloric acid. Further research effort must therefore be directed toward the synthesis of photostable catalysts of the anthraquinone type.

The overall back reaction B→A (see Fig. 2, Type III) necessary with energy storage in mind

$$Cl_2 + 2e^- \rightarrow 2Cl^-$$
$$H_2O \rightarrow \tfrac{1}{2}O_2 + 2H^+ + 2e^-$$
$$Cl_2 + H_2O \rightarrow 2HCl + \tfrac{1}{2}O_2$$

has not yet been verified.

An alternative could be the utilization of the chemical energy of chlorine by an electrochemical fuel cell with hydrogen as electron donor.

Table 1. UV/VIS data of components of selected photochemical storage systems. *s* = shoulder.

Compound	λ_{gr} [nm]	λ_{max} [nm]	ε_{max} [l mol^{-1} cm^{-1}]
(1a)		205 s	2100 [23, 81]
		214 s	1480
		220 s	870
		235	200 [23]
(2a)		205	400 [49]
Acetophenone	366 [83]	243	13000 [82]
(Sensitizer)		280	1020 [84]
		313	60
(1a)	388 [85]	253	7900 [53]
as CuCl complex		300 s	1000
(1b)	334 [26]	238	3800 [86]
		275 s	1500
(2b)		220	3000 [87]
(3)	366 [26]	278	39 [63]
(4)		297	39 [63]
trans-(5)	610 [88]	570	6300 [28]
cis-(5)		430	3800 [28]
		505 s	3500
NOCl	600 [26]	334	32 [21]
		478	6
		600	3
NO			
Cl_2		334	80 (Cl_2) [21]
(7) (Catalyst)	420 [89]	333	5100 [75]

Table 2. Efficiencies $\eta_{w(opt)}$ of a selection of photochemical storage systems and Q factors. $\eta_{abs} = 1$.

System [a]	η_E	ϕ_B^A	η_a	Q-factor [%] [b]	$\eta_{w(opt)} \cdot 100$ [%] [c]
(1a)/(2a) with acetophenone in $CHCl_3$	0.33	0.9 [52]	0.008	30	0.23
(1a)/(2a) as CuCl complex in $CHCl_3$	0.35	0.4 [23]	0.015	14	0.21
(1b)/(2b) in CH_3CN	0.22	0.5 [87]	0.0015	11	0.02
(3)/(4) in CH_3CN	0.21	0.4 [22]	0.008	8	0.07
trans-(5)/cis-(5)	0.17	0.2 [28]	0.273	3.5	0.95
$NOCl_{(g)}/NO_{(g)} + \frac{1}{2}Cl_{2(g)}$	0.19	1.0 [21, 26]	0.261	19	4.93
$2HCl_{(aq)} + \frac{1}{2}O_2/Cl_{2(g)} + H_2O$ *(7)* as catalyst	0.17	0.15 [75]	0.040	2.6	0.10

[a] The UV spectra of the substances *(1)—(4)* and *(7)* were recorded with a Cary 14 spectrometer on punched tape for processing with a Dietz computer (Mincal 621/8). The UV spectra of the other compounds were taken from the literature [21, 28].
[b] The Q factor was determined according to *G. Jones* [26, 30] as $\Delta\bar{H} \cdot \phi_B^A / \varepsilon_{gr}$; $\varepsilon_{gr} = N_A \cdot h \cdot c / \lambda_{gr}$. $Q = \phi_B^A \cdot \eta_E \cdot 100$.
[c] Calculated for $\eta_{abs} = 1$.

Table 2 shows, for all the systems discussed, the complementary trend of the factors in equation (2). It can be seen that the Q-factor[42] does not correctly characterize the efficiency of a photochemical solar energy storage system[26,30], and moreover leads to wrong conclusions, as in the case of norbornadiene *(1a)*/acetophenone and nitrosyl chloride.

5. Efficiency of Solar Energy Storage in Photosynthesis

According to Table 2 comparable efficiency values for the photosynthetic process can be obtained under the following assumptions:

1) Only the overall chemical reaction is considered[25,35]
$$CO_2 + H_2O \rightarrow \tfrac{1}{6}C_6H_{12}O_6 + O_2$$
2) The stored energy is 470 kJ per mol CO_2 assimilated, corresponding to the thermal value of the glucose formed[18] or $\Delta\bar{H} = 467$ kJ/mol[25,35].
3) The assimilation of one mole of CO_2 requires *ca.* 10 Einstein[18], *i.e.* the quantum yield is ≈ 0.1[90].
4) The limiting wavelength is 700 nm and thus $\varepsilon_{gr} = 180$ kJ/mol and $\eta_a = 0.36$ (from Figure 5).

The above-mentioned assumptions lead to a formal η_E-value of 2.6. This value is larger than 1 (cf. Section 3.1), because photosynthesis essentially requires more than one photon and the fraction of energy provided by dark reactions involved cannot be estimated. Thus the Q-value is 26% and $\eta_{w(opt)} \cdot 100 = 8\%$. This value for the efficiency is large compared to those for abiotic systems but it is reduced to 0.1—0.3% under realistic field conditions[17,18,42].

6. Dependence of the Efficiency η_w on the Absorption Parameters of the Light Absorber

Table 2 shows the $\eta_{w(opt)}$-values of the systems investigated, that is the efficiency [eq. (2)] for the condition $\eta_{abs} = 1$.

Figure 8 shows the dependence of η_w on the product of absorber concentration and path length of the absorption cell.

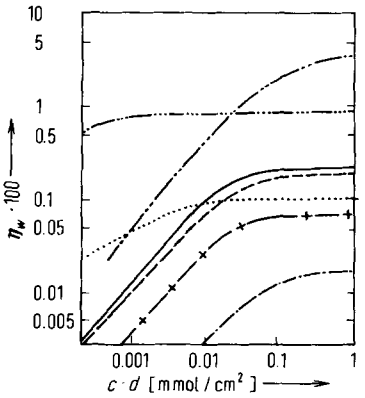


Fig. 8. Dependence of η_w on the quantity of photon absorber per area. c = concentration of light absorber; d = path length of absorption cell. ——≙ *(1a)/(2a)* with acetophenone; - - - - -≙ *(1a)/(2a)* as Cu^1Cl complex; -·-·-≙ *(1b)/(2b)*; —+—≙ *(3)/(4)*; —··—≙ *trans-(5)/cis-(5)*; ——··—≙ NOCl/NO + $\frac{1}{2}Cl_2$; ..... ≙ *(7)* as catalyst.

Hence it is seen that the efficiency η_w of a photochemical storage system is also strongly dependent on the absorption parameters of the photon absorber [cf. eq. (5)]. The required quantities of starting material A, Sens, and Cat can be calcu-

lated with the aid of the efficiency η_{abs}, thus providing an economic evaluation of the various systems.

Table 3 shows that *trans*-diacetylindigo, *trans-(5)*, is able to store 0.05% of incident solar energy at the smallest expense of material. For the same storage efficiency a 2000-fold quantity of the dienone *(3)* would be required, while the value of 0.05% cannot even been reached at all with the ester *(1b)*. Also in the range of optimal η_w-values, the diacetylindigo system *(5)* offers by far the best storage properties. The dramatic difference between *trans-(5)* (2.9 g/m^2) and NOCl (1500 g/m^2) is due to the difference in the extinction coefficients [ε_{max}(*trans-(5)*)/ε_{max}(NOCl) ≈ 2000 (cf. Table 1)].

Table 3. Required quantities and optimum storage capacity of selected photochemical storage systems. The required quantity is calculated for a fixed η_w value of 0.0005 and for a substance specific value of $0.9 \cdot \eta_{w(opt)}$. The storage capacity refers to the substance specific value only.

System	Quantities required [lg/m^2] for η_w = 0.0005	for η_w = $0.9 \cdot \eta_{w(opt)}$	Storage capacity [a] [mW/g] [b]	[g/m^2 h] [c]
(1a)/(2a) [91]	92	92	2.25	0.63
Acetophenone as Sens.	5.4	118	1.75	
(1a)/(2a) [92]	6.6	105	1.8	0.57
CuCl	7.1	113	1.7	
(1b)/(2b)	—	520	0.035	0.17
(3)/(4)	50.5	84.1	0.75	0.48
trans-(5)/cis-(5)	0.025	2.9	294.8	28.0
$NOCl_{(g)}/NO_{(g)} + \frac{1}{2}Cl_{2(g)}$	0.83	1500	2.96	27.5
(7) as catalyst [d]	3.6	34.7	2.6	0.58

[a] Relative to 100 W/m^2 [1] of the AM2 spectrum [31]. [b] Relative to substance A or Sens or Cat. [c] Relative to the energy-rich product(s) B. [d] System $2HCl_{(aq)} + \frac{1}{2}O_2/Cl_{2(g)} + H_2O$.

Thus absorbers with smaller extinction coefficients must be used in larger quantities per unit area in order to achieve optimal utilization of the incident energy. Concomitantly, however, the storable energy per gram of starting material is reduced (cf. Table 3, column 3). Thus the required quantity of *trans*-diacetylindigo is 100-fold more productive than the corresponding quantity of NOCl.

From the last column in Table 3 it can be seen, that the optimum production of energy-rich compound B in the case of *trans*-diacetylindigo and NOCl is about 50-fold compared to the other systems, which, however, has to be paid for by large amounts of material in the case of NOCl (cf. Table 3, second column).

The amounts of material required can be reduced if energy is withdrawn from a system during the storage. Cycles corresponding to Figures 2 and 9 have to be passed through. Then, however, the stability of the light absorbers and the extent of side reactions play an important role.

7. The Stability of Photochemical Storage Systems A, B

7.1. Types I and II

Figure 9 shows the possibility of the starting material A and the product B maintaining or breaking the storage cycle.

a) Deactivation:

$$A^* \rightsquigarrow A \text{ or } (Sens^* + A \rightsquigarrow Sens + A)$$

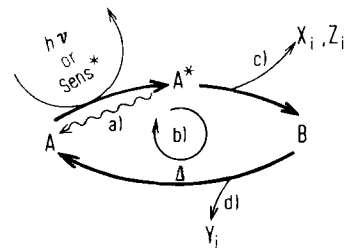


Fig. 9. Cycle referring to energy storage and recovery by a system A/B (cf. Fig. 2, I and II). The starting material A is excited to A* by absorption of a photon or interaction with an excited sensitizer Sens* and the product B is formed. (Further explanations, see text.)

b) Useful cycle

c) Wasteful photoreactions:

$$A^* \rightarrow \sum X_i,\ B \notin \{X_i\} \text{ or } (Sens^* + A \rightarrow Z_i,\ B \notin \{Z_i\})$$

d) Wasteful thermal reactions:

$$B \xrightarrow{\Delta} Y_i,\ A \notin \{Y_i\}$$

The lifetime of a storage system A/B depends on the fraction of side reactions X_i (or Z_i) and Y_i, *i.e.* on the probability ϕ_A of the recovery of A after the absorption of a photon (or interaction with Sens*) and after the possible processes a) to d).

Provided that A is thermally stable, the probability ϕ_A can be expressed by the measurable values ϕ_B^A [see eq. (2) and [40,93]], η_Δ (yield of the thermal back-reaction) and ϕ_{-A} (the quantum yield of the degradation of A after absorption of a photon or interaction with Sens*[93]).

$$\phi_A = 1 - \phi_{-A} + \phi_B^A \eta_\Delta \tag{6}$$

This probability has a formal value of 1 before the first absorption of a photon (or interaction with Sens*); it is $(\phi_A)^n$ after the n-th absorption of a photon (or n-th interaction with Sens*). Thus the expression

$$P_A = \sum_{n=0}^{\infty} (\phi_A)^n = 1/(1-\phi_A), \quad \phi_A < 1 \tag{7}$$

describes the sum of all probabilities with which a molecule A is successively available for renewed absorption of a photon (or interaction with Sens*) according to Figure 9. In this manner P_A is also the sum of all photons (or all Sens* molecules) with which A can react. The combination of equations (6) and (7) yields:

$$P_A = \frac{1}{\phi_{-A} - \phi_B^A \eta_\Delta} \tag{8}$$

as the mean number of possible excitations of A by a photon or Sens* molecule.

7.2. Type III

An analogous measure of the photostability of a catalyst accelerating a process corresponding to Type III in Figure 2 can be obtained from eq. (8), if the photon absorber A in

Figure 9 is replaced by the catalyst Cat. Assuming that Cat only forms Cat* and irreversible degradation products X_i ($\eta_\Delta = 0$), one obtains

$$P_{Cat} = 1/\phi_{-Cat} \tag{9}$$

as the mean number of photon absorptions, which can be endured by a molecule Cat before its complete degradation.

Eq. (9) is also valid for the stability of a sensitizer Sens in the cyclic system II (cf. Fig. 2) and in general for the photostability of light-absorbing substances (*e.g.* dyes). Thus the chlorophyll molecule in a leaf has a P_{Chl}-value of about 10^5[17], which corresponds to a degradation quantum yield of 10^{-5}.

8. The Number of Possible Storage Cycles

8.1. Types I and II

As one excitation of A is followed by a complete cycle (Fig. 9) with the probability $\phi_B^A \cdot \eta_\Delta$, the mean number of available cycles is:

$$P_{cy} = P_A \cdot \phi_B^A \cdot \eta_\Delta \tag{10}$$

Combination of equations 8 and 10 yields

$$P_{cy} = 1 \Big/ \left(\frac{\phi_{-A}}{\phi_B^A \cdot \eta_\Delta} - 1 \right) \tag{11}$$

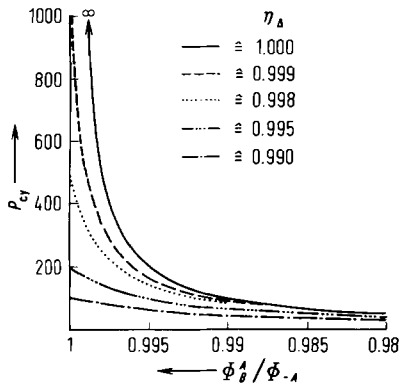


Fig. 10. The number of attainable storage cycles P_{cy} as a function of the yield of the photoreaction and of the thermal back-reaction. Definition of the parameters see Section 7.1; ϕ_B^A/ϕ_{-A} is the chemical yield of the photoreaction.

Figure 10 illustrates how "clean" both the photochemical and the thermal reaction must be in order to obtain appreciably more than 100 storage cycles. Even the number of cycles of 100[26], assumed by *Jones* for purposes of comparison, can only be achieved under the following conditions:

a) the photochemical step has no side reactions ($\phi_B^A/\phi_{-A} = 1$) and the thermal reaction has a yield $\geq 99\%$ ($\eta_\Delta \geq 0.99$), or

b) both the photochemical and the thermochemical steps have yields $\geq 99.5\%$ (*i.e.* ϕ_B^A/ϕ_{-A} and $\eta_\Delta \geq 0.995$), or

c) the thermal reaction is quantitative ($\eta_\Delta = 1$) and the photochemical step has a yield $\geq 99\%$ ($\phi_B^A/\phi_{-A} \geq 0.99$).

8.2. Type III

If a complete cycle according to Types I and II cannot be formulated, then in the case of a photocatalytic reaction the following relationship can be derived from eq. (9)

$$P_B = P_{Cat} \cdot \phi_B^A \tag{12}$$

where P_B is the mean number of product molecules B which can be generated with the photocatalyst Cat, if A is present in sufficient amount.

9. Capacity of Photochemical Energy Storing Systems

9.1. Types I and II

Multiplication of P_{cy}, the mean number of storage cycles, by the energy ΔH stored and recovered per cycle yields the maximum amount of energy, which can be converted up to complete degradation of A (Fig. 9):

$$W_{max} = P_{cy} \cdot \Delta H \tag{13}$$

9.2. Type III

By analogy with equation (13), for systems of Type III we have

$$W_{max}^{Cat} = P_B \cdot \Delta H \tag{14}$$

for the maximum value of the energy which can be stored through Cat up to its complete degradation. Equation (14) is also valid for photochemically unstable sensitizers.

Since the quantum yields of feasible solar energy storage systems described in the literature are not sufficiently accurate or not even given (*e.g.* ϕ_{-A}), it is difficult to make a comparison of the stabilities and capacities of the systems listed in Section 4. Nevertheless, if equations (11) and (13) are solved for the available literature values on the assumption that ϕ_B^A/ϕ_{-A} equals the chemical yield of the photoreaction and η_Δ is the optimum yield of the thermal back-reaction, the W_{max}-values in Table 4 are obtained.

From these W_{max} values, it can be seen that with sufficiently photo- and thermostable substances the combustion value of carbohydrates (15600 J/g; $C_6H_{12}O_6$) can be achieved by "pumping".

Table 4. Estimation of the number of cycles P_{cy} and of the storage capacity W_{max} of some abiotic systems (illustrations, see text).

System	η_Δ	ϕ_B^A/ϕ_{-A}	P_{cy}	W_{max} [J/g]
(1a)/(2a) with acetophenone [93]	1 [50]	1 [55]	"∞"[a]	"∞"[a]
(1a)/(2a) as CuCl complex	0.9 [23]	1 [55]	9	10710
(3)/(4)	0.98 [22]	0.95 [22]	13	6110
trans-(5)/cis-(5)	1 [28]	1 [28]	"∞"[a]	"∞"[a]

[a] According to Fig. 10, these values show extreme variations on slight modification of the yield parameters.

10. Concluding Remarks

The application of the criteria presented here to a potential photochemical system of Type I, II, or III enables one to estimate its storage capacity for solar energy in the form of chemical energy. In doing this the photochemical and chemical stability of the system have to be taken into account.

The factors η_w [eq. (1) and (2)], P_{cy} [eq. (11) and (12)] and W_{max} [eq. (13) and (14)] will be obtained from time-independent experimental data. For their determination very precise methods have to be developed. In so far as the production of material is concerned these factors are optimal values, which do not, or only indirectly, take into account the behavior of the systems over a long period of time. With these factors it is however possible to decide, if and how much experimental effort is justified in solving the problem of finding an acceptable storage system. The chemical problem to be solved is similar to that concerning the light stability of dyes. So long as it is uncertain from basic research whether a system is suitable or not, economical aspects such as price of starting material, *etc.*, environmental influences and technological considerations should be ignored in the initial studies.

11. Appendix

The Lambert-Beer law gives the intensity $I_\lambda(x)$ of the sunlight per unit of the wavelength at the distance x from the entrance area of the cell as

$$I_\lambda(x) = I_\lambda \cdot 10^{-e_\lambda x} \tag{15}$$

$$\text{with} \quad e_\lambda = \sum_i c_i(t) \cdot \varepsilon_{i\lambda} \tag{16}$$

[$c_i(t)$ is the time-dependent concentration of the i-th substance and $\varepsilon_{i\lambda}$ the corresponding molar decadic extinction coefficient, which depends on the wavelength.] The total extinction in the cell of length d is:

$$E_\lambda = e_\lambda \cdot d \tag{17}$$

Per unit time and wavelength, the volume element $F \cdot \Delta x$ absorbs the energy:

$$I_\lambda \cdot 10^{-e_\lambda x} \cdot e_\lambda \cdot \ln 10 \cdot F \cdot \Delta x \tag{18}$$

The fraction which is absorbed by A is

$$I_\lambda \cdot 10^{-e_\lambda x} \cdot \varepsilon_{A\lambda} \cdot c_A(t) \cdot \ln 10 \cdot F \cdot \Delta x \tag{19}$$

If stirring makes the concentration independent of x integration of eq. (19) from 0 to d gives the total amount of energy which has been absorbed by the substance A per unit wavelength and time:

$$(\varepsilon_{A\lambda} \cdot c_A(t)/e_\lambda) I_\lambda \cdot F \cdot (1 - 10^{-E_\lambda}) = (E_{A\lambda}/E_\lambda) I_\lambda \cdot F (1 - 10^{-E_\lambda}) \tag{20}$$

$$\text{with} \quad E_{A\lambda} = \varepsilon_{A\lambda} \cdot c_A(t) \cdot d \tag{21}$$

Division of equation 20 by $h \cdot c \cdot N_A/\lambda$ yields the light quanta (in Einstein) absorbed by the substance A at the wavelength λ per unit time and wavelength. Multiplication by the quantum yield ϕ_λ gives the amount of B (in mol) formed at the wavelength λ per unit time and wavelength. Integration from $t=0$ to $t=t_B$ and from $\lambda=0$ to $\lambda=\infty$ one obtains

$$\int_0^{t_B} \mathrm{d}t \int_0^{\infty} \mathrm{d}\lambda \, (E_{A\lambda}/E\lambda) I_\lambda \cdot F \cdot \phi_\lambda \cdot (1 - 10^{-E_\lambda}) \lambda/(h \cdot c \cdot N_A) = n \tag{22}$$

n = amount of substance B (in mol)

If the concentrations are independent of time (addition of A, removal of B) or if one considers only small yields (small n), integration over the time gives:

$$t_B = n \cdot h \cdot c \cdot N_A \Big/ \left(F \int_0^{\infty} I_\lambda \cdot (1 - 10^{-E_\lambda}) \cdot \lambda \, (E_{A\lambda}/E_\lambda) \, \phi_\lambda \, \mathrm{d}\lambda \right) \tag{23}$$

Assuming ϕ_λ to be independent of λ for $\lambda \leq \lambda_{gr}$ and to be zero for $\lambda > \lambda_{gr}$ (λ_{gr} = threshold wavelength (cf. Fig. 1)), *i.e.*

$$\begin{aligned} \phi_\lambda &= \phi_B^A \quad \text{for} \quad \lambda \leq \lambda_{gr} \\ \phi_\lambda &= 0 \quad \text{for} \quad \lambda > \lambda_{gr} \end{aligned} \tag{24}$$

equation (23) affords:

$$t_B = n \cdot h \cdot c \cdot N_A \Big/ \left(F \cdot \phi_B^A \int_0^{\lambda_{gr}} I_\lambda \cdot \lambda \cdot (E_{A\lambda}/E_\lambda)(1 - 10^{-E_\lambda}) \, \mathrm{d}\lambda \right) \tag{25}$$

and thus, after rearrangement, we obtain from (1) equations (2) (see Section 3) and (26) for the efficiency η^w:

$$\eta_w = n \cdot \Delta\bar{H} \Big/ \left(t_B \cdot F \int_0^{\infty} I_\lambda \, \mathrm{d}\lambda \right) \tag{1}$$

$$= \Delta\bar{H} \cdot \phi_B^A \int_0^{\lambda_{gr}} I_\lambda \cdot \lambda \, (E_{A\lambda}/E_\lambda)(1 - 10^{-E_\lambda}) \, \mathrm{d}\lambda \Big/ \left(h \cdot c \cdot N_A \int_0^{\infty} I_\lambda \, \mathrm{d}\lambda \right)$$

$$= \frac{\Delta\bar{H}}{h \cdot c \cdot N_A/\lambda_{gr}} \cdot \phi_B^A \cdot \frac{1}{\lambda_{gr}} \cdot \frac{\int_0^{\lambda_{gr}} I_\lambda \cdot \lambda \cdot \mathrm{d}\lambda}{\int_0^{\infty} I_\lambda \mathrm{d}\lambda} \cdot \frac{\int_0^{\lambda_{gr}} I_\lambda \cdot (E_{A\lambda}/E_\lambda)(1 - 10^{-E_\lambda}) \, \mathrm{d}\lambda}{\int_0^{\lambda_{gr}} I_\lambda \cdot \lambda \cdot \mathrm{d}\lambda} \tag{26}$$

$$\eta_w = \eta_E \cdot \phi_B^A \cdot \eta_a \cdot \eta_{abs} \tag{2}$$

We thank the "Deutsche Forschungsgemeinschaft" for providing the laboratory data system (Mincal 621 and periphery), the "Minister für Wissenschaft und Forschung des Landes NRW" for financial support, the "Stiftung Volkswagenwerk" for providing the Cary 14 Spectrometer, and the "Fonds der chemischen Industrie" for material support and Deutsche Shell AG for norbornadiene.

Received: February 23, 1979 [Z 285 IE]
German version: Angew. Chem. 91, 696 (1979)

[1] 100 W/m² is the mean value for Central and Northern Europe averaged per 24 hours per day and 365 days per year (see [15], p. 77).
[2] *M. M. Eisenstadt, K. E. Cox*, Sol. Energy *17*, 59 (1975); *K. F. Knoche:* Vorträge N 267 der Rhein.-Westf. Akademie der Wissenschaften, Westdeutscher Verlag, Opladen 1977.
[3] *O. M. Williams, P. O. Carden*, Sol. Energy *22*, 191 (1979).
[4] *T. A. Chubb*, Sol. Energy *17*, 129 (1975); Mil. Eng. *68*, 456 (1976); *W. E. Wentworth, E. Chen*, Sol. Energy *18*, 205 (1976); *H. W. Prengle jr., Chi Hua Sun*, Sol. Energy *18*, 561 (1976).
[5] *M. Calvin*, Acc. Chem. Res. *11*, 369 (1978).
[6] *M. Aizawa, M. Hirano, S. Suzuki*, Electrochim. Acta *23*, 1185 (1978).
[7] *G. Porter*, Pure Appl. Chem. *50*, 263 (1978).
[8] *H. Ti Tien, B. Karvaly* in *J. R. Bolton:* Solar Power and Fuels. Academic Press, New York 1977, p. 167.

[9] *A. Hengelein, M. Grätzel* in *J. R. Bolton:* Solar Power and Fuels. Academic Press, New York 1977, p. 53; *J. Kiwi, M. Grätzel,* Angew. Chem. *90,* 900 (1978); Angew. Chem. Int. Ed. Engl. *17,* 860 (1978).

[10] *H. Kuhn,* J. Photochem. *10,* 111 (1979).

[11] *H. Gerischer* in *J. R. Bolton:* Solar Power and Fuels. Academic Press, New York 1977, p. 77.

[12] *W. J. Albery, A. W. Foulds,* J. Photochem. *10,* 41 (1979).

[13] *A. Fujishima, K. Honda,* Nature *238,* 37 (1972); *S. Paleocrassas,* Sol. Energy *16,* 45 (1974); *V. Balzani, L. Moggi, F. Manfri, R. Bolletta, M. Gleria,* Science *189,* 852 (1975); *M. Wrighton, D. S. Ginley, P. T. Wolczanski, A. B. Ellis, D. L. Morse, A. Linz,* Proc. Nat. Acad. Sci. USA *72,* 1518 (1975); *D. G. Witten, F. R. Hopf, F. H. Quina, G. Sprintschnik, H. W. Sprintschnik,* Pure Appl. Chem. *49,* 379 (1977); *H. Maruska, A. K. Ghosh,* Sol. Energy *20,* 443 (1978); *J.-M. Lehn, J. P. Sauvage,* Nouv. J. Chim. *1,* 449 (1978); *N. Sutin,* J. Photochem. *10,* 19 (1979).

[14] *N. Lichtin:* The Current State of Knowledge of Photochemical Formation of Fuel. Report of a Workshop, Boston University's Osgood Hill Conference Center, Sept. 1974.

[15] Solar-Energy, a UK-Assessment. UK Section of the International Solar Energy Society, The Royal Institution, 21 Albemarle Street, London W1X 4BS, 1976.

[16] *S. Claessen, W. Engström:* Solar Energy Photochemical Conversion and Storage. Lyber Tryck, Stockholm 1977.

[17] *J. R. Bolton,* Science *202,* 705 (1978).

[18] *P. Böger,* Naturwissenschaften *65,* 407 (1978).

[19] *M. Almgren,* Photochem. Photobiol. *27,* 603 (1978); *R. T. Ross, T.-L. Hsiao,* J. Appl. Phys. *48,* 4783 (1977).

[20] *S. Levine, H. Halter, F. Mannis,* Sol. Energy *2,* 11 (1958).

[21] *R. J. Marcus, H. C. Wohlers,* Sol. Energy *5,* 44 (1961).

[22] *G. Jones II, B. R. Ramachandran,* J. Org. Chem. *41,* 798 (1976).

[23] *D. P. Schwendiman, C. Kutal,* Inorg. Chem. *16,* 719 (1977); *C. Kutal, D. P. Schwendiman, P. Grutsch,* Sol. Energy *19,* 651 (1977).

[24] *R. R. Hautala, J. Little, E. Sweet,* Sol. Energy *19,* 503 (1977).

[25] *J. R. Bolton,* Sol. Energy *20,* 181 (1978).

[26] *G. Jones II, T. E. Reinhardt, W. R. Bergmark,* Sol. Energy *20,* 241 (1978).

[27] *T. Mukai, Y. Yamashita,* Tetrahedron Lett. *1978,* 357.

[28] *R. E. Schwerzel, R. J. Barlett, J. R. Kelly, N. E. Klostermann, R. A. Nathan, B. E. Sherwood, G. H. Stickford, R. E. Wyant:* Poster-Contribution, 2nd Conference on Solar Energy Conversion. Cambridge (England), Aug. 1978.

[29] *E. Schuhmacher,* Chimia *32,* 193 (1978).

[30] *G. Jones II, Sh. Chiang, P. T. Xuan,* J. Photochem. *10,* 1 (1979).

[31] AM2 spectrum taken from: Handbook of Geophysics. Chapter 16—19. United States Air Force. McMillan Company, New York 1960.

[32] Instead of ΔH (= stored energy recoverable as heat) ΔG should be used for redox systems which can supply energy in another form.

[33] *G. Porter, M. D. Archer,* Interdisc. Sci. Rev. *1,* 119 (1976).

[34] *M. D. Archer,* Sol. Energy *20,* 167 (1978).

[35] *J. R. Bolton,* J. Solid State Chem. *22,* 3 (1977).

[36] *D. Trivich, P. A. Flynn* in *F. Daniels, J. A. Duffie:* Solar Energy Research. Thames & Hudson, London 1955.

[37] *J. J. Loferski,* J. Appl. Phys. *27,* 777 (1956).

[38] *W. Shockley, H. J. Queisser,* J. Appl. Phys. *32,* 510 (1961).

[39] *M. Wolf,* Energy Convers. *11,* 63 (1971).

[40] Concerning determination and definition of photochemical quantum yields, cf. *H. Mauser:* Formale Kinetik, Bertelsmann Universitätsverlag, 1974, pp. 133ff.; *H.-D. Scharf, J. Fleischhauer* in Houben-Weyl: Methoden der Organischen Chemie, Vol. 4/5a, Part. Vol. 1. Thieme, Stuttgart 1976. The expression ϕ_B' used in this paper describes the ratio of the number of molecules B produced to the number of photons absorbed by A, Sens, and Cat, respectively. This is also the probability of formation of B after absorption of one photon by A, Sens, or Cat, respectively.

[41] *H. Leismann, H. W. Gaidetzka, J. Berix, J. Mattay, H.-D. Scharf,* Tetrahedron Lett. *1976,* 3927.

[42] *J. G. Calvert* in *A. M. Zarem, D. D. Erway:* Introduction to the Utilization of Solar Energy. McGraw-Hill, New York 1963.

[43] *K. B. Wiberg, H. A. Connon,* J. Am. Chem. Soc. *98,* 5411 (1976).

[44] *D. S. Kabakoff, J. C. G. Bünzli, J. F. M. Oth, W. B. Hammond, J. A. Berson,* J. Am. Chem. Soc. *97,* 1510 (1975).

[45] *N. A. Belikova, L. G. Vol'fson, K. V. Kuznetzova, N. N. Mel'nikov, A. I. Person, A. F. Plate, M. A. Pryanishnikova,* Zh. Prikl. Khim. *33,* 454 (1960).

[46] *G. S. Hammond, N. J. Turro, A. Fischer,* J. Am. Chem. Soc. *83,* 4675 (1961).

[47] *S. J. Cristol, R. L. Snell,* J. Am. Chem. Soc. *76,* 5000 (1954) [for *(1)/(2)*, R = COOH].

[48] *S. J. Cristol, R. L. Snell,* J. Am. Chem. Soc. *80,* 1950 (1958) [for *(1)/(2)* R = COOH].

[49] *W. G. Dauben, R. L. Cargill,* Tetrahedron *15,* 197 (1961).

[50] *G. S. Hammond, P. Wyatt, C. D. DeBoer, N. J. Turro,* J. Am. Chem. *86,* 2532 (1964).

[51] *H. Prinzbach, J. Rivier,* Tetrahedron Lett. *1967,* 3713.

[52] *St. Murov, G. S. Hammond,* J. Phys. Chem. *72,* 3797 (1968).

[53] *D. P. Schwendiman, C. Kutal,* J. Am. Chem. Soc. *99,* 5677 (1977).

[54] *P. A. Grutsch, C. Kutal,* J. Am. Chem. Soc. *99,* 6460 (1977).

[55] *H. Hogeveen, H. C. Volger,* J. Am. Chem. Soc. *89,* 2486 (1967).

[56] *H. C. Volger, H. Hogeveen,* Recl. Trav. Chim. Pays-Bas *86,* 1066 (1967).

[57] *J. Manassen,* J. Catal. *18,* 38 (1970).

[58] *H. Hogeveen, B. J. Nusse,* Tetrahedron Lett. *1973,* 3667.

[59] *H. Hogeveen, B. J. Nusse,* Tetrahedron Lett. *1974,* 159.

[60] *R. B. King, E. M. Sweet,* J. Org. Chem. *44,* 385 (1979).

[61] *K. C. Bishop III,* Chem. Rev. *76,* 461 (p. 467) (1976).

[62] *M. Frey,* J. Chem. Soc. *1964,* 365.

[63] *R. C. Cookson, J. Hudec, R. O. Williams,* J. Chem. Soc. *C 1967,* 1382.

[64] Shell Development Company.

[65] By analogy with *G. Bernhard, F. Korte,* Angew. Chem. *77,* 133 (1965); Angew. Chem. Int. Ed. Engl. *4,* 149 (1965).

[66] *F. Wilkinson, J. T. Dubois,* J. Chem. Phys. *39,* 377 (1963); *A. Gupta, G. S. Hammond,* J. Am. Chem. Soc. *98,* 1218 (1976).

[67] *B. C. Roquitte,* J. Am. Chem. Soc. *85,* 3700 (1963).

[68] *K. Alder, F. H. Flock,* Chem. Ber. *87,* 1916 (1954).

[69] *G. O. Schenck, R. Steinmetz,* Chem. Ber. *96,* 520 (1963).

[70] *J. Blum, C. Zlotogorski, H. Schwarz, G. Höhne,* Tetrahedron Lett. *1978,* 3501.

[71] *D. Vorländer, J. v. Pfeiffer,* Ber. Dtsch. Chem. Ges. *52,* 325 (1919).

[72] *G. B. Kistiakowsky,* J. Am. Chem. Soc. *52,* 102 (1930).

[73] *E. Müller,* Pure Appl. Chem. *16,* 153 (1968).

[74] *H. Gerischer,* Ber. Bunsenges. Phys. Chem. *80,* 1046 (1976); *H. Tributsch,* Nachr. Chem. Tech. Lab. *26,* 509 (1978).

[75] *H.-D. Scharf, R. Weitz,* Tetrahedron, in press.

[76] *A. Eckert,* Ber. Dtsch. Chem. Ges. *58,* 318 (1925); *60,* 1691 (1927).

[77] *H.-D. Scharf, R. Weitz:* Twelfth Jerusalem Symposium on Quantum Chemistry and Biochemistry. Jerusalem, April 1979. Reidel/Elsevier, Dordrecht 1979.

[78] *W. F. Engel, M. I. Waale, S. Müller,* Chem. Ind. (London) *1962,* 76.

[79] *F. R. Mintz, R. Schliebs,* Chem. Unserer Zeit *12,* 135 (1978).

[80] *O. P. Studzinskii, N. I. Rtishchev, A. V. El'tsov, A. V. Devekki,* Zh. Org. Khim. *4,* 774 (1972).

[81] *C. F. Wilcox, S. Winstein, W. G. MacMillan,* J. Am. Chem. Soc. *82,* 5450 (1960), UV spectrum in ethanol.

[82] From: Handbook of Chemistry and Physics; 56th Ed. CRC Press, Cleveland (Ohio) 1975/1976.

[83] λ_{kr} is assumed to be the longest wavelength shoulder of the UV spectrum in $CHCl_3$.

[84] Measured in our laboratory in $CHCl_3$.

[85] λ_{kr} at $\varepsilon = 0.01$.

[86] *G. Kaupp, H. Prinzbach,* Justus Liebigs Ann. Chem. *725,* 52 (1969).

[87] *G. Kaupp, H. Prinzbach,* Helv. Chim. Acta *52,* 956 (1969).

[88] λ_{kr} at 10% of ε_{max}.

[89] λ_{kr} is assumed to be the longest wavelength maximum of the phosphorescence excitation spectrum at 77 K [75].

[90] a) *R. Godvindjee, E. Rabinowitch, Godvindjee,* Biochem. Biophys. Acta *162,* 539 (1968); b) *Govindjee, R. Govindjee* in *Govindjee:* Bioenergetics of Photosynthesis. Academic Press, New York 1975.

[91] [Norbornadiene *(1a)*] = 0.02 mol/l; this is sufficient for an energy tranfer yield > 99% [94], assuming that the triplet lifetime of acetophenone is about 6×10^{-7} s [66] and energy transfer is diffusion-controlled. By way of comparison the thickness of the absorption cell is assumed to be $d = 5$ cm; this value refers to a volume of 50 l/m^2.

[92] Stoichiometric amount of norbornadiene *(1a)* used on the assumption that $CuCl_2$ is complexed up to > 99% [53].

[93] Optimum energy transfer yield has to be established in the case of sensitized reaction. The required condition is [94]:
$K_{ET} \cdot [A] \gg 1/\tau_{Sens^*}$;
K_{ET} = rate constant of energy transfer $Sens^* \rightarrow A$;
τ_{Sens^*} = triplet lifetime of sensitizer.

[94] *H.-D. Scharf, H. Leismann, H. W. Gaidetzka,* Bimolekulare Photoreaktionen in Lösung, Aufklärung von Reaktionsmechanismen mit Hilfe von Konzentrations- und wellenlängenabhängigen Produktquantenausbeuten. Forschungsbericht des Landes Nordrhein-Westfalen, Nr. 2748, Westdeutscher Verlag GmbH, Opladen 1978.

[95] *O. Diels, K. Alder,* Ann. *490,* 230 (1932).

Rates of Reactive Removal of Anthropogenic Emissions in the Atmosphere[**]

By Heinz Georg Wagner and Reinhard Zellner[*]

Anthropogenic emissions such as SO_2, CO, NO_x, and hydrocarbons constitute a perturbation of the natural equilibrium of the atmosphere. On a global scale, the extent of this perturbation does not significantly exceed the natural background levels as a result of direct or indirect photochemical "clean-up" processes in the atmosphere. Regionally, however, considerably increased concentrations of these trace components may occur. They are degraded by free radical reactions having widely differing yet substance-specific rates.

1. Introduction

The composition of the natural atmosphere is determined by a dynamic equilibrium between its components and by mass exchange with the hydrosphere and the biosphere[1]. Man-made, *i.e.* anthropogenic, emissions represent a perturbation of this equilibrium; the amounts and nature of compounds emitted vary widely with time and location. As a result, differing effects on the environment can be expected. Whereas on a global scale so far all emissions (except CO_2[2]) do not extend far beyond their natural levels, very prominent enhancements can be detected on a local or regional scale.

Table 1. Global emissions and characteristic concentrations of some atmospheric trace gases. R = enhancement (concentration ratio).

	Amount emitted [10^6 t a^{-1}]		Concentration [ppm]		
	natural	anthropogenic	pure air	polluted air	R
CO_2	1000000	14000	320	400	1.3
CO	33	300	0.1	60	600
CH_4	1600	50	1.5	2.5	1.7
NO_x	1090	53	0.001	0.2	200
SO_2	5	70	0.0002	0.2	1000

Table 1 surveys the global emissions of some important trace gases[3–5], subdivided into anthropogenic and natural contributions, and their characteristic concentrations in pure[3] and polluted air[6]. It is seen that the concentrations of CO, NO_x, SO_2 in polluted air are higher than their concentrations in clean air by 2—3 orders of magnitude; this does not apply to CH_4 and CO_2, a fact which clearly exemplifies the complexity of the relation between the amount of a compound emitted and its perturbation of the natural equilibrium. The extent of the enhancement of the pollutant concentrations is only loosely related to the relative strengths of the anthropogenic and natural sources (*i.e.* CO, SO_2). An additional important factor is the absolute concentration level in clean air: compounds with low concentrations in clean air (*i.e.* NO_x) are readily enhanced even by relatively weak anthropogenic sources. In contrast, compounds with high concentrations in clean air (CO_2) are hardly enhanced even by strong pollution sources. These considerations reflect the dynamics of the atmosphere which is determined by transport processes, causing spread and dilution of the emissions, as well as by chemical reactions, establishing concentration levels.

The extent of anthropogenic emissions from all groups of emitters (industry, energy production, transport) are well known[3,4,7]. Moreover, records of local and regional levels have been kept for many years. Although such immission monitoring is important for estimates of air quality (particularly near the ground), they tell us nothing about the rate of degradation of anthropogenic emissions. For such information we must turn to laboratory studies. Within the last five years the results from such investigations of homogeneous gas reactions (elementary reactions of free radicals and reactive trace components, simulation experiments of complex gas reactions, smog chamber experiments), as well as heterogeneous reactions (reactions on aerosol surfaces), and also from the investigation of photochemical primary and consecutive processes, have accumulated to such a stage that the important aspects of the rates of removal of anthropogenic emissions seem to be becoming clear. This is particularly true of emissions with relatively short lifetimes and clearly identified sinks. For emissions with longer lifetimes (removal rates of only a few percent per year) the sinks are not easily identifiable, so that their removal rates cannot yet be given precisely enough. This applies, for example, to the tropospheric removal of fluorocarbons such as CCl_3F (F-11) and CCl_2F_2 (F-12)[8].

This article is concerned with the rates and (probable) mechanisms of reactive degradation of characteristic anthropogenic emissions. We shall be concentrating on removal by homogeneous gas reactions which, together with surface adsorption, wash-out, and also heterogeneous chemical reaction, account for a fair proportion of degradation processes. Only the chemistry of the troposphere (0 to *ca.* 10 km high) will be considered. Owing to the relatively slow rate of mass transfer between troposphere and stratosphere[1], the former is by far the most important region for the removal of anthropogenic emissions.

2. Characterization of Emissions

Anthropogenic emissions are very unevenly distributed between the different groups producing emissions. This applies to the individual compounds and the occurrence of the emissions. Furthermore, this distribution will also depend upon the industrial conditions within a given country. The situation will be illustrated below for the Federal Republic of

[*] Prof. Dr. H. Gg. Wagner, Dr. R. Zellner
Institut für Physikalische Chemie der Universität
Tammannstrasse 6, D-3400 Göttingen (Germany)

[**] Based on a Plenary Lecture delivered at ACHEMA 79 on June 18, 1979.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0909-0663 $ 02.50/0

Germany. Figure 1 summarizes the total annual emissions[9] of SO_2, CO, NO_x, as well as hydrocarbons and dusts recorded for 1974 in the Federal Republic. The compounds are subdivided according to: energy production (including domestic space heating), chemical industry, transport, and coal, iron, and steel. Characteristically, in this survey and in comparable compilations for other countries, individual substances are seen to be particularly associated with specific groups of emitters. Thus the emission of SO_2, NO_x, and dust is ascribable mainly to energy production and that of CO to automotive transport. The emission of hydrocarbons is distributed somewhat more evenly over the sectors energy, chemistry, and transport. The contribution of the chemical industry to the overall emission is comparatively small.

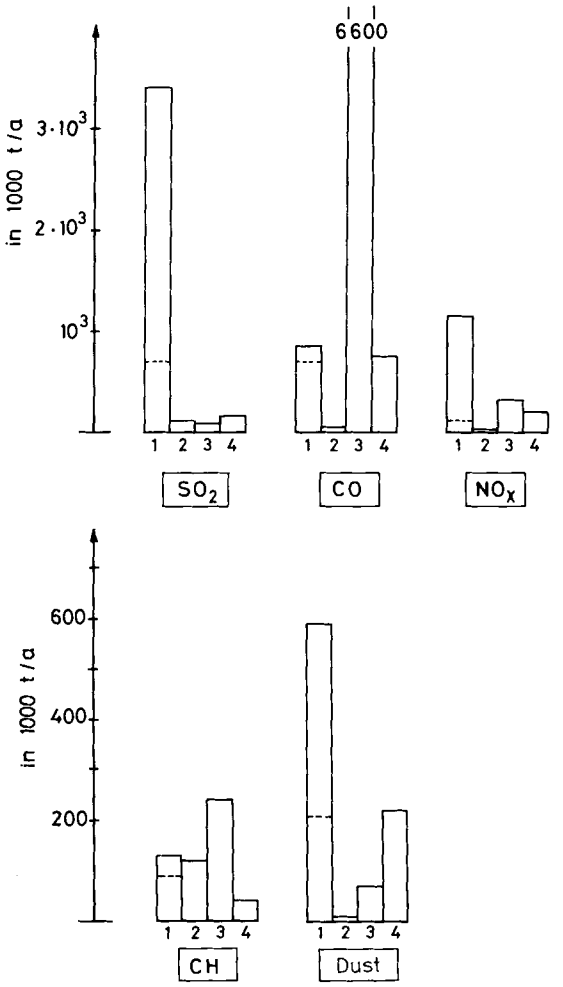


Fig. 1. Total annual emission (Federal Republic of Germany, 1974) of SO_2, CO, NO_x ($=NO_2$, NO), hydrocarbons, and dust, classified according to source. 1, energy production (including domestic space heating); 2, chemical industry; 3, transport; 4, coal, iron, and steel industry. Data in tonnes/year; the dashed line in (1) indicates contribution of domestic space heating [9].

With respect to the total burden of pollutant emissions, it is of interest to put these numbers on a more relative scale. To do this we go back to the emissions arising in connection with energy production. An emission of 3.3×10^6 t/a (SO_2) and of 1×10^6 t/a (NO_x) is caused by a total consumption of 225×10^6 t/a of primary fossil energy sources. The latter figure corresponds to a per capita consumption in West Germany of 3.7 t/a. The corresponding pollution is therefore 55 kg of SO_2 and 15 kg of NO_x per capita and annum. In this context, it is very important to indicate that the pollutant emissions are of the order of 1% by weight of the primary energy sources and further reductions cannot be achieved without considerable expense.

It should not go unmentioned that political and other decisions leading to a redistribution of the relative contributions of primary energy sources (*e.g.* less oil and more coal) will clearly lead to a redistribution of the relative anthropogenic emissions. However, this will essentially remain of a qualitative nature as long as there is no pronounced shift to non-fossil primary energy sources (nuclear and hydroelectric power), which are certainly far more favorable with regard to anthropogenic emissions.

It has already been pointed out that industry's contribution to the total emission is comparatively small. However, industrial emissions are responsible for the large variety of pollutants. This is demonstrated by Figure 2 for organic gases and vapors, and by Figure 3 for inorganic gases and vapors, in a typical pollution area (Cologne-Düsseldorf) with heavy chemical industry.

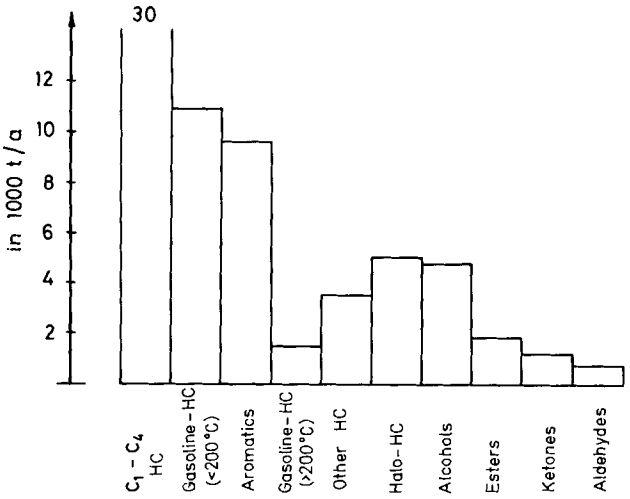


Fig. 2. Annual emission of organic gases and vapors from industrial sources in a typical pollution area (Cologne-Düsseldorf). HC = hydrocarbons.

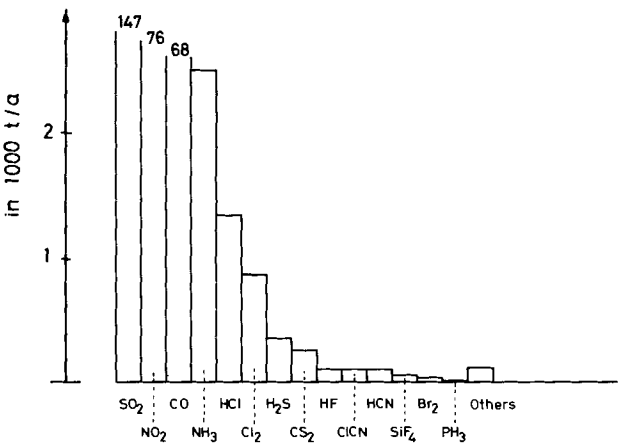


Fig. 3. Annual emission of inorganic gases and vapors from industrial sources in a typical pollution area (Cologne-Düsseldorf).

The classes of compounds and individual compounds accounting for most of the gaseous emissions (hydrocarbons, SO_2, NO_x, CO) affect the quality of air on a local and regional scale through their direct toxicological effect on humans (SO_2, NO_2), by their corrosive action on metal and stone

(SO_2), and by participation in photochemical smog (olefins, NO_x, CO) and its consequences (formation of peroxyacetyl nitrates and ozone, reduction of visibility). Moreover, unpleasant-smelling substances such as amines, H_2S, and thiols also impair the quality of air, although their total amount is very small. Among the emissions of particulate matter, dusts and soot from combustion processes are of interest in connection with their content of trace metals (Pb, Sb, Cd, Ni, Cr, Zn, V) and their possible catalysis of heterogeneous reactions. The metals are present as chelates in crude oil, often with porphyrin ligands. Since incorporation of metals occurs by condensation on soot particles forming in the cooling-down region, small particles ($<3\,\mu m$) have much higher metal contents than larger ones. This "enrichment" in small particles is of particular importance in connection with the toxicological action of suspended solids on absorption in the respiratory system.

3. Tropospheric Loss Processes of Anthropogenic Emissions

The removal of gaseous industrial emissions occurs predominantly by homogeneous gas reactions. This applies in particular to pollutants with short lifetimes ($\tau<1$ year) (see Section 4). Moreover, there are a number of other removal processes which assist in reducing the concentration of pollutants in the troposphere and which shall be briefly mentioned.

3.1. Physical Processes

3.1.1. Rain Out and Wash Out

Rain out (during the formation of clouds and fogs) and wash out (by falling rain drops) are removal processes for aerosol particles and for gases. Aerosols with radii $<0.1\,\mu m$ (so-called Aitken particles) are condensation nuclei which are subject to wet removal with a lifetime between 3—30 days[10]. The removal of gaseous compounds depends on their solubility in rain water. The amount of the gaseous trace component removed may easily be calculated from Henry's law[11]:

$$\varepsilon = \frac{N_L}{N_0} \approx 1 \Big/ \left(1 + \frac{KM_{H_2O}}{RTL}\right)$$

where N_0 and N_L are the trace gas concentration before and after condensation in the liquid phase; K is the equilibrium constant, M is the molar mass of H_2O and L is the liquid-water content of the air (typically 1 g H_2O/m^3 of cloud-laden air).

Such gas-liquid equilibria are generally not very effective loss processes. The amount of gas dissolved, however, can sometimes be very strongly increased by subsequent reactions in the aqueous phase. This is apparently the case for "acidic" gases such as SO_2 whose solubility in H_2O increases considerably with increasing pH. However, other gases are also involved in subsequent equilibria in the liquid phase. Thus the solubility of, *e.g.* formaldehyde is greatly enhanced by complex formation with hydrogen sulfite[11].

$$CH_2O + H_2O \rightleftharpoons CH_2(OH)_2 \overset{HSO_3^-}{\rightleftharpoons} CH_2(OH)SO_3H + OH^-$$

The rate of equilibration in solution depends upon the concentration gradients at the liquid/gas interface. Given "inverse" gradients, trace gases may accumulate in the air, for example when a saturated raindrop falls through "clean" air[4].

3.1.2. Adsorption on Surfaces, Vegetation

Both aerosols and gases may be removed by adsorption on surfaces (dry deposition). The adsorption of gases is a very important precursor to chemical reactions on vegetation (CO_2 photosynthesis, O_3) and on soil (microbiological activity).

3.1.3. Transport

Mass transport in the atmosphere generally serves to spread and dilute emissions. It is not a genuine loss process. Only in cases where the loss of pollutants occurs in areas of the atmosphere far removed from the point of their emission (*i.e.* the removal of fluorocarbons by photolysis in the stratosphere[8]), can transport be considered as a removal process. Because of the relatively slow mass exchange with the stratosphere (due to a strong discontinuity of the eddy diffusion coefficient around the tropopause), transport as a loss process is only important for pollutants with relatively long lifetimes.

3.1.4. Sedimentation

Sedimentation is a special form of transport and a typically size-dependent property of aerosol particles. Whereas the dynamics of small particles ($<0.1\,\mu m$) can be described by diffusion, "giant" particles ($>1\,\mu m$) are subject to sedimentation. Particles with radius of $10^2\,\mu m = 0.1$ mm "fall" through the whole troposphere within 2 h.

3.2. Chemical Processes

3.2.1. Photolysis

Because of the strong attenuation of shortwave radiation by stratospheric ozone the solar radiation available to the troposphere is limited to wavelengths above 300 nm. Correspondingly, photolysis is a tropospheric loss process only for compounds which absorb above this wavelength: 1) Ozone (relatively weak absorption in the region of the Huggins ($300<\lambda<360$ nm) and Chappuis bands ($450<\lambda<850$ nm); 2) NO_2 (very strong absorption in the whole visible region with photodissociation up to wavelengths of $\lambda=420$ nm); 3) HNO_2 (strong absorption and photodissociation up to 390 nm); 4) CH_2O (relatively weak absorption and photolysis below 360 nm)[11] and higher aldehydes which show a continuous absorption up to about 340 nm[12]; 5) SO_2 (weak triplet absorption $340<\lambda<390$ nm; strong singlet absorption $\lambda\leq320$ nm; but no photodissociation). The photochemical primary processes and the integrated tropospheric photodissociation rates

$$J^{TR} = \int_{300}^{\lambda} \phi(\lambda) f(\lambda)\, d\lambda$$

are shown in Table 2.

3.2.2. Heterogeneous Chemical Reactions (Reactions on Aerosol Surfaces)

It has been mentioned before that aerosols can be responsible for the heterogeneous removal of industrial emissions, mainly because of their trace contents of metals which may catalyze heterogeneous oxidation. For example, the oxidation of SO_2 is catalytically enhanced by $MnSO_4$-aerosols and by dusts from power plants in the presence of humidity[15].

other concentrations are estimated from photostationary relations, *e.g.* for $O(^3P)$:

$$NO_2 + h\nu \rightarrow NO + O$$
$$O + O_2 + M \rightarrow O_3 + M$$
$$\rightarrow d[O]/dt \approx 0 \Rightarrow J_{NO_2}[NO_2] = k_2[O][O_2][M]$$
$$\rightarrow [O]_{ss} = J_{NO_2}[NO_2]/k_2[O_2][M] \approx 10^5 \text{ molecules/cm}^3 \text{ for } [NO_2] = 50 \text{ ppb}$$

Table 2. Photochemical primary processes and tropospheric photodissociation rates for O_3, NO_2, HNO_2, CH_2O, and SO_2. All data for J^{TR} apply to 50° latitude in the northern hemisphere and maximum photon flux (summer, midday).

	Primary process	J^{TR} [s^{-1}]	Ref.
1)	$O_3 + h\nu$ ($\lambda \leq 313$) $\rightarrow O_2(^1\Delta_g) + O(^1D)$		
	($313 < \lambda < 360$) $\rightarrow O_2(^1\Delta_g) + O(^3P)$	4.5×10^{-4}	[13]
	($450 < \lambda < 850$) $\rightarrow O_2(^3\Sigma_g^-) + O(^3P)$		
2)	$NO_2 + h\nu$ ($300 < \lambda < 420$) $\rightarrow NO(x^2\pi) + O(^3P)$	8×10^{-3}	[13]
3)	$HNO_2 + h\nu$ ($300 < \lambda < 390$) $\rightarrow OH(x^2\pi) + NO(x^2\pi)$	2.8×10^{-3}	[13]
4)	$CH_2O + h\nu$ ($\lambda < 360$) $\rightarrow CHO(A') + H(^2S)$	5.4×10^{-5}	[11]
	$\rightarrow CO(^1\Sigma^+) + H_2(^1\Sigma_g^+)$		
5)	$SO_2 + h\nu$ ($\lambda < 320$) $\rightarrow SO_2^*(^1B_1)$	6.3×10^{-5}	[14]
	($340 < \lambda < 390$) $\rightarrow SO_2^*(^3B_1)$	4.5×10^{-7}	

As a result, SO_2 oxidation of up to 5% is observed within the stack plumes of common SO_2 and aerosol source strengths (40–300 mg dust/m^3; 0.5–5 g SO_2/m^3) at high relative humidities.

3.2.3. Homogeneous Chemical Reactions

Degradation by homogeneous gas reactions (reactions with radicals and reactive trace compounds) is nearly always the principal removal process for short-lived gaseous emissions. We shall therefore now consider such processes in greater detail.

4. The Troposphere as a Homogeneous Gas Phase Reactor

Before considering individual homogeneous gas phase reactions, let us first define the conditions under which such reactions occur in the troposphere.

4.1. Free Radicals and Reactive Trace Components

The basis for any chemical conversion in the troposphere is direct or indirect photochemical activation. The energy requirement for reactions between typical atmospheric components, *e.g.*

$$CO + O_2 \rightarrow CO_2 + O;\ E_A = 60 \text{ kcal/mol}$$
$$CO + NO_2 \rightarrow CO_2 + NO;\ E_A = 27.5 \text{ kcal/mol}$$

is too large for a chemical conversion to occur on a realistic time scale. The chemistry of the atmosphere is initiated by reactive trace components, like O_3 and $O_2(^1\Delta_g)$, or by free radicals (H, O, $O(^1D)$, OH, HO_2) which are formed from photochemical precursors. Table 3 summarizes formation processes and stationary tropospheric concentrations of these species. Only the concentrations of O_3 and OH (the latter with considerable uncertainty) were measured directly. All the

or from solution of the one-dimensional stationary continuity equation. (M = inert collision partner (N_2, O_2) subscript ss = steady state.)

Table 3. Formation processes and concentration range of free radicals and reactive trace compounds in the troposphere. The maximum concentration refers to the conditions of photochemical smog. 1 cm^3 of gas contains 2.3×10^{19} molecules at 0 °C and 1 bar.

Species	Formation process	Concentration [molecules/cm^3] max.	yearly average
H	$CH_2O + h\nu \rightarrow CHO + H$; $OH + CO \rightarrow CO_2 + H$		$< 10^{-1}$
O	$NO_2 + h\nu \rightarrow NO + O$	10^5	$\ll 10^5$
$O(^1D)$	$O_3 + h\nu \rightarrow O_2^* + O(^1D)$		$< 10^{-1}$
OH	$O(^1D) + H_2O \rightarrow 2OH$; $HONO + h\nu \rightarrow OH + NO$; $HO_2 + NO \rightarrow OH + NO_2$	5×10^6	5×10^5
HO_2	$H + O_2 + M \rightarrow HO_2 + M$	5×10^8	10^8
O_3	$O + O_2 + M \rightarrow O_3 + M$	5×10^{12}	10^{12}
$O_2(^1\Delta_g)$	$O_3 + h\nu \rightarrow O + O_2(^1\Delta_g)$; $NO_2^* + O_2 \rightarrow O_2^*(^1\Delta_g) + NO_2$		$< 10^7$

These formation processes are strongly coupled. The extremely small stationary concentration of H atoms for example is due to its fast conversion with O_2 to form HO_2. On the other hand, the concentration of OH is to a large extent determined by the fast conversion of HO_2 into OH in the presence of NO. This process is responsible for the enhancement of the OH concentrations in NO_x-catalyzed photochemical smog.

4.2. Spread of Emissions

Industrial emissions normally originate from point sources (stacks). Their *horizontal* spread is caused by a flow (winds), superimposed by eddy diffusion. The latter can be described by a Gaussian diffusion model. The corresponding spread in the *vertical* direction, however, is largely determined by the

local stability of the air layers. As shown by Figure 4, this stability is related to the vertical temperature profiles. The spread of emissions is said to be "neutral" if the actual temperature profile of the lower air layers is given by the adiabatic lapse rate (Fig. 4, case 2). For the troposphere, the average lapse rate is 6.5°/km and it is considerably lower than the adiabatic lapse rate for dry air (9.8°/km). Actual temperature profiles of the lower air layers, which correspond to

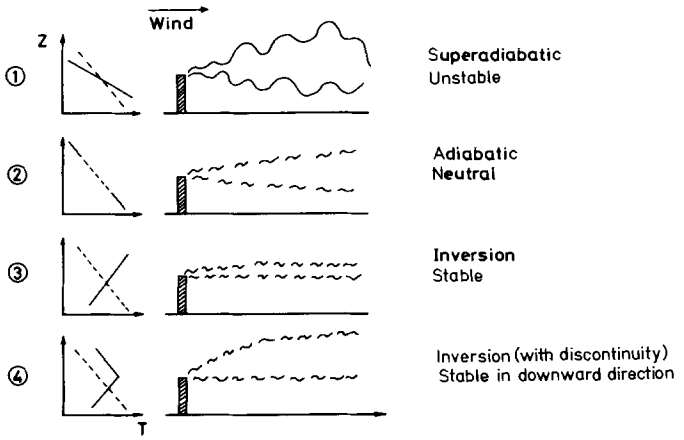


Fig. 4. Tropospheric temperature profiles and stability of low-lying layers of air. Left: plot of temperature T (x axis) *versus* tropospheric height z (y axis) for four cases of possible temperature profile (solid lines). The dashed line represents the mean adiabatic temperature gradient of the troposphere of 6.5°/km. Right: vertical propagation of emission from point sources (stacks) resulting from the given temperature profiles as a function of the horizontal distance from the site of emission. A wind of the direction indicated is superimposed upon the propagation. Pronounced vertical mixing is observed only for unstable layers (case 1). Propagation is "neutral" in case 2. In contrast, stable air layers (inversion, case 3) inhibit vertical mixing. In an inversion with discontinuity, stability is generated in an upward direction (not shown) or in a downward direction (case 4).

lapse rates higher (case 1) or lower (case 3) than adiabatic result in unstable or stable situations, respectively, with increased or decreased mixing. Of special interest in this context is a situation with inversion, in which the vertical mixing is strongly hampered and in which a local enrichment of emissions close to the surface is observed (case 4).

4.3. Definition of Lifetime

Assuming pseudo-first order reactions, the total rate of removal of a component A by homogeneous gas reactions can be described by the following expression:

$$R_A = -\frac{d\ln[A]}{dt} = \sum_i k_i[X_i]$$

where X_i represents all potential reactants (*e.g.* O, OH, HO_2, O_3). k_i are the corresponding rate constants. Assuming time independent (photostationary) concentrations for X_i, we may define "partial" lifetimes:

$$\tau_{Ai} = \{k_i[X_i]\}^{-1} \quad \text{(in time units)}$$

The total lifetime of A is then given by:

$$\tau_A = 1/\sum_i \tau_{Ai}^{-1}$$

An alternative formulation, which is used equally often, is the rate of removal R_i in %/time. It is related with the lifetime τ_i *via*

$$R_i = \tau_i^{-1} \cdot 63 \quad \text{(in units of \%/time)}$$

The preceding formulation of the lifetime of a compound A is only correct to a first approximation. It assumes that k_i and $[X_i]$ are independent of time and location. Owing to the uncertainty connected with the concentration of X_i, it will frequently suffice to use time- and site-averaged quantities. The lifetimes given in Tables 4 to 13 were obtained in this way. It should be emphasized, however, that a more precise approach (which becomes reasonable when X_i is known with sufficient accuracy) will require consideration of further effects:

1) Because of their coupling to tropospheric photochemistry, (*i.e.* to the altitude of the sun) the concentrations of some of the free radicals and reactive trace components are not constant, but show diurnal as well as annual variations[16, 17].
2) The concentration of the reactive component X_i may be influenced by the pollutant A to be degraded. In this case A appears in the steady state equation for X_i:

$$[X_i] = P_i / \sum_i k_i[M_i]$$

where P_i is a general production term and $\sum k_i[M_i]$ is a removal term with A as component of M_i. As a consequence, the concentration of X_i itself sinks to a minimum at site x_0 after emission of A (Fig. 5). Removal of A will then occur only in the boundary zones where A has become so dilute that it no longer affects X_i. The lifetime of A is, roughly speaking, enhanced by the corresponding transport time. This effect will be particularly large if A has a short lifetime, *i.e.* if A reacts fast with X_i.

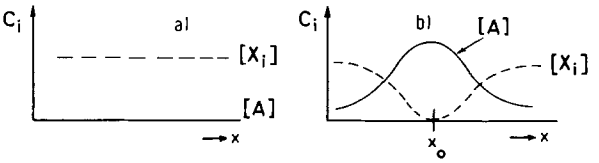


Fig. 5. Plot of concentration of a radical or a reactive trace compound X_i and an emitted substance A *versus* horizontal distance x. a) Prior to emission of A the value of $[X_i]$ is constant and independent of displacement and [A] is zero. b) After emission of A a gaussian diffusion profile is set up for [A] around the site of emission (x_0). (There is assumed to be no wind.) If the concentration of X_i is dependent upon A, then $[X_i]$ decreases with a minimum at x_0. As a result, A is removed only in boundary regions, in which it is sufficiently dilute.

3) Because of the relatively strong temperature gradients in the troposphere, the temperature dependence of the rate constants k_i of bimolecular reactions has to be considered for reactions having significant activation energies (E_i):

$$k_i(z) = k_i^0 \exp[-E_i/R(T_0 - lz)]$$

where T_0 (290 K) is the average temperature at the surface, $k_i^0 = k_i$ at 290 K; $l = 6.5°$/km is the adiabatic lapse rate, and z is the altitude in km.

Correspondingly we obtain for the "partial" lifetimes[18] in the troposphere:

$$\tau_i^{-1} = (1/z_T)\int_0^{zT} k_i(z)dz$$

$$= [X_i]k_i^0\left[1-\exp\left(-\frac{E_i}{R}\alpha z_T\right)\right]\Big/\left(\frac{E_i}{R}\alpha z_T\right)$$

where $\alpha = 1/T_0^2$, and z_T is the average height of tropopause (10 km).

In the case of recombination reactions, *e.g.*

$$OH + NO_2 + M \rightarrow HNO_3 + M$$

the rate constants show an additional dependence on the total pressure ("fall-off" behavior). As a consequence, the variation of the rate constants with atmospheric height, $k_i(z)$, does not show a simple exponential dependence upon z but has to be described by effective "fall-off" curves of rather complex form[19].

5. Rates and Mechanisms of the Reactive Removal of Selected Anthropogenic Emissions

5.1. Removal of SO_2

Studies on homogeneous oxidation of SO_2 have shown that the reaction with OH radicals

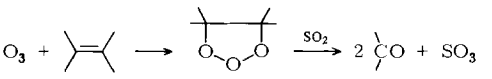
$$OH + SO_2(+M) \rightarrow HSO_3(+M)$$

is the most important oxidation reaction from which, for a mean OH concentration of 10^6 mol/cm^3, a SO_2 lifetime of about 11 days results (see Table 4).

Recombination with oxygen atoms is two orders of magnitude slower and of no importance as a removal process. Nor does the reaction with HO_2 radicals

$$HO_2 + SO_2 \rightarrow OH + SO_3$$

make any significant contribution to the oxidation of SO_2, although $[HO_2] > [OH]$. Little is known about the rate of oxidation by alkoxy (RO) and alkylperoxy radicals (RO_2). The lifetime given in Table 4 is estimated from assumed rate constants[20]. If heterogeneous oxidation is also considered, then an overall lifetime τ_{SO_2} of about one week is calculated[20]. That is somewhat more than half of the lifetime for oxidation by OH only. Recent studies have shown that SO_2 hardly reacts with NO_2, O_3, or NH_3 in the homogeneous gas phase. In the presence of olefins, however, and under conditions of photochemical smog, SO_2 is oxidized by intermediates of the olefin/O_3 reaction[21]:



The assumed mechanism of the principal oxidation of SO_2 under atmospheric conditions—induced by OH—is shown in Figure 6[20]. The occurrence of nitrosyl hydrogen sulfate ($NOHSO_4$) has been confirmed by recent photolysis studies on NO_2/SO_2[23]. The final products of SO_2 oxidation are sulfuric acid aerosols.

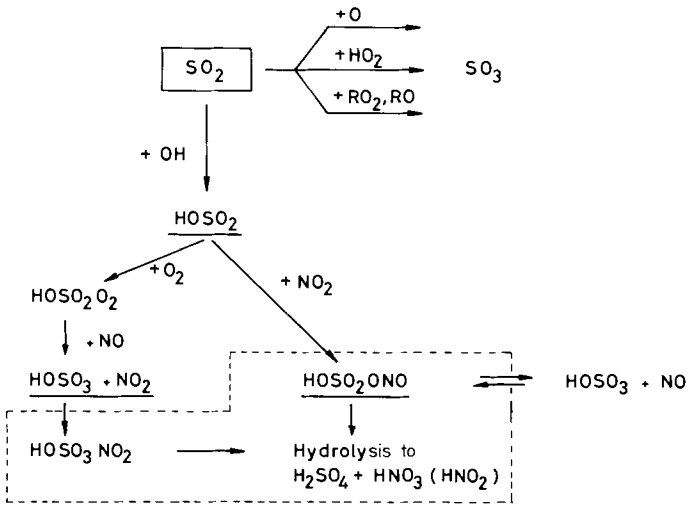


Fig. 6. Tropospheric oxidation of SO_2 by OH radicals. The initial step is recombination with formation of the $HOSO_2$ radical [19] (for thermochemical data of $HOSO_2$, see [22]). The final products of SO_2 oxidation are sulfuric acid aerosols (hatched box). The lifetime of SO_2 with respect to OH oxidation is 11 d; this is considerably less than in oxidations by O, HO_2, or RO/RO_2.

5.2. Removal of NO_x

In unpolluted air (no O_3, HO_2, RO_2) NO is oxidized only very slowly by the termolecular reaction

$$NO + NO + O_2 \rightarrow 2NO_2$$

At 50 ppb of NO, the "lifetime" (calculated for a decrease to 1/e of initial concentration) for oxidation by O_2 is about half a year. In the presence of O_3, HO_2, and RO_2, however, its oxidation is strongly accelerated (Table 5). This acceleration is characteristic of photochemical smog.

Table 4. Tropospheric oxidation of SO_2 by homogeneous gas reactions: primary reactions, rate constants, and partial lifetimes.

Reaction	k [cm^3 molecule^{-1} s^{-1}]	τ [days] [a]
$OH + SO_2(+M) \rightarrow HSO_3(+M)$	$\sim 10^{-12}$	~ 12
$O + SO_2(+M) \rightarrow SO_3(+M)$	1.8×10^{-14}	$>5\times10^3$
$HO_2 + SO_2 \rightarrow OH + SO_3$	8×10^{-16}	140
$(RO_2, RO) + SO_2 \rightarrow SO_3 + (RO, R)$		25
$SO_2 + h\nu \rightarrow SO_2(\tilde{a}^3B_1) \xrightarrow{O_2} SO_4$ (?)		360

[a] Here and in all the following tables the lifetimes τ have been calculated for the following concentrations of reactive components: $[OH] = 1\times10^6$, $[O] = 1\times10^5$, $[HO_2] = 1\times10^8$; $[O_3] = 1\times10^{12}$; $[RO] = 5\times10^5$; $[RO_2] = 1\times10^8$ molecules/cm^3. In this and the following tables, k and τ are for NTP unless otherwise stated.

Table 5. Homogeneous NO oxidation processes and NO lifetimes in the troposphere.

Reaction	k [cm^3 molecule^{-1} s^{-1}]	τ
$NO + NO + O_2 \rightarrow 2NO_2$		{ 0.5 a / 50 ppb NO }
$NO + O_3 \rightarrow NO_2 + O_2$	1.8×10^{-14}	1 min
$NO + HO_2 \rightarrow NO_2 + OH$	8×10^{-12}	20 min
$NO + CH_3O \rightarrow CH_3ONO$	8×10^{-14}	290 d
$\rightarrow CH_2O + HNO$		
$NO + CH_3O_2 \rightarrow CH_3O + NO_2$	1.2×10^{-12}	2 h
$NO + OH(+M) \rightarrow HNO_2(+M)$	1×10^{-11}	27 h

The oxidation of NO to NO_2, however, does not represent a removal process. Because of the photochemical instability

of NO_2, NO is regenerated with a lifetime of only 2 min. NO and NO_2 are always coupled *via* the photostationary relation $J_{NO_2}[NO_2] = k[NO][O_3]$, which has been experimentally established for numerous photochemical smog simulation studies.

The only true removal processes for NO_x are the recombination reactions

$$OH + NO_2(+M) \rightarrow HNO_3(+M)$$
$$HO_2 + NO_2(+M) \rightarrow HO_2NO_2(+M)$$

where the products may be washed out, as well as the formation of peroxyacetyl nitrate (PAN), whose rate of formation is probably several hours (Table 6). These results are shown schematically in Figure 7.

Table 6. Tropospheric removal processes and lifetimes of NO_2.

Reaction	k [cm^3 molecule^{-1} s^{-1}]	τ
$NO_2 + OH(+M) \rightarrow HNO_3(+M)$	1.5×10^{-11}	18 h
$NO_2 + HO_2(+M) \rightarrow HO_2NO_2(+M)$	10^{-12}	[b]
$NO_2 + CH_3O \rightarrow CH_3ONO_2$	3×10^{-13}	80 d
$CH_3CO(O_2) + NO_2 \rightarrow CH_3CO(O_2)NO_2$ (PAN)	—	several h
$NO_2 + h\nu \rightarrow NO + O$	$J = 8 \times 10^{-3}$ s^{-1} [a]	2 min

[a] This is the maximum photodissociation rate (summer, midday, 50° latitude, northern hemisphere) for NO_2. Since the photolytic lifetime of $NO_2 \ll 1$ d, correspondingly smaller photodissociation rates must be used for other times of day and year.
[b] Due to the low dissociation energy the reaction product (HO_2NO_2) is thermally unstable in the lower troposphere. There, an equilibrium is established from which NO_2 can be removed by wash out; the NO_2 lifetime is determined by the wash-out rate of HO_2NO_2 and not by its rate of formation.

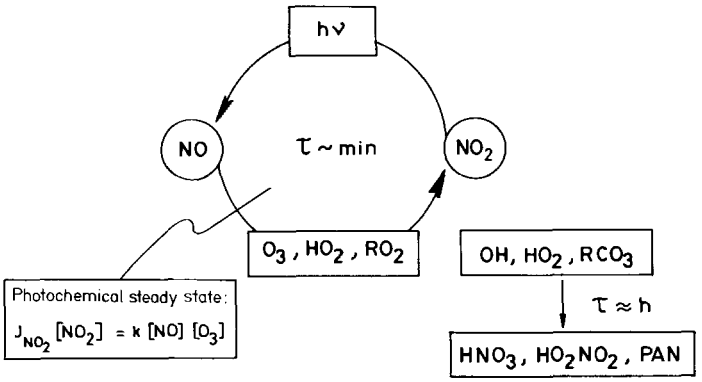


Fig. 7. NO/NO_2 conversion and NO_2 removal in the troposphere. The chemistry of NO_x is characterized by a relatively fast (several minutes) photostationary interconversion and comparatively slow degradation of NO_2 by recombination reactions with OH, HO_2, and RCO_3.

5.3. Removal of CO

The only significant removal reaction for CO is oxidation by OH radicals

$$OH + CO \rightarrow CO_2 + H$$

leading to a lifetime of *ca.* 40 d. Other oxidation reactions ($CO + O + M$, $CO + HO_2$) are unable to compete (Table 7).

Owing to the unique situation that the trace compound CO is oxidized exclusively by OH, the concentration of OH can be derived from the steady state concentration level of CO and its known rate of formation (see, *e.g.* [24]).

Table 7. Tropospheric oxidation processes and lifetimes of CO.

Reaction	k [cm^3 molecule^{-1} s^{-1}]	τ
$OH + CO \rightarrow CO_2 + H$	1.5×10^{-13} (several torr) 2.8×10^{-13} (760 torr) [a]	40 d
$CO + HO_2 \rightarrow CO_2 + OH$	10^{-19}	$>10^3$ a
$CO + O + M \rightarrow CO_2 + M$	5×10^{-17} (760 torr)	6×10^3 a

[a] This distinction is intended to indicate that the rate constant of the reaction $OH + CO$ increases with the total pressure, at least in the presence of O_2 [25].

5.4. Removal of Aliphatic Hydrocarbons

The oxidative removal of saturated hydrocarbons occurs almost exclusively by reaction with OH radicals. The corresponding reactions with O atoms are slower by several orders of magnitude (see Table 8)[*]. The calculated lifetimes decrease with increasing chain length of the alkane ($\tau_{CH_4} \approx 3.5$ a). The course of oxidative removal of saturated hydrocarbons under atmospheric conditions is shown in Figure 8.

Table 8. Tropospheric lifetimes of some aliphatic hydrocarbons with respect to their oxidation by O atoms and OH radicals.

Hydrocarbon	k_O [cm^3 molecule^{-1} s^{-1}]	k_{OH}	τ_O	τ_{OH}
Methane	6×10^{-18}	9×10^{-15}	5×10^4 a	3.5 a
Ethane	1×10^{-15}	3×10^{-13}	3×10^2 a	38 d
n-Butane	2.2×10^{-14}	3×10^{-12}	6.3 a	3.8 d
Isobutane	1×10^{-13}	2.5×10^{-12}	3.1 a	4.6 d

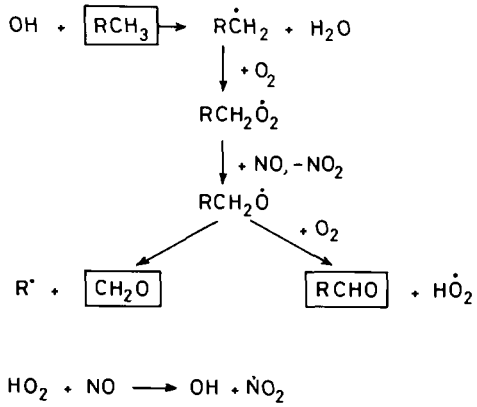


Fig. 8. Tropospheric oxidation of saturated hydrocarbons. The reactions lead either to oxidation of the terminal C atom ($RCHO + HO_2$) or to simultaneous C C cleavage ($CH_2O + R$). The branch of the reaction leading to $RCHO + HO_2$ is the basis of a chain reaction (regeneration of OH *via* $HO_2 + NO \rightarrow OH + NO_2$), through which 2 moles of NO are oxidized to NO_2 per mole of hydrocarbon. This reaction course is one of the causes of photochemical smog.

The mechanism involves the recombination with O_2 of the alkyl radical, formed in the primary step. The resulting alkylperoxy radical is then reduced by reaction with NO. The product of this process, the alkoxy radical, may then undergo unimolecular decomposition or be further oxidized by O_2 to give formaldehyde or a higher aldehyde. Halogenated alkanes (fluorocarbons) have lifetimes of several years with respect to reaction with OH radicals[18]. Only the perhalogen-

[*] Although excited oxygen atoms ($O(^1D)$) react very fast with hydrocarbons, their concentration is too low to significantly enhance the rate of removal.

Table 9. Tropospheric lifetimes of some selected olefins with respect to their oxidation by O atoms, OH radicals, and ozone.

Olefin	k_O	k_{OH} [cm³ molecule⁻¹ s⁻¹]	k_{O_3}	τ_O	τ_{OH}	τ_{O_3}
Ethylene	8.1×10^{-13}	8×10^{-12}	1.7×10^{-18}	142 d	34 h	6.8 d
Propylene	3.6×10^{-12}	1.5×10^{-11}	1.3×10^{-17}	32 d	11 h	21 h
1-Butene	3.8×10^{-12}	3.5×10^{-11}	1.2×10^{-17}	30 d	8 h	23 h
2-Methyl-2-butene	6.3×10^{-11}	8.7×10^{-11}	—	1.8 d	3.2 h	—
1,3-Butadiene	2×10^{-11}	6.8×10^{-11}	2.6×10^{-16}	5.7 d	4 h	1 h

ated compounds such as $CFCl_3$ (F-11) and CF_2Cl_2 (F-12) fail to react with OH; their lifetimes are several decades[8].

5.5. Removal of Olefins

Olefins are considerably more reactive than saturated hydrocarbons and have correspondingly shorter lifetimes. Apart from reaction with OH radicals, which leads to the highest rate of removal, those with oxygen atoms and with ozone are also important (Table 9).

The course of the OH/olefin reaction is highly complex, owing to primary addition of the OH radical to the double bond and the many possibilities of subsequent degradation:

$$C_2H_4OH^* \rightarrow CH_3CHO + H$$
$$\rightarrow CH_3 + CH_2O \text{[26]}$$

The rate constant is accordingly pressure dependent; the activation energy is negative[27]. Under atmospheric conditions, however, it can be assumed that the OH-olefin adduct is stabilized and reacts with O_2 to give aldehydes (Fig. 9).

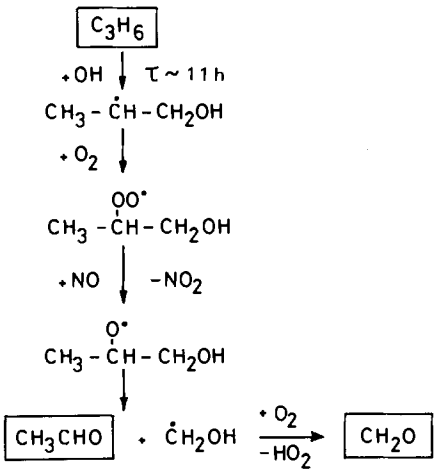
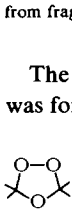


Fig. 9. Tropospheric oxidation of olefins (example: propylene), induced by OH radicals. This reaction course has not been unequivocally established; however, it appears that the double bond is preferentially oxidized. Aldehydes are formed from fragments of C–C cleavage.

The extremely complex course of the O_3/olefin reaction was formerly known only for the liquid-phase reaction—formation of the secondary ozonide of type *(1)*. Recent investigations by *Martinez et al.*[28] seem to indicate that the Criegee intermediate methylene peroxide (H_2COO) decomposes *via* a dioxirane in the gas phase (Fig. 10). Moreover, at low pressures the O_3/olefin reaction is accompanied by luminescence arising from decomposition of dioxetanes such as *(2)*[29].



(1)

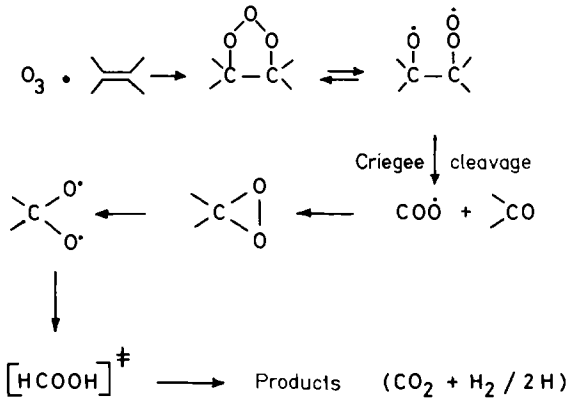
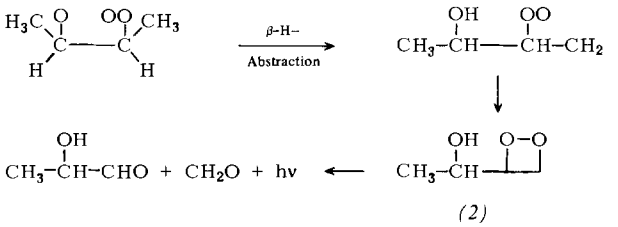


Fig. 10. Tropospheric ozone/olefin reaction illustrated for ethylene. The Criegee intermediate (methylene peroxide) presumably rearranges *via* a dioxirane [28] and decomposes to CO_2 *via* a highly excited formic acid molecule.



(2)

5.6. Removal of Aromatic Hydrocarbons

Reaction with OH is again the only significant pathway for removal of aromatic hydrocarbons. The lifetime of benzene is several days; it becomes considerably shorter on substitution by alkyl or OH groups (several hours, see Table 10).

Table 10. Tropospheric lifetimes of selected aromatic hydrocarbons with respect to their oxidation by OH radicals [27].

	k [cm³ molecule⁻¹ s⁻¹]	τ_{OH}
Benzene	1.2×10^{-12}	9.6 d
Toluene	6.4×10^{-12}	1.8 d
Ethylbenzene	7.9×10^{-12}	34 h
o-Xylene	1.4×10^{-11}	20 h
o-Cresol	3.4×10^{-11}	8 h

The OH radical adds preferentially to the ring; oxidation of ring C atoms occurs, and possibly also ring cleavage. Oxidation of alkyl side chains is observed to a slight extent (see *e.g.* [27]).

5.7. Removal of Aldehydes and Alcohols

Oxidative removal of partially oxidized hydrocarbons is particularly interesting as they are themselves intermediates of the oxidation of hydrocarbons. Reactions with OH radicals are again important degradation processes (Table 11).

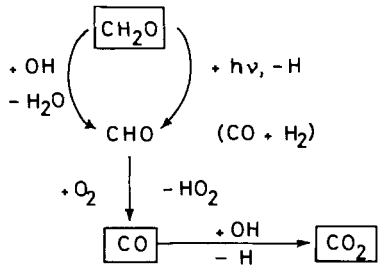
Table 11. Tropospheric removal processes and lifetimes of simple aldehydes and alcohols.

Reaction		k [cm^3 molecule^{-1} s^{-1}]	τ
$CH_2O + OH$	$\rightarrow H_2O + CHO$	9×10^{-12}	1.2 d
$CH_2O + h\nu$	$\rightarrow CO + H_2$ $\rightarrow CHO + H$	$J = 1.8 \times 10^{-5}$ s^{-1} [a]	15 h
$CH_3CHO + OH$	$\rightarrow CH_3CO + H_2O$	1.6×10^{-11}	17 h
$CH_3OH + OH$	$\rightarrow CH_2OH + H_2O$	1×10^{-12}	11.6 d
$C_2H_5OH + OH$	$\rightarrow$ Products	3×10^{-12}	3.8 d

[a] This is the photodissociation rate for 50° latitude, northern hemisphere, and annual average photon flux [11]. J is some three times higher at the maximum photon flux (summer, midday); the photolytic lifetime is correspondingly shorter.

Moreover, aldehydes are also photolabile. For example, photolytic degradation of formaldehyde is faster than its reactive removal by OH. The same final products are formed in either case (CO and HO_2; from $CHO + O_2 \rightarrow CO + HO_2$). Owing to the UV shift of the absorption spectrum, photolysis can no longer compete with the OH reaction in the case of higher aldehydes.

The course of oxidation of CH_2O and CH_3CHO by OH radicals is shown in Figure 11. The presumed formation of the acetyl radical (CH_3CO) during CH_3CHO oxidation and its further reaction with O_2 are deduced from the existence of peroxyacetyl nitrate and CO_2 as final products. It therefore seems that the CO oxidation stage can be omitted in the case of higher aldehydes (as opposed to CH_2O).



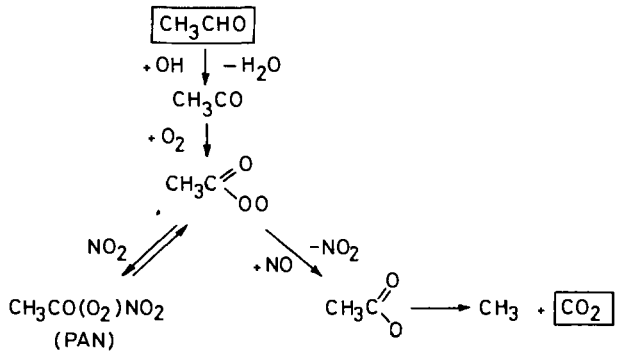


Fig. 11. Tropospheric removal of formaldehyde and of acetaldehyde. For CH_2O, both the OH reaction and photolysis are initiating primary processes. The resulting CHO radical is oxidized to CO by O_2. For CH_3CHO, photolysis cannot compete with the OH reaction. Primary oxidation by OH occurs at the aldehydic C atom. Final products are PAN and CO_2. Simultaneous oxidation of the methyl group is not observed.

5.8. Removal of Sulfur and Nitrogen Compounds

Emissions of H_2S, thiols, and aliphatic amines are also of importance as compounds with strong unpleasant odors owing to their low physiological thresholds. Their removal in the troposphere by reaction with O atoms and OH radicals, as well as the freshening of thiol-containing air by UV irradiation, have therefore been thoroughly investigated[30].

5.8.1. H_2S and Thiols

Rate constants for the removal reactions of some sulfur compounds and the lifetimes of these species are compiled in Table 12. They range from several hours to days for the reaction with OH radicals and months for the reaction with O atoms. Primary attack by O and OH leads preferentially to formation of alkylthio radicals (RS•) from which, as recently shown by *Kirchner* and *Vettermann*[30], SO_2 and aldehydes arise under atmospheric conditions; thus oxidative cleavage of the C–S bond occurs with accompanying oxidation of the C and S fragments (see Fig. 12).

Table 12. Tropospheric lifetimes of H_2S, alkanethiols, and $(CH_3)_2S$ with respect to their oxidation by O atoms and OH radicals.

	k_O	k_{OH} [cm^3 molecule^{-1} s^{-1}]	τ_O	τ_{OH}
H_2S	2.8×10^{-14}	3×10^{-12}	11 a	3.8 d
CH_3SH	1.6×10^{-12}	3.4×10^{-11}	72 d	8 h
CH_3SCH_3	—	1.0×10^{-11}	—	26 h
C_2H_5SH	2.5×10^{-12}	—	46 d	—
C_3H_7SH	2.6×10^{-12}	—	44 d	—

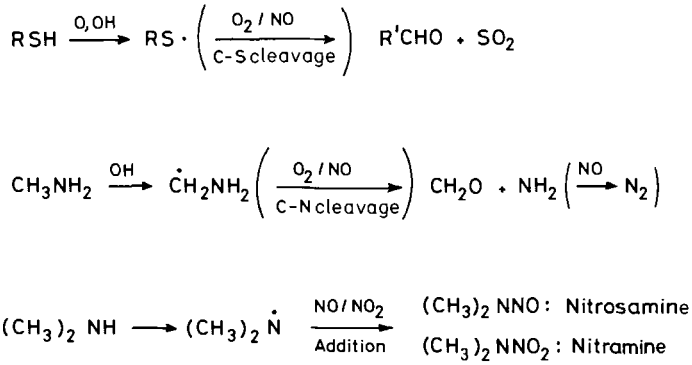


Fig. 12. Tropospheric removal of thiols and of primary and secondary amines, schematic.

5.8.2. NH_3 and Amines

Table 13 lists rate constants for the reactions of NH_3 and selected aliphatic amines with O and OH together with the respective lifetimes.

Table 13. Tropospheric lifetimes of NH_3 and amines with respect to their removal reactions with O atoms and OH radicals.

	k_O	k_{OH} [cm^3 molecule^{-1} s^{-1}]	τ_O	τ_{OH}
NH_3	1×10^{-16}	1.6×10^{-13}	$>10^3$ a	72 d
CH_3NH_2	3.4×10^{-13}	2.2×10^{-11}	1 a	12 h
$C_2H_5NH_2$	1.1×10^{-12}	2.7×10^{-11}	100 d	10 h
$(CH_3)_2NH$	5.3×10^{-12}	6.5×10^{-11}	22 d	4 h
$(CH_3)_3N$	1.5×10^{-11}	6.0×10^{-11}	8 d	4.6 h
$(C_2H_5)_2NOH$ (DEHA)	6.6×10^{-12}	—	17 d	—

The course of tropospheric degradation of amines is largely unexplained. However, comparison of the bond energies in primary and secondary amines [H—CH_2NH_2, 94.6 kcal/mol; CH_3NH—H, 103 ± 2 kcal/mol; $(CH_3)_2N$—H, 95 kcal/mol] suggests that a C_α—H atom is preferentially abstracted in primary amines; in contrast, N—H abstraction is expected in secondary amines. These reactions lead to different final products (see Fig. 12): primary amines are oxidized to aldehyde and N_2 *via* C—N cleavage, whereas the C—N bond is left intact in secondary amines; addition of NO and NO_2 presumably lead to nitrosamines[27] and nitramines, respectively.

It should be mentioned in conclusion that the reactions of O and OH with diethylhydroxylamine (DEHA) have been suggested as a means of inhibiting photochemical smog[31,32]. This inhibitory action consists in capture of O and OH which are the chain carriers of NO/NO_2 conversion in the presence of hydrocarbons (see Section 5.4 and Fig. 8).

As shown by *Filby* and *Güsten*[31], however, the reaction of diethylhydroxylamine with O atoms is too slow to compete with the O/hydrocarbon reaction unless rather dubiously high concentrations of the inhibitor (above the olfactory perception threshold) are sprayed into the atmosphere. Moreover, general reservations have been voiced concerning the possible combatting of the consequences of anthropogenic emissions (photochemical smog) by additional emission of inhibitors[33].

6. Summary and Outlook

Anthropogenic emissions are a burden on the environment. Such emissions are removed sufficiently fast on a global scale to dispel any misgivings about possible long term effects. We can aptly speak of a "self-cleaning action" of the atmosphere. However, the question of the limits of the self-cleaning capacity for individual classes of compounds remains open. For example, there is a slow but clearly detectable increase occurring in the concentration of CO_2. In the case of fluorocarbons, which we have purposely avoided discussing in this article, the present state of knowledge based on extremely broad-based and thorough studies would indicate that a slight reduction of the ozone concentration in the stratosphere by these substances cannot be ruled out in the long term.

These possible long-term global effects are certainly the exception rather than the rule. On a local and regional level, however, there is a significant pollution problem. What can be done?

A general requirement, which will certainly not be universally implementable, is to reduce the amounts of pollutants emitted. In addition, further studies are necessary on the removal and ecotoxological action of anthropogenic emissions, including those not discussed in this paper.

With regard to the predominant pollutants and classes of pollutants, it is most informative to consider the developments of the past fifteen years (Fig. 13). The situation in the Federal Republic of Germany again serves as example. There is a significant increase of NO_x, due to a) increased energy production in conventional power stations and b) increased motorization. SO_2 has remained roughly constant, in spite of increased energy production (improved sulfur removal from fuels and flue gases). Hydrocarbon emissions have likewise remained roughly constant. A significant decrease is seen only in the emission of particulate matter; this is due to improvements in electrostatic dust removal in coal-fired power stations, which are responsible for most of these emissions. The critical pollutants are therefore NO_x and SO_2.

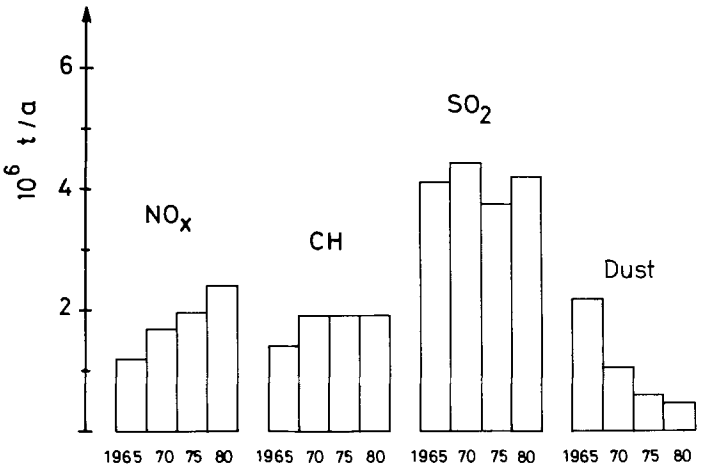


Fig. 13. Development of annual emission of NO_x, hydrocarbons, SO_2, and dust in the Federal Republic of Germany since 1965; values for 1980 estimated.

At this stage, the reader is again reminded that such emissions arise mainly from combustion of fossil fuels, at a rate of about 1% by weight; further reduction would incur enormous costs. Nobody would dispute that such reductions are technically feasible. With regard to the reduction of NO emissions from power stations, reference is made to fluidized-bed combustion[34]: Greatly improved heat transfer permits lower operating temperatures, and thus leads to considerably reduced formation of NO. This process was developed in its basic form more than 50 years ago at BASF; however, it has still not been employed in conventional power stations, apart from development work in pilot plant. Another process for reducing NO emission from combustion plant, recently patented by EXXON, involves the addition of NH_3/O_2 mixtures[35]. The observed drop in NO emission is due to the fast homogeneous gas reaction

$$NH_2 + NO \rightarrow N_2 + H_2O$$

A pilot plant has recently been built in Japan to test the technical applicability of this process.

Received: June 28, 1979 [A 287 IE]
German version: Angew. Chem. *91*, 707 (1979)

[1] *C. E. Junge*, Ber. Bunsenges. Phys. Chem. *82*, 1128 (1978).
[2] See, *e.g., G. M. Woodwell*, Sci. Am. *238* (1) 34 (1978); Spektrum der Wissenschaft, Erstedition 1978, p. 1, and references cited therein.
[3] *E. R. Robinson, R. C. Robbins* in *W. Strauss:* Air Pollution Control. Part II. Wiley, New York 1972.
[4] *A. C. Stern:* Air Pollution. Vol. I. 3rd Edit. Academic Press, New York 1976.
[5] *H. W. Georgii*, VDI-Ber. *314*, 57 (1978).
[6] *R. D. Cadle, E. R. Allen*, Science *167*, 243 (1970).
[7] Umweltgutachten 1978, Unterrichtung durch die Bundesregierung, Drucksache 8/1938, 1978.
[8] Halocarbons: Effects on Stratospheric Ozone. National Academy of Sciences, Washington 1976; see also *J. P. Jesson*, Angew. Chem. *89*, 507 (1977); Angew. Chem. Int. Ed. Engl. *16*, 513 (1977).
[9] Umweltfreundliche Technik. Forschungsbericht T 76-73, Bundesministerium für Forschung und Technologie, 1976.

[10] *R. Jaenicke*, Ber. Bunsenges. Phys. Chem. *82*, 1198 (1978).
[11] *P. Warneck, W. Kippel, G. Moortgat*, Ber. Bunsenges. Phys. Chem. *82*, 1136 (1978).
[12] *J. G. Calvert, J. N. Pitts, Jr.*: Photochemistry. Wiley, New York 1966.
[13] *I. M. Campbell*: Energy and the Atmosphere. Wiley, London 1977.
[14] *R. D. Penzhorn, W. G. Filby, H. Güsten*, Z. Naturforsch. *A 29*, 1449 (1974).
[15] *S. Jordan*, VDI-Ber. *314*, 53 (1979).
[16] *P. Fabian, J. A. Pyle, R. J. Wells*, Lecture at Bunsentagung 1978, Constance (Germany).
[17] *J. W. Bottenheim, O. Strausz*, IXth Int. Conference on Photochemistry, Cambridge 1978; *J. Chang, D. J. Wuebbles, D. D. Davis*, J. Geophys. Res., in press.
[18] *V. Handwerk, R. Zellner*, Ber. Bunsenges. Phys. Chem. *82*, 1161 (1978).
[19] *R. Zellner*, Ber. Bunsenges. Phys. Chem. *82*, 1172 (1978).
[20] *U. Schurath, H. Seitz, J. Löbel*, VDI-Ber. *314*, 33 (1978).
[21] *R. A. Cox, S. A. Penkett*, J. Chem. Soc. Faraday Trans. I *68*, 1735 (1972).
[22] *S. W. Benson*, Chem. Rev. *78*, 23 (1978).
[23] *W. H. Schroeder, P. Urone*, Environ. Sci. Technol. *12*, 545 (1978); *R. D. Penzhorn*, VDI-Ber. *314*, 27 (1978).
[24] *D. H. Ehhalt, A. Volz, A. Khedim*, Ber. Bunsenges. Phys. Chem. *82*, 1136 (1978).
[25] See, *e.g. H. W. Biermann, C. Zetzsch, F. Stuhl*, Ber. Bunsenges. Phys. Chem., in press.
[26] *K. H. Hoyermann, R. Sievert*, Ber. Bunsenges. Phys. Chem., in press.
[27] *R. Atkinson, K. R. Darnall, A. C. Lloyd, A. M. Winer, J. N. Pitts*, Adv. Photochem., in press.
[28] *R. I. Martinez, R. E. Huie, J. T. Herron*, Chem. Phys. Lett. *51*, 457 (1977).
[29] See, *e.g. J. Heicklen*: Atmospheric Chemistry. Academic Press, New York 1976.
[30] *K. Kirchner, R. Vettermann*, Ber. Bunsenges. Phys. Chem. *82*, 1223 (1978).
[31] *W. G. Filby, H. Güsten*, Atmos. Environ. *12*, 1563 (1978).
[32] *R. K. M. Jayanty, R. Simonaitis, J. Heicklen*, Atmos. Environ. *8*, 1283 (1974).
[33] *T. H. Haugh II*; Science *193*, 871 (1976); *J. Tinker*, New Sci. *9*, 530 (1976).
[34] See, *e.g. W. Jost*: Globale Umweltprobleme. Steinkopf Verlag, Darmstadt 1974.
[35] *R. K. Lyon*, Int. J. Chem. Kinet. *8*, 315 (1976); *R. K. Lyon, J. P. Longwell*, 4th Int. Clean Air Congress, Tokyo 1977; *R. K. Lyon, D. Benn*, Proceedings of the 17th Symp. (Int.) on Combustion, Leeds 1978.

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 New Bridging Mode of Carbon Disulfide in a Dinuclear Cobalt(I) Complex

By *Claudio Bianchini, Carlo Mealli, Andrea Meli, Annabella Orlandini*, and *Luigi Sacconi*[*]

The only X-ray structure determination[1] so far reported for a dinuclear complex containing a bridging CS_2 group shows a metal dithiocarboxylato fragment bonded *via* the two sulfur atoms to the second metal. Only IR and NMR information is available for analogous complexes[2], and suggests that the bridging CS_2 group is probably linked to one metal either *via* the carbon atom or *via* a η^2-bonded C=S linkage, while one sulfur atom is σ-bonded to the second metal.

By reaction of CS_2 with cobalt(II) tetrafluoroborate, $NaBPh_4$, and 1,1,1-tris(diphenylphosphinomethyl)ethane (triphos) we have obtained the dinuclear diamagnetic complex $[\{(triphos)Co\}_2CS_2](BPh_4)_2$ *(1)*. Its molecular structure has been established by single crystal X-ray analysis[3]. In the complex cation of *(1)*, a CS_2 molecule is found to hold together two Co(triphos) fragments. One cobalt atom is π-bonded to one C=S group, and the other forms two σ-bonds to the two sulfur atoms.

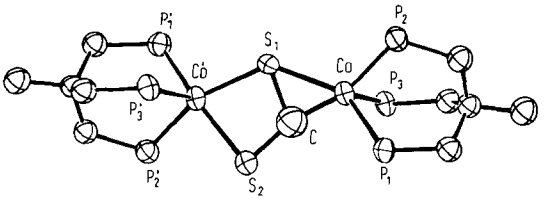


Fig. 1. ORTEP drawing of skeleton of the complex cation of *(1)*. Population parameters of S(1), S(2), and C atoms fixed at 0.5. Important distances [Å] and angles [°] are: Co P(average) = 2.22(2), Co S(1) = 2.27(1), Co S(2) = 2.31(1), Co S(1) = 2.29(1), Co C = 1.72(5), C S(1) = 1.75(7), C S(2) = 1.72(7), S(1) C S(2) = 112.2(3.7), S(1) Co S(2) = 77.7(5), C Co S(2) = 49.3(2.2).

The S—C—S angle of 112.2(3.7)° is somewhat smaller than that found in the structure of the mononuclear cobalt(0) complex with triphos and a terminally η^2-bonded CS_2 molecule (133.8(8)°)[4]. The two C—S distances (C—S(1) = 1.75(7), C—S(2) = 1.72(7) Å) are similar to each other and longer than those found in the above mononuclear complex (1.68(1), 1.62(1) Å). These geometrical details suggest a partial loss of double bond character of the C—S linkages and a consequent delocalization of the electron density toward the metal atoms. The absence of IR bands attributable to C=S stretching modes seems to support this view. Interestingly, the two Co—S σ-bonds are approximately of the same length (Co—S(1) = 2.27(1), Co—S(2) = 2.31(1) Å) indicating that the participation of CS_2 in π-bonding does not lead to any great difference in the σ-donor capacities of the two sulfur atoms.

Considering the CS_2 molecule as a 6-electron donor and adding the 16 electrons of the Co^I ions and the 12 electrons of the two triphos ligands, a configuration of 34 valence electrons is reached for the dinuclear complex cation. Particular stability has been predicted for such 34-electron species. The diamagnetism of the complex is thus also rationalized.

Procedure

All operations performed under N_2 and with oxygen-free solvents. CS_2 is bubbled for 5 min through a hot mixture of triphos (1 mmol) in acetone (40 ml) and $Co(BF_4)_2 \cdot 6H_2O$ (1 mmol) in butanol (30 ml). On addition of $NaBPh_4$ (2 mmol)

[*] Prof. Dr. L. Sacconi, Dr. C. Bianchini, Dr. C. Mealli, Dr. A. Meli, Dr. A. Orlandini
Istituto di Chimica generale e Inorganica
dell'Università, Laboratorio CNR
Via J. Nardi 39, I-50132 Firenze (Italy)

in ethanol (20 ml) and slow evaporation of the solvent, brownish black crystals are formed which are recrystallized from acetone/ethanol; yield 50%.

Received: May 16, 1978
revised: February 19, 1979 [Z 11a IE]
German version: Angew. Chem. *91*, 739 (1979)
Publication delayed at authors' request

[1] *J. M. Lisy, E. D. Dobrzynski, R. J. Angelici, J. Clardy,* J. Am. Chem. Soc. *97*, 656 (1975).

[2] *J. E. Ellis, R. W. Fennel, E. A. Flom,* Inorg. Chem. *15*, 2031 (1976); *M. Herberhold, M. Süss-Fink, C. G. Kreiter,* Angew. Chem. *89*, 191 (1977); Angew. Chem. Int. Ed. Engl. *16*, 193 (1977); *P. V. Yaneff,* Coord. Chem. Rev. *23*, 183 (1977); *U. Oehmichen, T. G. Southern, H. Le Bozec, P. Dixneuf,* J. Organomet. Chem. *156*, C29 (1978); *H. Werner, K. Leonhard, Ch. Burschka, ibid. 160*, 291 (1978); *W. P. Fehlhammer, A. Mayr, H. Stolzenberg,* Angew. Chem. *91*, 661 (1979); Angew. Chem. Int. Ed. Engl. *18*, 626 (1979).

[3] Philips PW 1100 automatic diffractometer. $a=18.120(4)$, $b=14.074(4)$, $c=12.705(3)$ Å, $\alpha=91.3(2)$, $\beta=106.1(3)$, $\gamma=111.8(3)°$, space group $P\bar{1}$. One formula unit of *(1)* and two molecules of solvent acetone per unit cell. $R=0.076$ for 4187 reflections with $I \geq 3\sigma(I)$. The crystal structure is affected by statistical disorder due to a pseudo center of inversion midway between the metal atoms, two enantiomeric dinuclear cations therefore overlapping in the X-ray observable mean unit cell.

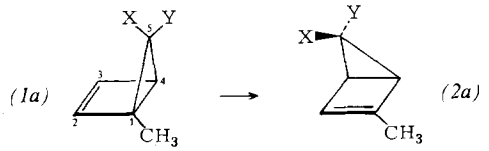
[4] *C. Bianchini, C. Mealli, A. Meli, A. Orlandini, L. Sacconi,* to be published.

Thermal "Walk"-Rearrangement in the Bicyclo[2.1.0]pent-2-ene System[**]

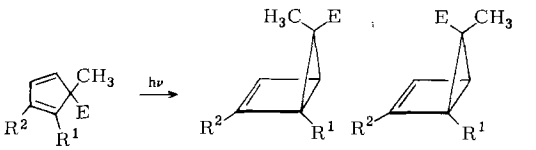
By *Frank-Gerrit Klärner* and *Friedhelm Adamsky*[*]

In a large number of five-membered heterocycles, *e.g.* derivatives of furan, pyrrole, and thiophene, a photochemical isomerization is observed leading to a redistribution of the ring atoms. This unusual reaction has often been explained in terms of "walk" rearrangements in the intermediate valence tautomeric hetero-bicyclo[2.1.0]pent-2-enes[1a]. According to *Lemal et al.*[1b] a rapid "walk" rearrangement takes place in perfluorotetramethyl-5-thiabicyclopentene and its *exo-S*-oxide also on thermal excitation.

In the carbocyclic bicyclopentene system most of the interest was hitherto focused on the electrocyclic ring opening, which leads to chemically activated 1,3-cyclopentadienes[2a–c]. A "walk" rearrangement was observed only on photochemical excitation[2d]. We report here on the thermal "walk" rearrangement *(1a)*→*(2a)*, which precedes the competing bicyclopentene-cyclopentadiene isomerization and proceeds with high stereoselectivity even at 0 °C.



For experimental verification of this rearrangement the bicyclopentene derivatives *(1a), (1b), (2a), (2b),* and *(3a), (3b)* were synthesized by photolysis of the cyclopentadienes *(4), (5),* and *(6),* respectively (−50 °C, Hg low-pressure lamp NK25/7 Hanau, dimethyl ether)[3]. The assignment of the diastereomers *(1a), (1b), (2a), (2b)* and *(3a), (3b)* separated by column chromatography at −10 °C was largely based on the ^{1}H-NMR spectroscopic comparison with *exo-* and *endo*-5-methylbicyclo[2.1.0]pent-2-ene[2c,4].



$R^1=CH_3$, $R^2=H$ *(4)* — *(1a)* *(1b)*
$R^1=H$, $R^2=CH_3$ *(5)* — *(2a)* *(2b)*
$R^1=R^2=H$ *(6)* — *(3a)* *(3b)*
$E=CO_2CH_3$

At 0 °C the 1,5-dimethyl derivative *(1a)* already undergoes complete reorganization yielding two products (GC 93:7)[5]. The major product is identical with the independently synthesized 2,5-dimethyl derivative *(2a)*. The minor product proved to be the starting cyclopentadiene *(4)*. ^{1}H-NMR spectroscopic monitoring of the isomerization *(1a)*→*(2a)* at 0 °C gave a rate constant $k_{(1a),(2a)}$ of 2.4×10^{-5} [s^{-1}] and thus a Gibbs activation energy of $\Delta G^{+}=21.7$ kcal/mol.

A similar thermal behavior is exhibited by the diastereomeric 1,5-dimethyl derivative *(1b)*. However, in this case 97% electrocyclic ring opening *(1b)*→*(4)* and only 3% "walk" rearrangement *(1b)*→*(2b)* is observed.

The 2,5-dimethyl derivatives *(2a)* and *(2b)* are thermally more stable than *(1a)* and *(1b)*, comparable with *(3a)* and *(3b)* and with the parent system. Above room temperature *(2a), (2b)* and *(3a), (3b)* isomerize to the cyclopentadiene derivatives *(5)* and *(6)*, respectively. Their kinetic parameters are listed, together with those of the parent system, in Table 1. Thermolysis of *(2a)* leads not only to *(5)* (95%) but also to the 1,5-dimethylcyclopentadiene *(4)* (5%), whose formation indicates the "walk" rearrangement *(2a)*⇌*(1a)* to be reversible to a slight extent. In no case is an *exo-endo* isomerization at C-5 observed. This finding rules out a migration of C-5 with retention in the bicyclopentene systems, a process which was calculated by semi-empirical MO-methods[6] to be the favored one[6]. The observed stereochemistry corresponds to an inversion at C-5 and is in accord with the stereochemical requirements for an orbital symmetry controlled process[7].

The Gibbs activation energy of the reaction *(1a)*→*(2a)* is surprisingly small; it is considerably smaller than that of the "walk" rearrangements of the correspondingly substituted vinylogous systems *cis*-bicyclo[4.1.0]hepta-2,4-diene (180 °C, $\Delta G^{+}=37.1$ kcal/mol)[8a] and *cis*-bicyclo[6.1.0]nona-2,4,6-triene (102.5 °C, $\Delta G^{+}=28.8$ kcal/mol)[8b]. The observed activation parameter for the rearrangement of bicy-

Tabelle 1. Kinetic parameters at 50 °C.

Reaction	Halflife [min]	ΔG^{+} [kcal/mol]	ΔH^{+} [kcal/mol]	ΔS^{+} [cal K^{-1} mol^{-1}]
(2a)→*(5)*	165	25.2		
(2b)→*(5)*	83	24.7		
(3a)→*(6)*	67	24.5	25.4±0.3	2.3±1.6
(3b)→*(6)*	38	24.2	25.6±0.2	3.7±0.8
Bicyclo[2.1.0]pent-2-ene→1,3-Cyclopentadiene [a]	112	24.9	26.3±0.3	4.3±0.9

[a] *J. I. Brauman, D. M. Golden,* J. Am. Chem. Soc. *90*, 1920 (1968); Trans. Faraday Soc. *65*, 464 (1969).

[*] Doz. Dr. F.-G. Klärner, Dipl.-Chem. F. Adamsky
Abteilung für Chemie der Universität
Postfach 102148, D-4630 Bochum 1 (Germany)

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

clo[6.1.0]nonatriene has been interpreted by a participation of an aromatic transition state. The *ca.* 7 kcal/mol lower Gibbs activation energy of *(1a)*→*(2a)* would accordingly suggest an aromatic transition state for the bicyclopentene rearrangement. We assume, however, that the lower activation barrier of the bicyclopentene rearrangement does not only result from the resonance stabilization of the transition state, but largely from the high ground-state enthalpy of the bicyclopentene system. The heat of hydrogenation of the olefinic double bond in the parent compound, bicyclo[2.1.0]pent-2-ene (25 °C: $\Delta H = 42.5$ kcal/mol) is higher by *ca.* 9 kcal/mol than that of the double bond in bicyclo[2.2.0]hex-2-ene and bicyclo[3.2.0]hept-6-ene[9]. The additional energy content of 9 kcal/mol is attributed to an antiaromatic destabilization of the bicyclo[2.1.0]pent-2-ene ground state and must be considered for estimating the resonance stabilization of the transition state of the "walk" rearrangement *(1a)*→*(2a)*.

Received: March 21, 1979 [Z 271 IE]
German version: Angew. Chem. *91*, 738 (1979)

CAS Registry numbers:
(1a), 71215-49-1; *(1b)*, 71242-66-5; *(2a)*, 71215-50-4; *(2b)*, 71242-67-6; *(3a)*, 71215-51-5; *(3b)*, 71276-51-2; *(4)*, 71215-52-6; *(5)*, 71242-68-7; *(6)*, 71215-53-7

[1] a) *J. A. Barltrop, A. C. Day, R. W. Ward*, J. Chem. Soc. Chem. Commun. *1978*, 131; Review: *J. A. Barltrop, J. D. Coyle:* Excited States in Organic Chemistry. Wiley, New York 1975, pp. 298ff.; b) *J. A. Ross, R. P. Seiders, D. M. Lemal*, J. Am. Chem. Soc. *98*, 4325 (1976); *C. H. Bushweller, J. A. Ross, D. M. Lemal, ibid. 99*, 629 (1977).

[2] a) *M. C. Flowers, H. M. Frey*, J. Am. Chem. Soc. *94*, 8636 (1972); b) *W. E. Farneth, M. B. D'Amore, J. I. Brauman, ibid. 98*, 5546 (1976); c) *G. D. Andrews, J. E. Baldwin, ibid. 99*, 4853 (1977), references cited therein; d) *ibid. 99*, 4851 (1977).

[3] *(4)* and *(5)* were prepared analogously to the procedure for *(6)* (*H. Müller, G. E. Herberich*, Chem. Ber. *104*, 2772 (1971)).

[4] ^{1}H-NMR (60 MHz, CCl_4, TMS, −15 °C): *(1a)*: τ=4.10 (m, 2-, 3-H), 6.43 (s, OCH_3), 7.72 (m, 4-H), 8.44 (s, 1-CH_3), 8.62 (s, 5-CH_3); *(1b)*: τ=4.05 (m, 2-, 3-H), 6.41 (s, OCH_3), 8.27 (m, 4-H), 8.50 (s, 1-CH_3), 8.80 (s, 5-CH_3); *(2a)*: τ=4.45 (m, 3-H), 6.47 (s, OCH_3), 7.81 (d, 1-, 4-H), 8.37 (d, 2-CH_3), 8.52 (s, 5-CH_3); *(2b)*: τ=4.45 (m, 3-H), 6.41 (s, OCH_3), 8.08 (d, 1-, 4-H), 8.47 (d, 2-CH_3), 8.86 (s, 5-CH_3); *(3a)*: τ=4.01 (m, 2-, 3-H), 6.40 (s, OCH_3), 7.61 (m, 1-, 4-H), 8.41 (s, 5-CH_3); *(3b)*: τ=3.97 (m, 2-, 3-H), 6.37 (s, OCH_3), 7.88 (m, 1-, 4-H), 8.83 (s, 5-CH_3).

[5] GC: 42 m "Marlophen" glass capillary column (T=30 °C). We thank Dr. *F. Scheidt* for designing and constructing the GC column.

[6] *W. W. Schoeller*, J. Am. Chem. Soc. *97*, 1978 (1975).

[7] *R. B. Woodward, R. Hoffmann*, Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).

[8] a) *F.-G. Klärner*, Angew. Chem. *86*, 270 (1974); Angew. Chem. Int. Ed. Engl. *13*, 268 (1974); *F.-G. Klärner, S. Yaslak, M. Wette*, Chem. Ber. *112*, 1168 (1979); b) *F.-G. Klärner*, Angew. Chem. *84*, 892 (1972); Angew. Chem. Int. Ed. Engl. *11*, 832 (1972); *F.-G. Klärner, M. Wette*, Chem. Ber. *111*, 282 (1978).

[9] *W. R. Roth, F.-G. Klärner, H.-W. Lennartz*, Chem. Ber., in press.

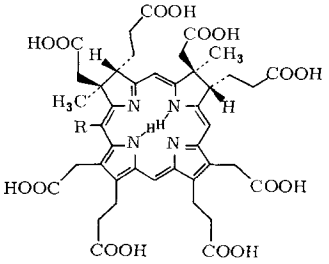
A Synthetic Approach to the Isobacteriochlorin Macrocycle[**]

By *Franz-Peter Montforts, Silvio Ofner, Vittorio Rasetti, Albert Eschenmoser, Wolf-Dietrich Woggon, Keith Jones*, and *Alan R. Battersby*[*]

The chemistry and biochemistry of porphinoid natural products has recently been enriched by the emergence of isobacteriochlorin systems *(1)* into the forefront of interest. The first example from Nature, sirohydrochlorin *(2a)*[1,2], was isolated in 1973 by *Siegel et al.*[1] from *E. coli*, where the iron complex of *(2a)* serves as cofactor for the enzyme sulfite reductase. Recently, *(2a)* (probably as a dihydro derivative) has been shown to be important in the biosynthesis of vitamin B_{12}[1–3]; this work led to the definitive structure *(2a)* for sirohydrochlorin. Then 20-methylsirohydrochlorin *(2b)* was isolated from organisms producing vitamin B_{12}[2c,4] and was shown to be converted biosynthetically into the vitamin[4]. These interlocking studies have given a new and unexpected direction to researches on the biosynthesis of vitamin B_{12}.



(1)



(2a), R = H
(2b), R = CH_3

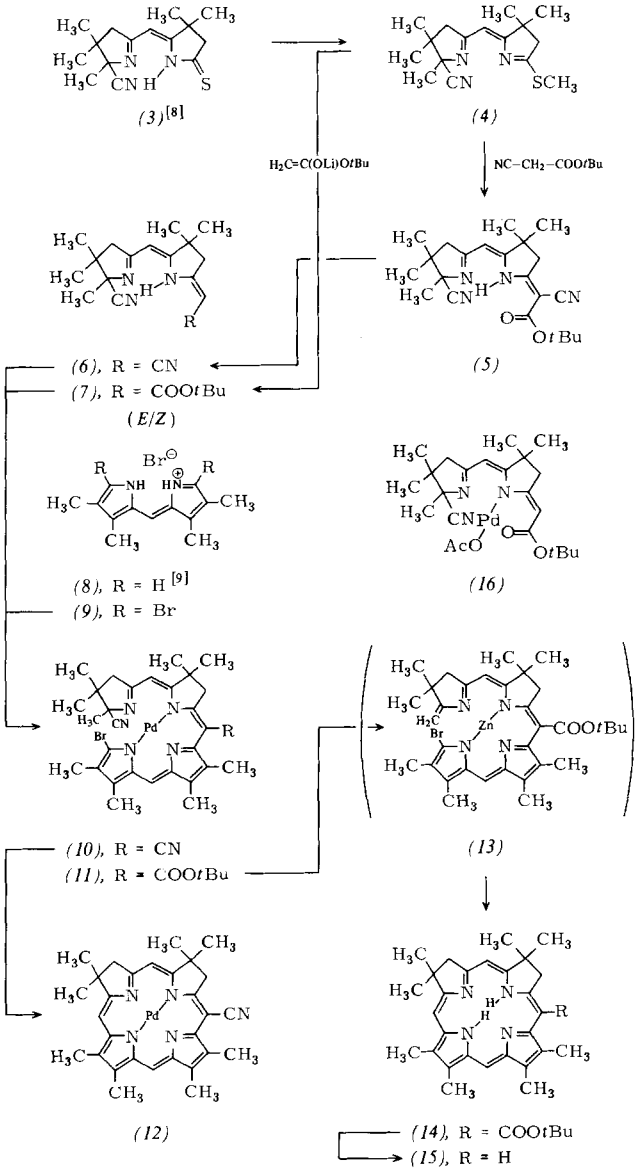
The chemistry of isobacteriochlorins is largely unknown. Though "an octaethyl derivative" had been prepared by reduction of iron(II)-octaethylporphinate[5] or of iron(II)-octaethylchlorinate[5a] with sodium in isoamyl alcohol[6], no rational synthesis of this type of substance has so far been available[7]. We report here such a route (Scheme 1).

The synthesis in principle involves the combination of a corrinoid A/B-component of type *(6)* or *(7)* with a porphinoid C/D-partner of type *(9)*. The components *(6)* and *(7)* are prepared from the bicyclic thiolactam *(3)*[8b,c], by methods dependent on earlier synthetic studies on corrins[8], and *(9)* is available by bromination of the tetramethyldipyrromethene *(8)*[9] or of the corresponding tetramethyldipyrromethane-α,α′-dicarboxylic acid[10]. It was not possible to accomplish a base-catalyzed coupling of *(6)*+*(9)*→*(10)* either directly or with the help of "mild" coordinating metal ions such as zinc(II) or nickel(II). However, the reaction succeeded in the presence of palladium(II) owing to its known "hard" tendency towards planar coordination; this exerts a template effect which is often decisive for inducing a condensation step[11]. The coupling of *(6)* with *(9)* in the presence of palladium(II) diacetate and ethyldiisopropylamine gave a mixture of the palladium complexes *(10)* and *(12)*. The *seco*-complex *(10)* readily cyclizes to the palladium(II) isobacteriochlorinate *(12)*; the base acts by releasing the exocyclic methylidene double-bond (enamine) in ring A (cf. ref. [8,11]).

Neither the metal ion, nor the cyano group bound to the chromophore, could be removed from the palladium complex *(12)* without further changes [the cyano group of *(6)* served the purpose of fixing the enamine double bond in an exocyclic position]. The synthesis of metal-free isobacteriochlorins without a cyano group *(15)* therefore proceeded from the A/B-component *(7)* having *tert*-butyloxycarbonyl as the fixing group and this approach gave the *seco*-palladium complex *(11)*. In agreement with earlier experience[12] that corrinoid *seco*-complexes can be very readily demetalated (in contrast to the corresponding stable macrocyclic complexes), palladium(II) was removed smoothly from *(11)* by potassium cyanide. Potassium *tert*-butoxide in the presence of zinc(II) ions then cyclized the free *seco*-ligand to the zinc complex of *(14)* *via* the putative complex *(13)*. Acid ca-

[*] Prof. Dr. A. Eschenmoser, Dr. F.-P. Montforts, dipl.-Naturwiss. V. Rasetti, dipl.-Chem. S. Ofner
Organisch-chemisches Laboratorium der ETH
Universitätstrasse 16, CH-8092 Zürich (Switzerland)
Prof. Dr. A. R. Battersby, Dr. W.-D. Woggon, K. Jones
University Chemical Laboratory,
Lensfield Road, Cambridge CB2 1EW (England)

[**] The work of the Zürich group was supported by the Swiss National Science Foundation and that in Cambridge by the Nuffield Foundation and the Science Research Council. *W.-D. W.* thanks the Swiss National Science Foundation for a postdoctoral award.



Scheme 1. Reaction conditions [13]: *(3)→(4): (3)* [8] + 3 $(CH_3)_3O^+BF_4^-$ + *ca.* 0.1 diazabicycloundecene (DBU) in CH_2Cl_2, RT, *(4)* used without purification. *(4)→(5):* cat. amount DBU in *tert*-butyl cyanoacetate, 100 °C [77% from *(3)*]. *(5)→(6):* a) 70 °C in CF_3COOH, b) melting of the carboxylic acid >180 °C (>90%), *(6)* used without purification. *(4)→(7):* 1 *O*-Lithio *tert*-butyl acetate in THF, −78 °C → RT (83% cryst. *E*/*Z*-mixture). *(8)→(9):* 3 Br_2 in HCOOH, RT, cryst. precipitate freed from Br_3^- by heating in acetone (80%). *(6)* + *(9)* → *(10)* + *(12):* 1.3 *(9)* (free base) + 1.0 *(6)* + 1.3 $Pd(OAc)_2$ + 1.8 ethyldiisopropylamine in toluene, 80 °C, under argon [28% cryst. *(10)* (procedure not optimized) + 5% cryst. *(12)*]. *(10)* → *(12):* in sulfolane/DBU (2.5:1), 80 °C under argon (72%). *(7)* + *(9)* → *(11):* a) *(7)* + 1.7 $Pd(OAc)_2 \cdot (DBU)_2$ [from $Pd(OAc)_2$ + 2 DBU in CH_3CN, RT] in CH_3CN, 75 °C, under argon [formation of *(16)*], b) 2.5 *(9)* and 1.0 DBU in CH_3CN added separately in 3 portions to *(16)* in CH_3CN, 80 °C, under argon [41% TLC-pure *(11)*]. *(11)* → *(14):* a) KCN in CH_3OH, RT, under argon, free ligand *(11)* worked up and, after drying, used without purification, b) 5 $Zn(ClO_4)_2 \cdot (CH_3CN)_x$ + 8 *t*-BuOK in *t*-BuOH (degassed), 80 °C, under argon, c) worked up with 10% HCl/H_2O [30—50% TLC-pure *(14)*]. *(14)* → *(15):* a) CF_3COOH, RT, b) 105 °C in glutaric acid [80% TLC-pure *(15)*, overall yield *(11)* → *(15)* up to 32%]. *(15)* can be crystallized with difficulty from CH_2Cl_2/ether/hexane at *ca.* −10 °C.

talysis removed zinc(II) and also the *tert*-butyloxycarbonyl to afford *(15)*.

The critical step in the synthesis is the coupling of *(7)* and *(9)* to give the *seco*-complex *(11)*. Yields reproducibly over 40% for this delicate step could be obtained by first forming the mixed complex *(16)* from *(7)* and the $(DBU)_2$-adduct of palladium(II) diacetate; *(16)* was then coupled using an equimolar amount of DBU with an excess of *(9)* added portionwise, the course of the reaction being followed by UV/VIS spectroscopy. The data in the Table and Figure establish the constitution for the target substance, *viz.* 2,2,7,7,12,13,17,18-octamethylisobacteriochlorin *(15)*.

Table 1. Analytical data for the compounds *(11)*, *(12)*, and *(15)*. All compounds in the reaction scheme except *(13)* were analyzed and characterized by spectroscopy (UV/VIS, IR, ^{1}H-NMR, MS) [13].

(11), m.p. >250 °C (from methyl acetate/hexane).—UV/VIS (CH_3CN): λ_{max} = 298 (log ε = 4.14), 325 (4.05), 380 (4.31), 405 (4.26), 430 sh (4.21), 507 sh (3.49), 562 sh (3.99), 609 (4.35) nm.—IR ($CHCl_3$): 1695 (m), 1595 (s), 1575 (m), 1540 (s), 1505 (m) cm^{-1}, *etc.*—MS: *m/e* = 739 (100%, M^+, ^{106}Pd, ^{81}Br) + isotope peaks, 683 (10%, M^+ − isobutene), *etc.*—^{1}H-NMR ($CDCl_3$; *ca.* 1:1 mixture of diastereoisomers): δ = 0.83 (s, CH_3, *endo*?), 1.15 (s, CH_3, *exo*?), 1.19/1.25/1.27/1.33 (4 s, 4 CH_3), 1.56 (s, *t*-Bu), 1.97 (br., CH_3), 2.08 (br., CH_3), 2.26 (br., 2 CH_3) with satellites, 2.72/2.84/3.00 (m, 2 CH_2), 5.30 (br., H-5), 7.04/7.08 (s, H-15)

(12), m.p. >230 °C (from CH_2Cl_2/methyl acetate).—UV/VIS (C_2H_5OH, red): λ_{max} = 280 (log ε = 3.82), 292 sh (3.80), 355 sh (4.42), 382 (4.77), 505 sh (3.72), 540 sh (3.99), 576 (4.54) nm.—IR ($CHCl_3$): *inter alia* 2210 (m/CN), 1645 (m), 1620 (s), 1600 (w), 1565 (m), 1500 (m) cm^{-1}.—MS: *m/e* = 555 (100%, M^+, ^{106}Pd) + isotope peaks, *etc.*—^{1}H-NMR ($CDCl_3$): δ = 1.72/1.74 (2 s, each 6H), 2.89/2.94/2.97/3.11 (4 s, each 3H), 4.01/4.19 (2 s/each 2H), 7.19/7.74/8.74 (3 sharp s, each 1H)

(15), m.p. >250 °C (from CH_2Cl_2/ether/hexane).—UV/VIS (C_2H_5OH, red-violet): λ_{max} = 261 sh (log ε = 4.25), 276 (4.29), 335 sh (4.42), 352 sh (4.71), 366 (4.90), 375 sh (4.85), 396 (4.52), 480 sh (3.73), 509 (3.94), 545 (4.17), 584 (4.37), 632 (3.69) nm; UV/VIS (C_2H_5OH + 1 drop CF_3COOH in 3 ml, blue): 283 (4.32), 297 sh (4.26), 332 sh (4.34), 350 sh (4.60), 365 (4.71), 380 (4.73), 400 (5.13), 463 sh (3.55), 488 (3.82), 520 (3.54), 579 (4.06), 623 (4.67).—IR ($CHCl_3$): *inter alia* 3375 (w/NH), 3280 (w/NH), 1642 (m), 1600 (s), 1575 (m) cm^{-1}.—MS: *m/e* = 428 (6%), 427 (33%), 426 (100%, M^+).—^{1}H-NMR ($CDCl_3$): δ = 1.66/1.71 (2 s, each 6H), 2.55 (s, br., 2 NH), 2.80 (s, 3H), 2.85 (s, 3H), 2.95 (s, 6H), 3.80/3.84 (2 s, each 2H), 6.94 (s, 1H), 7.46 (s, 1H), 7.54 (s broadened, 1H), 8.56 (s, 1H)

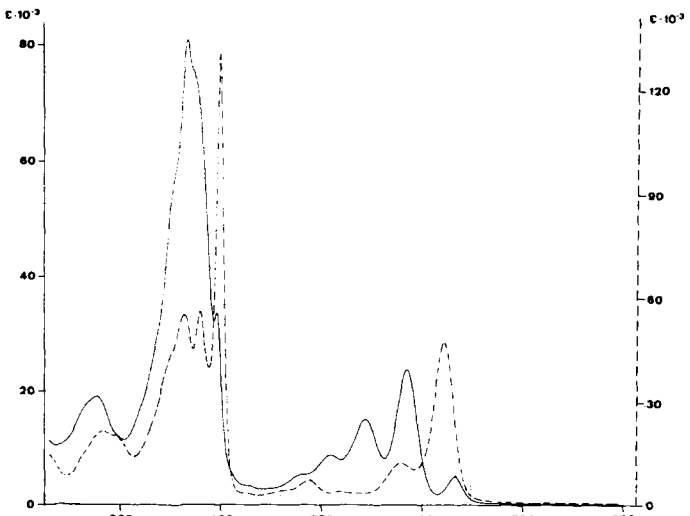


Fig. 1. UV/VIS spectrum of *(15)* in ethanol (——) and in ethanol + CF_3COOH (- - - -).

CAS Registry numbers:
(3), 51381-93-2; *(4)*, 71250-49-2; *(5)*, 71250-50-5; *(6)*, 71250-51-6; *(7)*, 71276-87-4; *(8)*, 6506-43-0; *(9)*, 71250-52-7; *(10)*, 71264-62-5; *(11)* isomer A, 71264-63-6; *(11)* isomer B, 71301-38-7; *(12)*, 71264-64-7; *(14)*, 71250-53-8; *(15)*, 71250-54-9; *(16)*, 71264-65-8; *tert*-butyl cyanoacetate, 1116-98-9; lithio-*tert*-butyl acetate, 53503-61-0; palladium(II) diacetate, 3375-31-3

Received: June 7, 1979 [Z 272 IE]
German version: Angew. Chem. *91*, 752 (1979)

[1] *L. M. Siegel, M. J. Murphy, H. Kamin*, J. Biol. Chem. *248*, 251 (1973); *M. J. Murphy, L. M. Siegel, H. Kamin, D. Rosenthal, ibid. 248*, 2801 (1973); *M. J. Murphy, L. M. Siegel, S. R. Tove, H. Kamin*, Proc. Nat. Acad. Sci. USA *71*, 612 (1974).

[2] a) *A. R. Battersby, K. Jones, E. McDonald, J. A. Robinson, H. R. Morris,* Tetrahedron Lett. *1977*, 2213; *A. R. Battersby, E. McDonald, H. R. Morris, M. Thompson, D. C. Williams, V. Ya. Bykhovsky, N. I. Zaitseva, V. N. Bukin, ibid. 1977*, 2217; b) *R. Deeg, H. P. Kriemler, K. H. Bergmann, G. Müller,* Hoppe-Seylers Z. Physiol. Chem. *358*, 339 (1977); c) *K. H. Bergmann, R. Deeg, K. D. Gneuss, H. P. Kriemler, G. Müller, ibid. 358*, 1315 (1977); d) *A. I. Scott, A. J. Irwin, L. M. Siegel, J. N. Shoolery,* J. Am. Chem. Soc. *100*, 316, 7987 (1978).

[3] *V. Ya. Bykhovsky, N. I. Zaitseva, N. V. Bukin,* Dokl. Akad. Nauk SSSR *224*, 1431 (1975); *V. Ya. Bykhovsky, N. I. Zaitseva, A. V. Umrikhina, A. N. Yavorskaya,* Prikl. Biokhim. Mikrobiol. *12*, 825 (1976); *A. R. Battersby, E. McDonald, M. Thompson, V. Ya. Bykhovsky,* J. Chem. Soc. Chem. Commun. *1978*, 150.

[4] *A. R. Battersby, E. McDonald,* Bioorg. Chem. *7*, 161 (1978); *A. R. Battersby, G. W. J. Matcham, E. McDonald, R. Neier, M. Thompson, W.-D. Woggon, V. Ya. Bykhovsky, H. R. Morris,* J. Chem. Soc. Chem. Commun. *1979*, 185; *N. G. Lewis, R. Neier, E. McDonald, A. R. Battersby, ibid. 1979*, 541. *G. Müller, K. D. Gneuss, H. P. Kriemler, A. I. Scott, A. J. Irwin,* J. Am. Chem. Soc. *101*, 3655 (1979).

[5] a) *U. Eisner,* J. Chem. Soc. *1957*, 3461; *R. Bonnet, I. A. D. Gale, G. F. Stephenson, ibid. C 1967*, 1168; b) *H. H. Inhoffen, J. W. Buchler, R. Thomas,* Tetrahedron Lett. *1969*, 1141.

[6] The "octaethylisobacteriochlorin" of [5a] and [5b] has been shown by NMR to be a mixture of *trans,trans,trans* and *trans,cis,trans* diastereoisomers, separable by HPLC (unpublished work by *K. Jones,* CPGS Thesis, Cambridge 1977, and *Ch. Angst,* ETHZ, 1977); see also *D. G. Whitten, I. C. Yau, F. A. Carroll,* J. Am Chem. Soc. *93*, 2291 (1971).

[7] For the formation of the Pd^{II} complex of *(15)* by thermolysis (200 °C) of palladium(II)-2,2,7,7,13,13,17,17-octamethylcorphinate chloride, see *P. M. Müller,* Diss. ETHZ No. 5135, Juris-Verlag, Zürich 1973, p. 146; see also *G. D. Egorova, K. N. Solov'ev, A. M. Shul'ga,* Zh. Obshchei Khim. *37*, 357 (1967).

[8] a) *Y. Yamada, D. Miljkovic, P. Wehrli, B. Golding, P. Löliger, R. Keese, K. Müller, A. Eschenmoser,* Angew. Chem. *81*, 301 (1969); Angew. Chem. Int. Ed. Engl. *8*, 343 (1969); b) *E. Götschi, W. Hunkeler, H. J. Wild, P. Schneider, W. Fuhrer, J. Gleason, A. Eschenmoser, ibid. 85*, 950 (1973), and *12*, 910 (1973), resp.; c) *P. Wehrli,* Diss. ETHZ No. 4043, Juris-Verlag, Zürich 1967, p. 123.

[9] *Y. Murakami, Y. Matsuda, K. Sakata,* Inorg. Chem. *10*, 1728 (1971).

[10] *H. Fischer, B. Walach,* Justus Liebigs Ann. Chem. *450*, 109 (1926).

[11] Cf. *A. P. Johnson, P. Wehrli, R. Fletcher, A. Eschenmoser,* Angew. Chem. *80*, 622 (1968); Angew. Chem. Int. Ed. Engl. *7*, 623 (1968).

[12] Cf. *A. Eschenmoser,* Pure Appl. Chem. *20*, 1 (1969).

[13] Experimental details will be described by *S. Ofner,* Diss. ETHZ (in preparation), *V. Rasetti,* Diss. ETHZ 1979, in press, and *K. Jones,* Thesis, Cambridge (in preparation).

2,2,4,4,6,6-Hexamethylcyclotristannatellurane, a Sn_3Te_3-Ring with C_2-Symmetry[**]

By *Axel Blecher* and *Martin Dräger*[*]

Dimethylstannane reacts with tellurium to give the title compound *(1)*[1a], which, however, must be separated from the Sn_3Te_2-ring compound[1b] formed at the same time. We have now been able to obtain pure, crystalline *(1)* by reaction of dichlorodimethylstannane with sodium hydrogen telluride in aqueous solution:

$$3\,(CH_3)_2SnCl_2 + 3\,NaHTe \xrightarrow{H_2O} [(CH_3)_2SnTe]_3 + 3\,NaCl + 3\,HCl$$

(1)

The NaHTe is generated from tellurium and $NaBH_4$ in the reaction mixture[2].

(1) crystallizes from petroleum ether in the form of yellow needles which are stable for several days at room temperature in the absence of air and in the dark. The X-ray structure analysis[3] at 110 K shows that the molecule of *(1)* approaches C_2 symmetry (Fig. 1: twofold axis through Sn1 and Te2) resulting in a chiral ring. The crystal contains both enantiomers A and B, transforming *via* pseudorotation in solution[4]. The average Sn—Te distance is 275(2) pm; the mean Sn—Te—Sn angle is 96(1)°, distinctly compressed compared to the analogous Sn—S—Sn[5] and Sn—Se—Sn angles[4]. The coordination at the tin atom deviates only slightly from a tetrahedron.

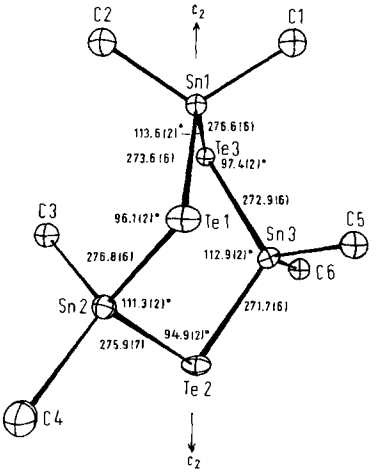


Fig. 1. Enantiomer A of *(1)* with distances [pm] and angles of the six-membered ring. Sn—C distances 220 (5) pm, C—Sn—C angles 113(2)°. Ring torsional angles [°]:

Te3—Sn1—Te1—Sn2 −34.2(2)	Sn3—Te3—Sn1—Te1 −33.3(2)
Sn1—Te1—Sn2—Te2 85.9(2)	Te2—Sn3—Te3—Sn1 84.1(2)
Te1—Sn2—Te2—Sn3 −44.5(3)	Sn2—Te2—Sn3—Te3 −41.2(3)

Procedure

All operations carried out under nitrogen and with nitrogen-saturated solvents: To a suspension of Te (3.7 g, 29 mmol) in H_2O (25 ml) is added a solution of $NaBH_4$ (2.3 g, 61 mmol) in H_2O (25 ml) and the mixture gently warmed. Te reacts vigorously and is dissolved. A solution of $(CH_3)_2SnCl_2$ (6.3 g, 29 mmol) in 25 ml H_2O is added dropwise with stirring to the red solution of NaHTe. A greenish-yellow precipitate is formed, which after 30 min is separated, dried and extracted with petroleum ether (b.p. 50—70 °C) in a Soxhlet apparatus. 5 g (62%) of yellow crystals of *(1)* precipitate from the solution, and on evaporation a further 1.5 g can be recovered.

Received: February 14, 1979 [Z 273 IE]
German version: Angew. Chem. *91*, 740 (1979)

[*] Prof. Dr. M. Dräger, Dipl.-Chem. A. Blecher
Institut für Anorganische Chemie und Analytische Chemie der Universität Johann-Joachim-Becher-Weg 24, D-6500 Mainz (Germany)

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

[1] a) *A. Blecher, B. Mathiasch,* Z. Naturforsch. *B 33*, 246 (1978); b) *B. Mathiasch,* Z. Anorg. Allg. Chem. *432*, 269 (1977).

[2] *D. L. Klayman, T. S. Griffin,* J. Am. Chem. Soc. *95*, 197 (1973).

[3] CAD4 diffractometer; 5219 reflections ($\lambda = 71.069$ pm), 2321 unobserved ($< 2\sigma$). Cell data: $a = 1314.2(3)$, $b = 995.6(3)$, $c = 4040.5(8)$ pm, $V = 5.286 \times 10^9$ pm^3, $Z = 12$, $\rho_{calc} = 3.12$ (110 K), $\rho_{exp} = 2.92$ g cm^{-3} (300 K), $\mu = 91.0$ cm^{-1}. In the space group Pnam, $R = 0.090$ (131 refined parameters), the asymmetric unit contains 1.5 molecules ($1/2$ molecule arranged randomly about a symmetry plane); in the space group $Pna2_1$, $R = 0.063$ (221 refined parameters), 3 molecules. Both space groups result in the same structure, with distinctly lower standard deviations for Pnam.

[4] *M. Dräger, A. Blecher, H.-J. Jacobsen, B. Krebs,* J. Organomet. Chem. *161*, 319 (1978).

[5] *B. Menzebach, P. Bleckmann,* J. Organomet. Chem. *91*, 291 (1975); *H.-J. Jacobsen, B. Krebs, ibid. 136*, 333 (1977).

Radical Complexes of Palladium and Platinum with Bisphosphane Derivatives of Maleic Anhydride

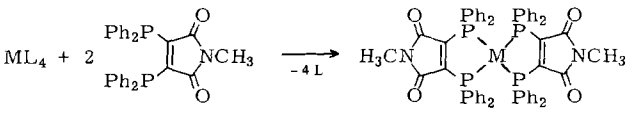
By *Walter Bensmann* and *Dieter Fenske*[*]

The intrinsic color of bis(diphenylphosphino)maleic anhydride, thioanhydride, and (*N*-methyl)imide (PP), and the deep color of their metal(0) complexes urged us to extend our

[*] Priv.-Doz. Dr. D. Fenske, Dr. W. Bensmann
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

investigations on this class of compounds[1]. We have found that not only normal diamagnetic metal(0) complexes of the type $(CO)_nM(PP)$ with M = Cr(Mo, W), Fe, Ni and $n = 4, 3, 2$ (in which (PP) is a neutral ligand) are formed, but also paramagnetic complexes of the type $(CO)_nM(PP)$ with M = Mn or Co and $n = 4$ or 3, respectively[2]. The magnetic measurements, ESR spectra, and the observed changes in bond lengths and vibration frequencies showed that in these complexes an electron is transferred from the metal into an antibonding orbital of the ligand, thus giving a complex of M^{1+} and $(PP)^-$ as radical anion ligand. (PP) was also intermediary to a complex bound radical anion in the reaction of nickelocene with (PP), but in this case a novel secondary reaction takes place in which a C_5H_5-group is inserted into a PC bond of the biphosphane ligand[3].

We now report on the ligand exchange reaction of metal(0) complexes of Ni, Pd, and Pt with bis(diphenylphosphino)maleic *N*-methylimide in the molar ratio 1:2.



(PP)

L = PPh_3; *(1)*, M = Pd
(2), M = Pt
L = CO; *(3)*, M = Ni

The product $Ni(PP)_2$ *(3)* is diamagnetic, air-stable, and its IR spectrum shows νCO bands which are characteristic for (PP) as neutral ligand. The analogous complexes of Pd and Pt, on the other hand, are very sensitive to air and special precautionary measures must be taken in their isolation. Their νCO bands appear at 1610 and 1665 cm^{-1}, about 100 cm^{-1} lower than in the case of the nickel complex. We conclude, therefore, that in the homologs *(1)* and *(2)* the ligands have become radical anions by taking up an electron from the metal. The ESR spectrum of *(1)* confirms this. In $C_2H_4Cl_2$ solution three groups of signals are observed in the ratio 1:2:1, corresponding to the coupling of the electron with the P-nuclei, with a hyperfine structure through coupling with N and the H-nuclei of the CH_3-group. The coupling constants ($a_p = 9.60$, $a_N = 3.0$, $a_{CH_3} = 0.68$ G) are very close to the values found for $(PP)Mn(CO)_4$ and $[PP]^-K^+$[2]. No coupling of the electron with Pd is detectable.

The X-ray structure analysis[4] on a single crystal of *(1)* confirms the spectroscopic findings. *(1)* crystallizes from 1,2-dichloroethane with five solvent molecules per unit cell. The solvent molecules are present in the two different conformations and are intercalated between layers of molecules of *(1)*. The Pd atom lies at the inversion center (0,0,0) and is square-planar coordinated by four P atoms (Fig. 1). The Pd–P distance of 237 pm falls within the range of values already observed in palladium-phosphane complexes[5]. This indicates that the tetrahedrally coordinated central atom in $Pd(PPh_3)_4$[5] changes its bonding symmetry in the course of the reaction.

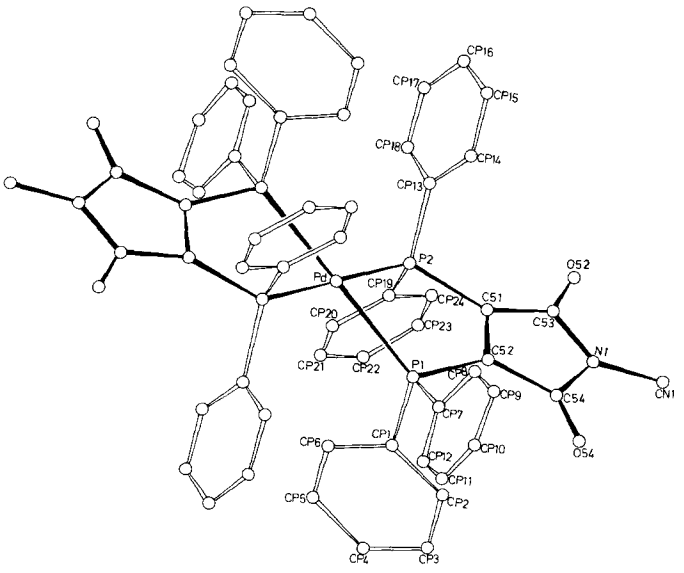


Fig. 1. Molecular structure of the palladium complex *(1)* in the crystal.

The bond angle P1–Pd–P2 has values of 83.4 and 96.6°, respectively, and the C atoms of the planar five-membered ring bound to P lie respectively 68 pm above and below the plane formed by the Pd and P atoms. The double bond in the five-membered ring is longer than that in comparable complexes which conform to the noble-gas rule[2], *e.g.* the C51–C52 distance of 139 pm is markedly longer than the corresponding CC double bond in $(PP)Fe(CO)_3$ (133 pm). Likewise the CO bond length of 124 pm is about 6 pm longer than in the Fe derivative. At the same time there is a noticeable shortening of the C51–C53 and C52–C54 bonds as well as a strengthening of the P2–C51 and P1–C52 (176 pm) bonds as compared to the P–C(phenyl) bonds (182–183 pm).

As in the case of $(PP)Co(CO)_3$ and $(PP)Mn(CO)_4$, it follows from these changes in bond lengths that low π^* acceptor levels of the ligand (PP) enable electron transfer from the Pd and Pt to the conjugated 6π-system of the maleic acid derivative. Therefore *(1)* is better regarded as $Pd^{2+}[PP^-]_2$—as is also reflected in the square-planar coordination typical for Pd^{2+}. It is still unclear why this does not apply in the case of the "more negative" nickel.

Procedure

Synthesis of *(1)*: A mixture of $Pd(PPh_3)_4$ (1 g, 0.87 mmol) and the bisphosphane ligand (0.83 g, 1.87 mmol) in $C_2H_4Cl_4$ (40 ml) is stirred at room temperature. An olive-colored solution is formed, from which *(1)* crystallizes at −20 °C in 45% yield. *(2)* is obtained analogously by reaction of $Pt(PPh_3)_4$ (1 g, 0.80 mmol) and ligand (PP) (0.77 g, 1.61 mmol).

Synthesis of *(3)*: To a solution of $(PP)Ni(CO)_2$ (1.61 g, 2.0 mmol) in xylene (50 ml) is added 0.96 g (2.0 mmol) (PP) and the mixture heated to boiling. Within 60 min the stoichiometric amount of CO is liberated and the solution turns intense green. On cooling, green crystals of *(3)* precipitate (yield 90%). *(3)* can also be obtained by direct reaction of $Ni(CO)_4$ with (PP).

Received: February 9, 1976 [Z 274a IE]
German version: Angew. Chem. *91*, 754 (1979)

CAS Registry numbers:
(1), 71277-47-9; *(2)*, 71277-48-0; *(3)*, 71277-49-1; $Pd(PPh_3)_4$, 14221-01-3; $(PP)Ni(CO)_2$, 56669-56-8; $Pt(PPh_3)_4$, 14221-02-4; $Ni(CO)_4$, 13463-39-3

[1] *D. Fenske, H. J. Becher*, Chem. Ber. *107*, 117 (1974); *108*, 2115 (1975); *H. J. Becher, W. Bensmann, D. Fenske, ibid. 110*, 315 (1977); *H. J. Becher, W. Bensmann, D. Fenske, B. Pfennig*, Monatsh. Chem. *109*, 1023 (1978).

[2] *D. Fenske*, Angew. Chem. *88*, 415 (1976); Angew. Chem. Int. Ed. Engl. *15*, 381 (1976); Chem. Ber. *112*, 363 (1979).

[3] *W. Bensmann, D. Fenske*, Angew. Chem. *90*, 488 (1978); Angew. Chem. Int. Ed. Engl. *17*, 462 (1978).

[4] Space group $P\bar{1}$; $a = 1199.8(3)$, $b = 1295.8(3)$, $c = 1366.8(4)$ pm, $\alpha = 65.65(2)$, $\beta = 72.38(2)$, $\gamma = 64.55(2)$, $Z = 1$; $\rho_{exp} = 1.48$, $\rho_{calc} = 1.50$ g/cm³; $\mu Mo(K\alpha) = 7.9$ cm^{-1}. Low-temperature measurement (−130 °C), Syntex-P2₁ diffractometer, up to $2\vartheta = 50°$ 6132 reflections, of which 5380 with $I > 1.96\sigma(I)$. Solution of structure: heavy atom method, anisotropic refinement of all positional parameters and temperature factors, $R_1 = 0.051$, $R_2 = 0.047$. In a subsequent difference Fourier synthesis all hydrogen positions could be located.

[5] *V. G. Andrianov, I. S. Akhrem, N. M. Chistovalova, Yu. T. Struchkov*, Zh. Strukt. Khim. *17*, 135 (1976); and references cited therein.

Novel Polycyclic Phosphanes and Arsanes: $P_{11}(SiMe_3)_3$ and $As_7(SiMe_3)_3$

By *Hans Georg von Schnering, Dieter Fenske, Wolfgang Hönle, Michael Binnewies,* and *Karl Peters*[*]

From the products formed on reaction of Na/K alloy with white phosphorus and chlorotrimethylsilane in monoglyme *Fritz* and *Hölderich*[1] were able to isolate polycyclic phosphane derivatives such as P_7R_3, $P_{14}R_4$ and $P_{13}R_5$ ($R=SiMe_3$) in yields of up to 40% P. We have now found that reaction of the pure phosphides Na_3P_{11} and Cs_3P_{11} and of the arsenide Rb_3As_7 with chlorotrimethylsilane in toluene leads in a surprisingly simple way and in high yields to $P_{11}(SiMe_3)_3$ and $As_7(SiMe_3)_3$, respectively.

$P_{11}(SiMe_3)_3$: When a suspension of 20 g of Na_3P_{11}[2] or Cs_3P_{11}[3,4] (previously finely ground under inert conditions) in O_2-free toluene is treated with an excess of Me_3SiCl and the vigorously stirred mixture is heated under reflux for two days, deep yellow-orange solutions are obtained from which NaCl and CsCl, respectively, separate out. After filtration, removal of Me_3SiCl and half of the toluene, and cooling to 0 °C, $P_{11}(SiMe_3)_3$ crystallizes in *ca.* 60% yield (based on P, not optimized).—In the preparation of Na_3P_{11} and Cs_3P_{11}, often Na_3P_7 and Cs_3P_7[5] are also formed; in this case large amounts of $P_7(SiMe_3)_3$ are also obtained.

$As_7(SiMe_3)_3$: An analogous reaction is carried out with about 30 g of Rb_3As_7 (described in the system Rb/As as $RbAs_2$[6]), though at room temperature and in the absence of light. A deep-red solution is obtained. After 24 hours, removal of RbCl by filtration, concentration of the filtrate to 50% of its original volume and cooling to 0 °C leads to crystallization of $As_7(SiMe_3)_3$ in 70% yield.

4,7,11-Tris(trimethylsilyl)pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecaphosphane, $P_{11}R_3$, forms bright-yellow flat rhombic (lentil shaped) crystals which are much more reactive (H_2O, O_2) than P_7R_3, both under the mother liquor as well as in the isolated form. The mass spectrum (QMS) at 150 °C shows fragments differing from one another by P_2 or P_4 units [*m/e*; abundance]: $P_{11}R_3^+$ [560; 66], $P_9R_3^+$ [498; 80], $P_7R_3^+$ [436; 18], $P_7R_2^+$ [363; 77], $P_3R_3^+$ [312; 20], $P_5R_2^+$ [301; 100], $P_4R_2^+$ [270; 30], PR_3^+ [250; 45], $P_3R_2^+$ [239; 95], $P_2R_2^+$ [208; 95].

Of these, $P_9R_3^+$ seems noteworthy to us as a possible derivative of a P_6 prism[5]; it has also already been observed by *Fritz* and *Hölderich*[1]. At $T>200$ °C we also found a small amount of $P_{16}R_2^+$ [*m/e*=642]. $P_{11}R_3$ crystallizes monoclinically in the space group $P2_1/c$ (No. 14) with $a=1912.8(8)$, $b=1137.8(5)$, $c=1227.3(9)$ pm, $\beta=90.73(4)°$, $Z=4$. The structure determination is not yet complete, since the isolated crystals rapidly decompose. The molecular structure is, however, confirmed (390 *hkl*; $R=0.15$). The asymmetrically substituted enantiomers of the "ufosane" polycycle P_{11}^{3-}[2] are present with mean P···P distances of 221.5 pm (Fig. 1, above).

3,5,7-Tris(trimethylsilyl)tricyclo[2.2.1.0^{2,6}]heptaarsane, As_7R_3, forms bright-yellow rhombohedral crystals up to 2 mm in length which are astonishingly air-stable in the isolated state. On exposure to moisture, air, and light, arsenic separates out after a few hours (in the mother liquor, immediately). Its solubility in toluene is lower than that of $P_{11}R_3$. The mass spectrum at 80 °C shows $As_7R_3^+$ [744; 71], $As_4R_3^+$ [519; 29], $As_3R_3^+$ [444; 100], and As_4^+ [300; 85]. As_7R_3 crystallizes rhombohedrally in the space group $R\bar{3}$ (No. 148) with $a_R=1298.9(3)$ pm, $\alpha=50.29(1)°$, $Z=2$ ($a_H=1103.8(3)$, $c_H=3395.4(9)$ pm, $Z=6$). The structure determination (1721 *hkl*; $R=0.05$) confirms the expected configuration of the homologs P_7R_3[7] (Fig. 1, below). The As···As bond lengths are A=244.4(2), B=242.7(2) and C=240.7(1) pm [As···Si =239.7(3) pm]; the sequence A>B>C corresponds to that observed in P_7R_3[7] and differs from the sequence A>C>B in the anion As_7^{3-}[8].

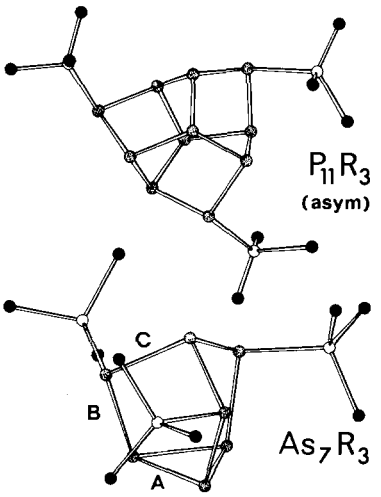


Fig. 1. Structures of the silyl-substituted polycyclic undecaphosphane $P_{11}R_3$ and of the heptaarsane As_7R_3 ($R=SiMe_3$).

Received: June 11, 1979 [Z 274b IE]
German version: Angew. Chem. *91*, 755 (1979)

[1] *G. Fritz, W. Hölderich*, Naturwissenschaften *62*, 573 (1975).
[2] *W. Wichelhaus, H. G. v. Schnering*, Naturwissenschaften *60*, 104 (1973).
[3] *W. Bues*, persönliche Mitteilung (1978).
[4] *H. G. v. Schnering et al.*, to be published.
[5] *H. G. v. Schnering* "Catenation of Phosphorus Atoms" in *A. L. Rheingold:* Homoatomic Rings, Chains and Macromolecules of Main-Group Elements. Elsevier, Amsterdam 1977.
[6] *S. Lohmeyer*, Dissertation, Universität Münster 1962.
[7] *W. Hönle, H. G. v. Schnering*, Z. Anorg. Allg. Chem. *440*, 171 (1978).
[8] *W. Schmettow, H. G. v. Schnering*, Angew. Chem. *89*, 895 (1977); Angew. Chem. Int. Ed. Engl. *16*, 857 (1977).

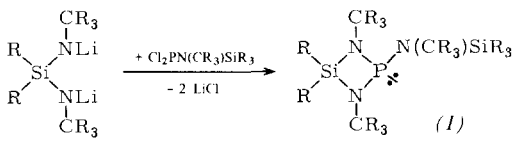
[*] Prof. Dr. H. G. von Schnering, Dr. W. Hönle, Dr. K. Peters
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)
Priv.-Doz. Dr. D. Fenske, Dr. M. Binnewies
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-4400 Münster (Germany)

Synthesis, Resolution, and Characterization of an Aminophosphane Rotamer Pair[**]

By *Otto J. Scherer* and *Michael Püttmann*[*]

On introduction of two different bulky substituents R^1, R^2 of the kind $X(CH_3)_3$ (X=C, Si, Ge), in addition to sterically active groups R, into aminophosphanes[1a] and -arsanes[1b] $R_2El-NR^1R^2$ (El=P, As), a pair of rotamers can be detected by NMR spectroscopy[1]; however, their resolution has so far proved impossible.

On reaction with a *N,N'*-bismetalated diaminosilane



(1)

R = CH_3

[*] Prof. Dr. O. J. Scherer, Dipl.-Chem. M. Püttmann
Fachbereich Chemie der Universität
Postfach 3049, D-6750 Kaiserslautern (Germany)

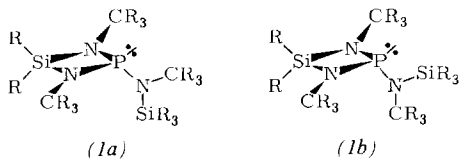
[**] This work was supported by the Fonds der Chemischen Industrie.

Table 1. Physical and NMR spectroscopic data of the aminophosphane rotamer pair *(1a)/(1b)*.

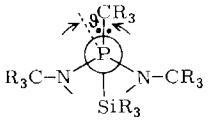
		^{1}H-NMR [a]				^{13}C{^{1}H}-NMR [a]						^{31}P{^{1}H}-NMR [a]
	M.p. [°C]	δSiR_2	$\delta NCR_{3(r)}$	$\delta NCR_{3(e)}$	$\delta NSiR_3$	$\delta NC_{(e)}$	$\delta NCC_{(e)}$	$\delta NC_{(r)}$	$\delta NCC_{(r)}$	$\delta NSiC_{(e)}$	$\delta NSiC_{(r)}$	δ
(1a)	122 [b]	0.34 (s)	1.28 (s)	1.53 (d) ^4J(PH) = 1.1 Hz	0.50 (s)	57.2 (d) J(PNC) = 33.0 Hz	34.5 (d) J(PNCC) = 18.9 Hz	51.2 (d) J(PNC) = 13.6 Hz	32.8 (d) J(PNCC) = 5.7 Hz	7.3 (d) J(PNSiC) = 0.6 Hz	7.6 (d) J(PNSiC) = 5.1 Hz 6.2 (s) [c]	142.2
(1b)	97—100 [b]	0.35 (s) 0.27 (s) [c]	1.28 (s)	1.59 (s)	0.48 (d) ^4J(PH) = 3.9 Hz	60.3 (d) J(PNC) = 3.7 Hz	33.3 (d) J(PNCC) = 2.3 Hz	51.3 (d) J(PNC) = 14.7 Hz	32.7 (d) J(PNCC) = 5.9 Hz	7.5 (d) J(PNSiC) = 22.6 Hz	6.7 (d) J(PNSiC) = 4.8 Hz 6.3 (d) [c] 0.5 Hz	125.4 −70 °C ^2J(Si(e)P) = 33.7 Hz

[a] *Ca.* 30% C_nD_n solution; ^{1}H- and ^{13}C: TMS internal, ^{31}P: 85% H_3PO_4 external; positive sign always means downfield shift (the problem of the sign of J is neglected except in one case); (r) = group on the ring nitrogen atom, (e) = group on the exocyclic nitrogen atom, R = CH_3. [b] Heat-up rate 5 °C/min beginning about 10 °C below the melting temperature given (*1a*) undergoes *ca.* 10% isomerization). [c] The signal showing a downfield shift is tentatively assigned to the $SiCH_3$ group located *cis* to the phosphorus "lone" pair.

we succeeded in synthesizing a cyclic aminophosphane derivative *(1)* which, owing to hindered rotation about the P—N bond of the three-coordinate phosphorus, forms a pair of rotamers *(1a)/(1b)* that has now been resolved and characterized individually[2].



(1a) *(1b)*



The rotamers differ in having the CR_3 group of *(1a)* (cf. Newman projection *(A)*), but the SiR_3 of *(1b)*, eclipsing the phosphorus "lone" pair.

(1a) initially predominates [*(1a)*:*(1b)* ≈ 4:1][3] in the synthesis of 1,3,2,4-diazaphosphasiletidine but is transformed into the thermodynamically more stable *(1b)* on distillation[4]. Both rotamers are very readily soluble in ether, pentane, and benzene; they differ considerably in their melting point and in some spectroscopic data (Table 1). In contrast to the ^{13}C-NMR results, *(1a)* shows only one signal for the SiR_2 group of the ring (accidental equivalence) in its ^{1}H-NMR spectrum even at 200 MHz. The greatest deviations of the values of *(1a)* and *(1b)* are found in the ^{31}P-NMR spectrum. For the groups bound to the exocyclic N atom we assign the greater coupling constant(s) to that located *cis* to the "lone" pair of the P atom (dihedral angle[5] of 0° for *(1a)*) (Table 1). Crystal structure analysis[7] of *(1a)* now confirms this assignment previously proposed for aminophosphane rotamers on the basis of ^{1}H-[6a], ^{13}C-[6b], and ^{29}Si-NMR[6c] data. Remarkably, the average value of 14.15 Hz calculated from 13.6 and 14.7 Hz for $J(PNC)_r$ agrees well with the value of 14.65 Hz calculated for a dihedral angle of 90°[8].

Synthesis of (1a)/(1b): A solution of $LiN(CR_3)SiR_3$ (R = CH_3) (50 mmol) in ether/hexane (*ca.* 80 ml) is added dropwise over 1.5 h to a solution of PCl_3 (6.97 g, 50.7 mmol) in ether (60 ml) at −18 °C and stirring is continued for 1 h at that temperature. $R_2Si[N(tBu)Li]_2$ (50 mmol) in toluene/hexane (*ca.* 110 ml) is then added dropwise within 1 h to the cooled (ice/salt) intermediate $Cl_2PN(CR_3)SiR_3$[9]. After warming to room temperature, the solvent is evaporated off, the residue dissolved in pentane (50 ml), LiCl filtered off, and the pentane is removed in vacuum. Crude yield: 16.3 g (87%) of a viscous dark red-brown oil containing *(1a)* and *(1b)* [≈4:1] accompanied by *ca.* 10% of $[ClPNtBu]_2$[9]. *(1a)* can be separated from the mixture by fractional recrystallization from acetonitrile. *(1b)* is isolated by repeated fractional distillation over a 5-cm Vigreux column; the fractions collected at 70—92 °C/10^{-3} torr (bath temp. 160—180 °C, cleanest fraction, 4.5 g) and 92—100 °C/10^{-3} torr (bath temp. 180—190 °C, 1.2 g) are finally purified by recrystallization from acetonitrile.

Received: February 8, 1979;
supplemented: June 18, 1979 [Z 275 IE]
German version: Angew. Chem. *91*, 741 (1979)

CAS Registry numbers:
(1), 71264-58-9; $Cl_2PN(C(CH_3)_3)Si(CH_3)_3$, 61916-04-9; $(CH_3)_2Si[N(t\text{-}Bu)Li]_2$, 54677-64-4; $LiN(C(CH_3)_3)Si(CH_3)_3$, 18270-42-3; PCl_3, 7719-12-2

[1] a) *R. H. Neilson, R. Chung-Yi Lee, A. H. Cowley*, J. Am. Chem. Soc. *97*, 5302 (1975); Inorg. Chem. *16*, 1455 (1977); b) *O. J. Scherer, W. Janssen*, Chem. Ber. *103*, 2784 (1970).

[2] The two rotamers were further characterized by C,H,N analysis, cryoscopic molecular weight determination (in benzene), and their mass spectra [18 eV: m/e = 375 (25% M^+ at *(1a)* and 4% at *(1b)*].

[3] Reaction of $R_2Si(NCR_3)_2PCl$ with $LiN(CR_3)SiR_3$, R = CH_3, for 6 d at room temperature gives the rotamers *(1a)* and *(1b)* in the ratio ≈3:7. Cf. exclusive formation of one rotamer of reaction of $Cl_2Si(NSiR_3)_2PCl$ with $LiN(CR_3)SiR_3$, R = CH_3: *U. Klingebiel, P. Werner, A. Meller*, Chem. Ber. *110*, 2905 (1977).

[4] *(1b)* was obtained from *(1a)* on heating in toluene to 80 °C in *ca.* 10% yield after 1 h and in *ca.* 20% after 3 h.

[5] In *(A)* the dihedral angle ϑ is defined as the angle between the plane of the atoms $P,N_{exocycl.},C$ and a plane through the center of the ring (with R_2Si and P); ϑ would be *e.g.* 0° for *(A)*.

[6] Cf. a) *A. H. Cowley, M. J. S. Dewar, W. R. Jackson, W. B. Jennings*, J. Am. Chem. Soc. *90*, 1085, 5206 (1970); b) *M.-P. Simonnin, R.-M. Lequan, F. W. Wehrli*, J. Chem. Soc. Chem. Commun. *1972*, 1204; c) *E. Niecke, W. Flick, S. Pohl*, Angew. Chem. *88*, 305 (1976); Angew. Chem. Int. Ed. Engl. *15*, 309 (1976).

[7] Some bond distances [pm] and angles [°] of *(1a)*: $PN_{(e)}$ 171.7, $PN_{(r)}$ 173.7/174.2, $NSi_{(e)}$ 176.4, $NSi_{(r)}$ 173.1/173.3, $N_{(e)}C$ 152.7, $N_{(r)}C$ 147.9/148.0. $N_{(r)}PN_{(r)}$ 82.8, $N_{(r)}SiN_{(r)}$ 83.4, $PN_{(r)}Si$ 94.6, $PN_{(e)}C$ 111.7, $PN_{(e)}Si$ 128.2, $CN_{(e)}Si$ 120.1. $Si_{(r)}PN_{(e)}SiC$ lie in a plane. (e) = exocyclic, (r) = in ring. We are grateful to Dr. *C. Krüger*, Mülheim, for the crystal structure analysis.

[8] By analogy with [6b], a negative sign would be assumed for $J(PNC)_e$ of *(1b)* for a dihedral angle of *ca.* 180°; *i.e.* the coupling constant has a value of −3.7 Hz.

[9] *O. J. Scherer, P. Klusmann*, Angew. Chem. *81*, 743 (1969); Angew. Chem. Int. Ed. Engl. *8*, 752 (1969); *N. Kuhn*, Dissertation, Universität Kaiserslautern 1975; cf. [1a].

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0909-0680 $ 02.50/0

Mono- and Bis(η^3-allylnickel) Derivatives of 1,8-Dihydroxyanthraquinone and of Some 1,3,5-Triketones

By *Borislav Bogdanović* and *Miguel Yus*[*]

The known mono- and dimetallic derivatives of 1,3,5-triketones[1] have recently become the subject of renewed investigations, particularly regarding their magnetic properties[2,3]. According to X-ray crystal structure analyses[3], the metal atoms in dinuclear complexes of type *(1)* are almost coplanar with the ligands and are bridged to each other *via* the two central oxygen atoms.

In connection with our investigations on organometallic pentanedionates and their catalytic properties[4] our interest was directed to compounds of type *(2)*, in which two metal atoms are located very close to each other and, moreover, bear reactive η^3-allyl groups.

(1) *(2)*

We report here on the synthesis and characterization of the bis(η^3-allylnickel) 1,3,5-triketonates *(3a—c)* and the 1,8-bis(η^3-allylnickeloxy)anthraquinone *(3d)*, the first organometallic compounds very probably having structures of type *(2)*[5]. For comparison we have also synthesized the mono(η^3-allylnickel) 1,3,5-triketonates *(4b, c)* and the 1-(η^3-allylnickeloxy)-8-hydroxyanthraquinone *(4d)*.

By analogy with the synthesis of η^3-allylnickel pentanedionate[4b], we attempted the preparation of compounds *(4)* and *(3)* by reaction of the triketones *(5)* and of 1,8-dihydroxyanthraquinone with bis(η^3-allyl)nickel in the molar ratio 1:1 and 1:2, respectively. However, at −30 to 0 °C in ether, the reaction always afforded only the mono(η^3-allylnickel) derivatives *(4b, c)* of the triketones and 1-(η^3-allylnickeloxy)-8-hydroxyanthraquinone *(4d)*, respectively (see Table 1, Method A). The mono(η^3-allylnickel) 1,3,5-triketonates *(4b, c)* can also be prepared from the monothallium triketonates[7] and η^3-allylnickel bromide[8] (see Table 1, Method B)[9]. The synthesis of bis(η^3-allylnickel) 1,3,5-triketonates *(3a—c)* and of 1,8-bis(η^3-allylnickeloxy)anthraquinone *(3d)* was achieved by reaction of the dithallium salts *(6)*[7] with η^3-allylnickel bromide in CH_2Cl_2 at −50 to −78 °C.

The compounds *(3a—d)*, which are soluble in CH_2Cl_2, can be separated from thallium bromide by decantation at −78 °C. Subsequent removal of part of the solvent and addition of ether leads to their precipitation. The compounds *(3a—d)* are sensitive to air and heat: their thermal stability decreases along the series *(3d)* > *(3b)* ≃ *(3c)* > *(3a)*.

The ^{1}H-NMR spectra of the bis(η^3-allylnickel) 1,3,5-triketonates *(3a—c)* (Table 1) show signals for each of the triketonate ligands, together with characteristic signals of the η^3-allyl groups. The ^{1}H-NMR spectrum of *(3b)* in which two signals each for the *syn*- and *anti*-protons (H_s and H_a) appear at −65 °C, can be interpreted in terms of the structure *(3')* or *(3'')*, in which the two "inner" *syn*- or *anti*-differ from the two "outer" *syn*- or *anti*-protons.

(3') *(3'')*

On increasing the temperature to *ca.* −20 °C the signals of the *syn*- and *anti*-protons coalesce, so the ^{1}H-NMR spectrum corresponds to that of a symmetric η^3-allyl group—a phenomenon which is also observed in the case of bis(η^3-allylnickel) 2,4,6-heptanetrithionediate[6]. The ^{1}H-NMR spectrum of *(3a)* at −65 °C shows, *inter alia*, four signals for *syn*-, (at least) three signals for *anti*-, and one signal for *meso*-protons (H_m), together with three signals for methine protons of the triketonate ligands, a possible indication that *(3')* and *(3'')* and other conceivable stereoisomers are present together[10].

(5) *(4b)*, R^1, R^4 = CO_2Et; R^2, R^3 = H
(4c), R^1, R^4 = CO_2Et; R^2-R^3 = $-(CH_2)_2-$
(4d)

(6) *(3a)*, R^1, R^4 = CH_3; R^2, R^3 = H
(3b), R^1, R^4 = CO_2Et; R^2, R^3 = H
(3c), R^1, R^4 = CO_2Et; R^2-R^3 = $-(CH_2)_2-$
(3d)

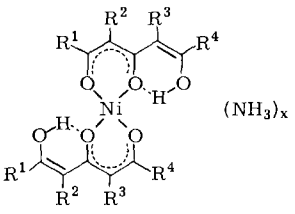
[*] Prof. Dr. B. Bogdanović, Dr. M. Yus [**]
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)
[**] New address: Departmento de Quimica Organica, Facultad de Ciencias, Oviedo (Spain)

Table 1. Data on the synthesis and characterization of compounds *(3a—d)* and *(4b—d)*.

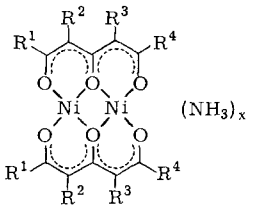
Cpd.	Yield [a]	IR spectra (KBr) cm^{-1}				^{1}H-NMR spectra [τ-value]							mol CO / mol *(3)* or *(4)*	NH_3-reaction
Color	[%]	$\nu_{C=O}$	$\nu_{C\ O}$	$\nu_{C=O(ester)}$	ν_{OH}	H_m	H_s	H_a	CH_3	CH_2	CH	OH	[b]	yield [%] [c]
(3a) yellow	95 (95)	—	1585 1510	—	—	4.45 m	6.22 d 6.27 d 6.72 d 7.63 d	7.94 d 8.14 d 8.70 d	8.40 s 8.50 s	—	5.16 s 5.28 s 5.47 s	— [d]	7.8	59
(3b) orange	90 (98)	1715	1620 1585 1545	1265	—	4.19 m 4.02 m	7.01 d 6.88 d 7.05 d	7.93 d 7.76 d 7.94 d	8.70 t 8.70 t	5.80 q 5.75 q	4.31 s 4.23 s	— [e] — [f]	6.6	77
(3c) red	95 (100)	1715	1590 1475	1230	—	4.10 m	6.98 d	7.90 d	8.71 t	5.73 q 7.18 s	—	— [e]	8.0	42
(3d) violet	96 (100)	1655	1590 [g] 1510	—	—				[h]				7.2	15
(4b) orange-brown	58 (A) [i] 66 (100) (B)	1725	1605 1530	1250	3430				[h]				2.0	10—15
(4c) orange	90 (A) [j] 70 (98) (B)	1720 1700	1625 1565 1480	1260	3420	4.37 m	7.40 d	8.13 d	9.02 t 9.08 t	7.16 s 5.97 q 6.07 q	—	−1.36 s [k]	1.8 [l]	75
(4d) violet	49 (A)	1650	1605 [g] 1595 1515 1485	—	3430				[h]				2.0	10—15

[a] Route A $(\eta^3\text{-}C_3H_5)_2Ni$ + *(5)*; Route B $(\eta^3\text{-}C_3H_5NiBr)_2$ + monothallium triketonate. Numbers in brackets: yields of TlBr. [b] Carbonylation at normal pressure in CH_2Cl_2. [c] Yields of $(\eta^3\text{-}C_3H_5)_2Ni$. [d] In $CDCl_3$ at −65 °C (100 MHz). [e] In $CDCl_3$ at −20 °C (60 MHz). [f] In $CDCl_3$ at −65 °C (60 MHz). [g] The absorptions of the aromatic groups also lie in this region. [h] No ^{1}H-NMR spectrum obtainable owing to sparing solubility. [i] Route A: at −30 °C in ether; Route B: at −30 °C in CH_2Cl_2. [j] Route A: at 0 °C in ether; Route B: at 20 °C in ether. [k] In C_6D_6 at 20 °C (60 MHz). [l] Carried out in THF.

The compounds *(4b—d)* and *(3a—d)* react with ammonia[4b] in ether at *ca.* −30 °C to give bis(η^3-allyl)nickel and the ammonia adducts of the mono- and dinickel derivatives, respectively, of the ligands *(7)* and *(8)* (see Table 1).

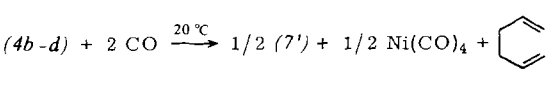


(7), x = 1-2
(7'), x = 0

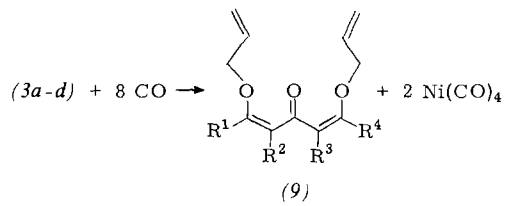


(8), x = 1.5-3

A characteristic difference in the reactivity between the mono- and bis(η^3-allylnickel) derivatives of the 1,3,5-triketones and those of 1,8-dihydroxyanthraquinone is demonstrated in their carbonylation: the mono(η^3-allylnickel) compounds *(4b—d)* react at −20 °C (1 bar) with *ca.* 2 mol CO/mol *(4)* to give tetracarbonylnickel and mononickelbis(triketonates) *(7')*; in the case of *(4c)*, 1,5-hexadiene was found to be formed in 45% yield.



The bis(η^3-allylnickel) derivatives *(3a—d)*, on the other hand, react with a total of *ca.* 8 mol CO/mol *(3)*, whereupon two thirds or even the whole of the CO is taken up at −78 °C. Tetracarbonylnickel and the bis(allyl enol ether) of each triketone or the 1,8-dihydroxyanthraquinone *(9)* are formed by reductive elimination.



(9)

Received: October 7, 1975 [Z 276a IE]
revised: May 23, 1979
German version: Angew. Chem. *91*, 742 (1979)
Publication delayed at authors' request

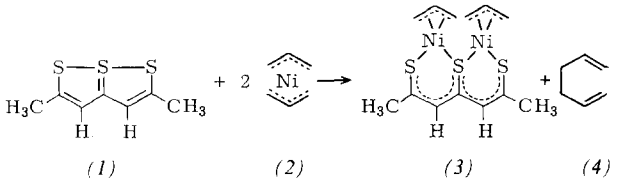
[1] *F. Feist*, Justus Liebigs Ann. Chem. *257*, 276 (1890); *M. Dünschmann, H. v. Pechmann, ibid. 261*, 175 (1891).
[2] *D. P. Murtha, R. L. Lintvedt*, Inorg. Chem. *9*, 1532 (1970).
[3] *R. L. Lintvedt, L. L. Borer, D. P. Murtha, J. M. Kuszaj, M. D. Glick*, Inorg. Chem. *13*, 18 (1974); *A. B. Blake, L. R. Fraser*, J. Chem. Soc. Dalton Trans. *1974*, 2554.
[4] a) *B. Bogdanović*, Angew. Chem. *77*, 1010 (1965); Angew. Chem. Int. Ed. Engl. *4*, 954 (1965); b) *U. Birkenstock, H. Bönnemann, B. Bogdanović, D. Walter, G. Wilke*, Adv. Chem. Ser. *70*, 250 (1968); c) *B. Bogdanović, G. Wilke*, Brennst.-Chem. *49*, 323 (1968); d) *B. Bogdanović, B. Henc, H.-G. Karmann, H.-G. Nüssel, D. Walter, G. Wilke*, Ind. Eng. Chem. *62*, (12) 34 (1970).
[5] Bis(η^3-allylnickel) 2,4,6-heptanetrithionediate, a sulfur analog of *(3a)* has been shown by X-ray structure analysis to have the structure type *(2)* [6].
[6] *B. Bogdanović, C. Krüger, O. Kuzmin*, Angew. Chem. *91*, 744 (1979); Angew. Chem. Int. Ed. Engl. *18*, 683 (1979).
[7] The mono- and dithallium salts of 1,3,5-triketones *(5)* and 1,8-dihydroxyanthraquinone were prepared according to the method of *R. C. Menzies, A. R. P. Walker*, J. Chem. Soc. *1936*, 1678.
[8] This method was first described by *S. D. Robinson, B. L. Shaw*, J. Chem. Soc. *1963*, 4806.
[9] Mono(η^3-allylnickel) 2,4,6-heptanetrionate *(4a)* could not be prepared by Method A or B.
[10] Two non-mirror image stereoisomers of the type *(3')* and *(3'')* are possible on twisting the molecule, as has been found in the case of bis(η^3-allylnickel) 2,4,6-heptanetrithionediate [6].

Bis(η^3-allylnickel) 2,4,6-Heptanetrithionediate

By *Borislav Bogdanović, Carl Krüger,* and *Oleg Kuzmin*[*]

We report here the synthesis, characterization, and X-ray crystal structure analysis of bis(η^3-allylnickel) 2,4,6-heptanetrithiodiate *(3)*, the first organometallic derivative of a 1,3,5-trithiotriketone[1]. Compound *(3)* was synthesized by reaction of 2,5-dimethyl-1,6,6aλ^4-trithiapentalene *(1)*[2] with bis(η^3-allyl)nickel *(2)* or η^3-allylnickel chloride. We have already prepared oxygen analogs of *(3) via* a different route[3].

(1) reacts with *(2)* in the molar ratio 1:2.0-2.2 in ether, tetrahydrofuran (THF) or toluene at 0 °C within 8—12 h to give intensely dark blue (in ether) or dark violet (in THF) solutions of *(3)*. Compound *(3)* crystallizes from the ethereal solutions at 0 or −78 °C as violet crystals having a metallic luster and can be isolated analytically pure in *ca.* 70% yield. In the synthesis of *(3)* in toluene, stoichiometric amounts of 1,5-hexadiene *(4)* could by isolated from the reaction products in addition to *(3)*.



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

Reaction of *(1)* with η^3-allylnickel chloride (molar ratio 1:2) in THF at 0 °C affords *(3)* and nickel chloride; filtration of the THF solution and subsequent crystallization from ether furnishes *(3)* in *ca.* 48% yield. A green compound, apparently analogous to *(3)*, is formed on reaction of 2,5-diphenyl-1,6,6aλ^4-trithiapentalene[2] with bis(η^3-allyl)nickel in THF at 0 °C.

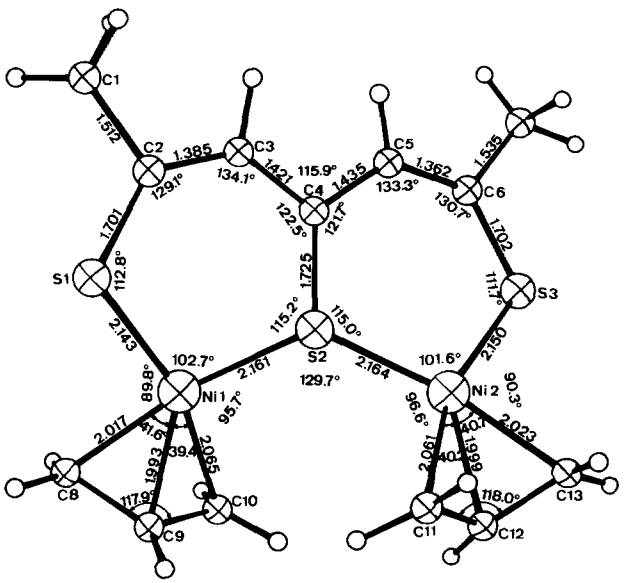


Fig. 1. Bond lengths [Å] and angles in bis(η^3-allylnickel) 2,4,6-heptanetrithionediate *(3)*.

The structure of *(3)* (Fig. 1) was confirmed by X-ray structure analysis[4]. Both nickel atoms are square planar coordinated; very slight and insignificant deviations arise due to steric hindrance of the neighboring opposingly oriented η^3-allyl groups. This hindrance causes distortion of the planar ligand[5] with maximum deviations of the plane through all S atoms of +0.17 Å (C2) and −0.24 Å (C6). S1 lies 0.898(8) Å above and S3 0.752(8) Å below a plane determined by Ni1, S2, Ni2. The S—S distances (3.361(1) and 3.342(1) Å, respectively) enlarge as a result of complexation; as a consequence there is no longer S—S bonding in the complex. The large distance between the neighboring Ni atoms (3.914(1) Å) likewise indicates an absence of metal-metal bonding. Apart from substantial broadening of the angles within the ring system at C2, C3, C5, and C6 (+12 to 13° w.r.t. the free ligand), the bond geometry of the sulfur ligand is maintained. Due to steric repulsion (C10, C11), or to a *trans*-effect of the different types of sulfur atoms S1—S2 and S2—S3, the η^3-allyl groups are bound asymmetrically to the nickel atoms. Their inclinations to the S—Ni—S planes[6] are 121.6 and 128.9 °C, respectively.

Consistent with X-ray structure analyses, the 100-MHz ^{1}H-NMR spectrum[7] of *(3)* in C_6D_6 at +10 °C shows the signals of two equivalent, asymmetric η^3-allyl groups: a signal for H_{meso} at $\tau = 5.15$ (m) and two signals each for H_{syn} and H_{anti} at $\tau = 6.98$ (d) and 7.17 (d) ($J_{meso,syn} = 7$ Hz) and 7.82 (d) and 7.96 (d) ($J_{meso,anti} = 14$ Hz), respectively. The signals of the methine protons and of the methyl groups of the trithiapentalene ligands appear as singlets at $\tau = 3.02$ and 7.59, respectively. An analogous spectrum with insignificant change in position of the signals is obtained at −50 °C in THF. On increasing the temperature to 20 °C the signals of the *syn*- and of the *anti*-protons coalesce. In the 60-MHz spectrum of *(3)* in C_6D_6 at 20 °C, the characteristic signals of symmetric η^3-allyl groups appear as a result of dynamic equilibration[8], the H_{meso} as a septet at $\tau = 5.07$ and H_{syn} and H_{anti} as sharp doublets at $\tau = 7.0$ and 7.86, respectively.

(3) reacts with carbon monoxide (1 bar) in toluene at 0 to 20 °C with uptake of *ca.* 3 mol CO/mol *(3)*. On distillation of the reaction mixture *in vacuo*, 37% of the nickel employed in the reaction is recovered as $Ni(CO)_4$; *(1)* can be recovered in 46% yield from the distillation residue by crystallization from THF at −78 °C.

The synthesis of *(3)* from *(1)* and *(2)* with formation of 1,5-hexadiene *(4)* and the reaction of *(3)* with CO to give $Ni(CO)_4$ and *(1)* respectively constitute C—C coupling reactions and formal redox processes with participation of two transition metal atoms.

Received: October 7, 1975 [Z 276b IE]
German version: Angew. Chem. *91*, 744 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(3a), 71277-50-4; *(3b)*, 71277-51-5; *(3c)*, 71277-52-6; *(3d)*, 71277-53-7; *(4b)*, 71277-54-8; *(4c)*, 71294-38-7; *(4d)*, 71277-55-9; *(5a)*, 25033-12-9; *(5b)*, 71264-95-4; *(5b)*, monothallium salt, 71277-56-0; *(5c)*, 53182-88-0; *(5c)*, monothallium salt, 71277-57-1; *(5d)*, 717-10-2; *(6a)*, 71277-58-2; *(6b)*, 71277-59-3; *(6c)*, 71277-60-6; *(6d)*, 71277-61-7; *(7b)*, 71277-62-8; *(7c)*, 71277-63-9; *(7d)*, 71277-64-0; *(9a)*, 71264-96-5; *(9b)*, 71264-97-6; *(9c)*, 71264-98-7; *(9d)*, 71264-99-8; bis(η^5-allyl)nickel, 12077-85-9; η^3-allylnickel bromide, 12012-90-7

[*] Prof. Dr. B. Bogdanović, Priv.-Doz. Dr. C. Krüger, Dr. O. Kuzmin [**]
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)

[**] DFG Fellow. Present address: Institute for Petrochemical Synthesis of the Academy of Science of the USSR, Moscow (USSR)

[1] Review of sulfur atoms as ligands in metal complexes: *H. Vahrenkamp*, Angew. Chem. *87*, 363 (1975); Angew. Chem. Int. Ed. Engl. *14*, 322 (1975); review of metal pentanedithionates: *S. W. Schneller*, Int. J. Sulfur Chem. *B7*, 295 (1972).

[2] *N. Lozac'h*, Adv. Heterocycl. Chem. *13*, 161 (1971).

[3] *B. Bogdanović, M. Yus*, Angew. Chem. *91*, 742 (1979); Angew. Chem. Int. Ed. Engl. *18*, 681 (1979).

[4] *(3)* violet plates from benzene/pentane. Crystal data: $a = 12.063(1)$, $b = 15.728(2)$, $c = 8.704(1)$ Å, $\beta = 107.04(1)°$, space group $P2_1/c$, $Z = 4$, $\rho_{calc} = 1.63$ g cm^{-3}. Refinement of the structural model derived by direct methods converged with data corrected for absorption (1887 reflections, *hkl*, $\bar{h}kl$, 100 reflections unobserved) to $R = 0.039$; several hydrogen atoms could

be located and refined by a difference Fourier synthesis; for the methodology of measurement and calculation see: *D. J. Brauer, C. Krüger, P. J. Roberts, Y.-H. Tsay*, Chem. Ber. *107*, 3706 (1974). Lists of atomic parameters and structure amplitudes are available from the author (*C. K.*) on request.

[5] *F. Leung, S. C. Nyburg*, Chem. Commun. *1969*, 137; *L. K. Hansen, A. Hordvik*, Acta Chem. Scand. *27*, 411 (1973).

[6] *B. L. Barnett, C. Krüger*, J. Organomet. Chem. *77*, 407 (1974).

[7] We thank Professor *E. G. Hoffmann* and *G. Schroth* for recording and interpreting the ^{1}H-NMR data.

[8] *G. Wilke, B. Bogdanović, P. Hardt, P. Heimbach, W. Keim, M. Kröner, W. Oberkirch, K. Tanaka, E. Steinrücke, D. Walter, H. Zimmermann*, Angew. Chem. *78*, 157 (1966); Angew. Chem. Int. Ed. Engl. *5*, 151 (1966).

An *ortho*-Palladated Complex of 2,5-Diphenyl-1,6,6aλ^4-trithiapentalene

By *Borislav Bogdanović, Carl Krüger,* and *Paolo Locatelli*[*]

The previously reported reaction of 2,5-dimethyl-1,6,6aλ^4-trithiapentalene with bis(η^3-allyl)nickel leading to bis(η^3-allylnickel) 2,4,6-heptanetrithionediate[1] prompted us to investigate the reactivity of 1,6,6aλ^4-trithiapentalene towards other metallic and organometallic compounds.

2,5-Diphenyl-1,6,6aλ^4-trithiapentalene *(3)*[2] reacts with $PdCl_2$ in boiling methanol/benzene (10:1) in the presence of LiCl with loss of HCl to give a violet, air-stable complex *(1)* (yield 97%).

According to an X-ray crystal structure analysis[3], compound *(2)*, the triphenylphosphane adduct of *(1)* crystallizing from toluene, is a square-planar palladium complex (±0.05 Å) whose coordination geometry is determined by a Cl-, a P-, a S-, and a σ-bonded phenyl C-atom.

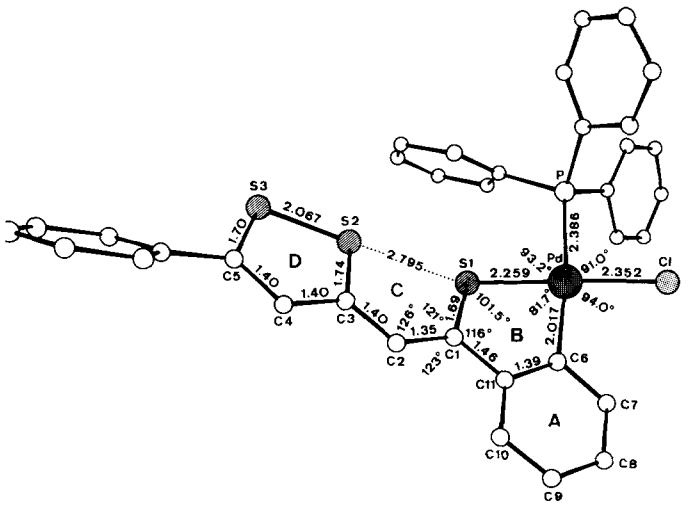
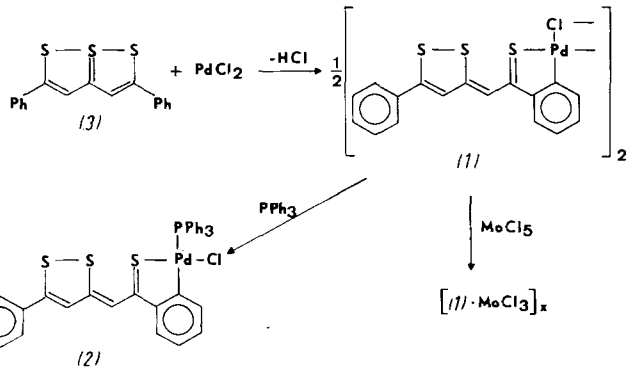


Fig. 1. Bond lengths [Å] and angles in the complex *(2)*.

The interaction of only one sulfur atom of the ligand with palladium leads to removal of the non-bonding resonance[4] in *(3)* and to rupture of a S—S bond. Whereas the S—S distances in *(3)* are 2.362 and 2.304[5], the S—S bond remaining in complex *(2)* is shortened to 2.067. This is accompanied by a disruption of the original planarity of the ligand with formation of planar (±0.01 Å) subunits (A, B, C, D; deviations from the best plane each ±0.01 Å) and an increase in the double bond character of the C1—C2 bond. The metallaheterocycle B is oriented along the S1—C6 vector (159°); the bond distances to the palladium correspond to those already reported in the literature[6].

By virtue of the structure of *(2)*, *(1)* is presumably a dimer with bridging chlorine atoms. The formation of *(1)* from *(3)* and $PdCl_2$ represents an example of the so-called *ortho*-metalation reaction[7] and can be compared with the *ortho*-palladation and -platination of diarylthioketones described by *Alper*[8].



Upon treatment of *(1)* with $PdCl_2$ in the presence of LiCl (molar ratio 1:1:3) in methanol/benzene (1:1) no reaction was observed even after five days' boiling under reflux. Thus, under analogous conditions as for the synthesis of *(1)*, palladation of the second phenyl group could not be accomplished. In contrast, reaction of *(1)* with $MoCl_5$ (molar ratio 1:1) in boiling toluene[9] quantitatively afforded a violet complex of the composition $[(1)\cdot MoCl_3]_x$ of presently unknown structure. Thus, the palladium compound *(1)* is suitable as starting material for the synthesis of complexes containing several different metal atoms.

Procedure[10]

Synthesis of *(1)*: To a suspension of *(3)* (3.10 g, 9.94 mmol)[2] in methanol (230 ml) and benzene (25 ml) was added 1.76 g (9.92 mmol) $PdCl_2$ and a solution of 1.33 g (31.3 mmol) LiCl in 20 ml methanol. The stirred suspension was heated for 3 h under reflux, and, after cooling to room temperature, the product was collected on a G3 filter. The mother liquor was shown to contain 93.6% of the liberated HCl by acidometric titration. The residue was washed with methanol and ether and dried at 10^{-3} torr; the yield of *(1)* (m.p. 304 °C, dec.) was 4.38 g (97%). *(1)* is soluble in pyridine, morpholine, and chloroform, but sparingly soluble in pentane, benzene, ether, ethanol, and tetrahydrofuran.

Synthesis of *(2)*: A mixture of *(1)* (0.36 g, 0.80 mmol) and triphenylphosphane (0.21 g, 0.80 mmol) in ether is stirred for 18 h at room temperature; the violet precipitate which is formed is filtered off, washed with ether, and dried at 10^{-3} torr. Yield of *(2)* (m.p. 203—205 °C): 0.50 g (87%).

Received: November 6, 1978 [Z 276c IE]
German version: Angew. Chem. *91*, 745 (1979)

CAS Registry numbers:
(1), 71328-64-8; *(2)*, 71264-59-0; *(3)*, 1033-90-5; $PdCl_2$, 7647-10-1

[*] Prof. Dr. B. Bogdanović, Priv.-Doz. Dr. C. Krüger, Dr. P. Locatelli [**]
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, D-4330 Mülheim-Ruhr 1 (Germany)

[**] Present address: Istituto di Chimica delle Macromolecole del C.N.R.
Via A. Corti 12, I-20133 Milano (Italy)

[1] *B. Bogdanović, C. Krüger, O. Kuzmin*, Angew. Chem. *91*, 744 (1979); Angew. Chem. Int. Ed. Engl. *18*, 683 (1979), and references cited therein.

[2] *E. Klingsberg*, J. Am. Chem. Soc. *85*, 3244 (1963).

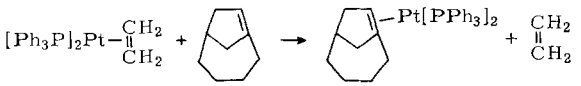
[3] Crystal data: $a = 10.004(1)$, $b = 13.826(3)$, $c = 15.534(2)$ Å, $\alpha = 65.35(1)$, $\beta = 81.69(1)$, $\gamma = 71.16(1)°$, $V = 1848$ Å^3, $Z = 2$, space group $P\bar{1}$, $\rho_{calc} = 1.52$ g cm^{-3}; 3426 reflections, 1757 unobserved, $R = 0.059$. The structural analysis was hampered by randomly disordered solvent (toluene) in the general position and about an inversion center. The solvent was included with partial occupation numbers in the final refinement of the structural model.

[4] *L. K. Hansen, A. Hordvik, L. J. Saethre*, J. Chem. Soc. Chem. Commun. *1972*, 222.
[5] *A. Hordvik*, Acta Chem. Scand. *25*, 1583 (1971).
[6] *D. L. Wheaver*, Inorg. Chem. 9, 2250 (1970); *M. A. Bennett, R. N. Johnson, G. B. Robertson, I. B. Tomkins, P. O. Whimp*, J. Am. Chem. Soc. *98*, 3514 (1976); *J. Dehaud, J. Fischer, M. Pfeffer, A. Mitschler, M. Zinius*, Inorg. Chem. *15*, 2675 (1976); *P. M. Maitlis*: The Organic Chemistry of Palladium. Vol. I. Academic Press, New York 1971, p. 38 and references cited therein.
[7] *G. W. Parshall*, Acc. Chem. Res. *3*, 139 (1970); *S. Trofimenko*, Inorg. Chem. *12*, 1215 (1973); *H.-P. Abicht, K. Issleib*, Z. Chem. *17*, 1 (1977); *M. I. Bruce*, Angew. Chem. *89*, 75 (1977); Angew. Chem. Int. Ed. Engl. *16*, 73 (1977).
[8] *H. Alper*, J. Organomet. Chem. *61*, C 62 (1973).
[9] The mixture was boiled under reflux for 2 h and then stirred for 20 h at 20 °C.
[10] We thank *Ursula Wilczok* for experimental assistance.

Metal Complexes of Bredt Olefins: Synthesis and Structure of Bicyclo[4.2.1]non-1(8)-enebis(triphenylphosphane)platinum(0)[**]

By *Erich Stamm, Konrad B. Becker, Peter Engel, Otto Ermer,* and *Reinhart Keese*[*]

Bredt olefins[1] derived from *trans*-cyclohexene or *trans*-cycloheptene[2] have been detected as labile intermediates[3], yet they have never been studied in detail. Because of their unusual structural and chemical properties we decided to check whether Bredt olefins can be reversibly stabilized with transition-metal compounds[4]. We have investigated the reaction of ethylenebis(triphenylphosphane)platinum(0) *(1)* with bicyclo[4.2.1]non-1-(8)-ene *(2)*, a Bredt olefin of the *trans*-cyclooctene series stable at room temperature, to give the complex *(3)* (see Procedure).



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

The structure of *(3)* was determined by X-ray crystallography[5] (Fig. 1). The bridgehead double bond is bound on the *exo* side to the bis(triphenylphosphane)platinum. The platinum atom is almost planar coordinated; the angle between the P1—Pt—P2 and C1—Pt—C8 planes is 6° (cf. [6, 4c]). The most important bond lengths are: Pt—P1 = 2.30, Pt—P2 = 2.26, Pt—C1 = 2.16 and Pt—C8 = 2.11 Å. The length of the bridgehead double bond C1—C8 (1.41 Å) is comparable with that observed in other complexed olefins of this type (*e.g. (1)*: 1.43 Å)[6a].

The conformation of bicyclo[4.2.1]non-1(8)-ene in the crystalline platinum complex *(3)* corresponds to the energetically preferred conformation[7] of the free olefin *(2)* as obtained by force field calculations. In Figure 1 the double-bond geometry observed in the crystalline complex *(3)* is compared with that calculated for the free olefin. As can be expected from the back-bonding influence of platinum(0) on the olefinic double bond, the torsional angle C2—C1=C8—C7 in the complex *(3)* (124°) is smaller than the value calculated for the free olefin *(2)* (136.5°). The increased pyramidal character at the olefinic bridgehead, *i.e.* the angle between the C1, C2, C8 and C1, C8, C9 planes ("out-of-plane bending" parameter, see [7]) is also in accord with this observation: The value found for this angle in *(3)* (39°) is greater than the value (33.3°) calculated for the corresponding angle in *(2)*. X-ray structure analysis is not accurate enough to provide more detailed information.

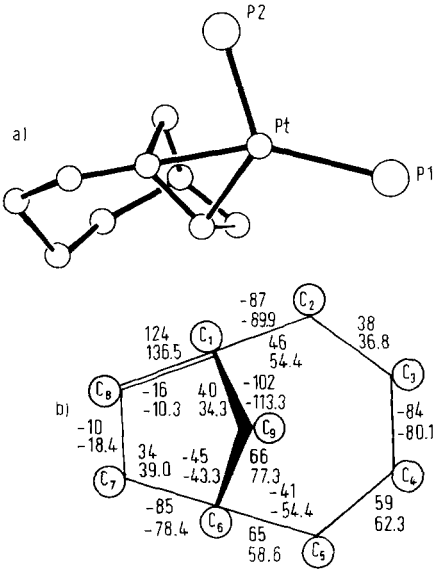


Fig. 1. a) Structure of bicyclo[4.2.1]non-1(8)-enebis(triphenylphosphane)platinum(0) *(3)* (phenyl groups not shown); b) torsion angles [°] in bicyclo[4.2.1]non-1(8)-ene *(2)*. Upper values: measured in complex *(3)*; lower values: calculated [7] for the free olefin *(2)*.

The complex *(3)* is stable at room temperature; surprisingly however, at higher temperatures in solution a mixture of four isomeric bicyclo[4.2.1]nonenes is formed[8]. Isomer-free bicyclo[4.2.1]non-1(8)-ene is obtained from *(3)* in toluene by addition of carbon disulfide or tetracyanoethylene (TCNE). Further experiments have revealed that the stability of complexes of the general formula $[(C_6H_5)_3P]_2Pt$—L in solution increases along the series $L = H_2C{=}CH_2 < (C_6H_5)_3P < O_2 < (2) < CS_2 \approx$ TCNE.

Procedure

To a solution of *(1)* (0.56 g, 0.75 mmol) in toluene (30 ml) is added *(2)* (0.095 g, 0.75 mmol) at −60 °C[9]. After 1 hour the mixture is allowed to warm to 0 °C and then concentrated *in vacuo*. The residue is dissolved in 1:1 ethyl acetate/dichloromethane (*ca.* 3 ml) and chromatographed at −10 °C on 60 g aluminum oxide (Camag, neutral, activity I). Olefins are eluted with hexane, and the complex *(3)* with hexane/ethyl acetate (1:1). The main fraction is concentrated *in vacuo* at 0 °C; the residue crystallizes spontaneously from ether at 0 °C. A total of 0.328 g (52%) of *(3)* is obtained as pale yellow crystals[10].

Received: June 8, 1979 [Z 278 IE]
German version: Angew. Chem. *91*, 746 (1979)

CAS Registry numbers:
(1), 12120-15-9; *(2)*, 23057-35-4; *(3)*, 71302-37-9

[*] Prof. Dr. R. Keese [+], Dr. E. Stamm
Institut für organische Chemie der Universität
Freiestrasse 3, CH-3012 Bern (Switzerland)
Priv.-Doz. Dr. P. Engel
Mineralogisch-petrographisches Institut der Universität
CH-3012 Bern (Switzerland)
Priv.-Doz. Dr. K. B. Becker
Institut für organische Chemie der Universität
CH-4056 Basel (Switzerland)
Dr. O. Ermer
Abteilung für Chemie der Universität
D-4630 Bochum (Germany)
[+] Author to whom correspondence should be addressed.

[**] Delivered in part in a lecture at the Conference of the Schweizerische Chemische Gesellschaft, Geneva, October 9, 1976.—This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Projects 2.103-0.74, 2.560-0.76 and 2.627-0.76).

[1] For the definition of "Bredt olefin" and "bridgehead olefin" cf. [3], p. 568 and 528, respectively, footnote [***].

[2] a) *J. Bredt*, Ann. Acad. Sci. Fenn. *29*, 2, 15 (1927); b) *J. R. Wiseman, W. A. Pletcher*, J. Am. Chem. Soc. *92*, 956 (1970).

[3] *R. Keese*, Angew. Chem. *87*, 568 (1975); Angew. Chem. Int. Ed. Engl. *14*, 528 (1975).

[4] a) *Inter alia*, [2+4]-cycloadditions are also suitable for reversible stabilization; however, furan adducts of 1-norbornene are stable up to 260 °C: *R. Keese, E. P. Krebs*, Angew. Chem. *83*, 254 (1971); *84*, 540 (1972); Angew. Chem. Int. Ed. Engl. *10*, 262 (1971); *11*, 518 (1972); *E. P. Krebs*, Dissertation ETH No. 4994, Zürich 1972; b) for similar examples cf. *M. E. Jason, J. A. McGinnety, K. B. Wiberg*, J. Am. Chem. Soc. *96*, 6531 (1974); c) *M. E. Jason, J. A. McGinnety*, Inorg. Chem. *14*, 3025 (1975); d) $Fe(CO)_4$ complex of bicyclo[4.3.1]deca-1(9),7-diene: *M. v. Büren, H. J. Hansen*, Helv. Chim. Acta *60*, 2717 (1977).

[5] *(3)*, triclinic, space group P1; $d_m = 1.46$, $d_x = 1.53$ g/cm³; $Z = 2$; $a = 11.34(1)$, $b = 11.90(1)$, $c = 16.14(1)$ Å, $\alpha = 79.4(1)$, $\beta = 70.4(1)$, $\gamma = 67.2(1)°$. $R = 9.5\%$ for 6280 reflections (isotropic refinement). Standard deviation for bond lengths 0.1 Å, for bond angles 5°. The unit cell contains two independent molecules of *(3)*; the structural parameters of one molecule are unreliable (possibly due to disorder) and are not considered here.

[6] a) *P. T. Cheng, S. C. Nyburg*, Can. J. Chem. *50*, 912 (1972); b) *J. J. de Boer, D. Bright*, J. Chem. Soc. Dalton Trans. *1975*, 662.

[7] *O. Ermer*, Z. Naturforsch. *B 32*, 837 (1977).

[8] *E. Stamm, K. B. Becker, P. Engel, R. Keese*, Helv. Chim. Acta, in press.

[9] *K. B. Becker*, Helv. Chim. Acta *60*, 81 (1977).

[10] M.p. = 137—141 °C (dec.); R_f (aluminum oxide, ethyl acetate/hexane, 1:1) = 0.8; ^{1}H-NMR (D_8-toluene, 80 MHz, −20 °C, TMS): δ = 0.95—3.4 (*ca.* 14 H), 7.12 (s, 18 H), 7.68 (12 H), contains a small amount of ether; ^{13}C-NMR (25.2 MHz, −20 °C, TMS internal): δ = 25.9, 28.9, 36.4 (2C), 39.1, 41.2, 47.2, 63.6, 70.4, signals of the C_6H_5 groups overlapping with D_8-toluene signals; ^{31}P-NMR (40.5 MHz, −20 °C, $(CH_3O)_3P$ external): δ = 107.7 [P_a; $J(P_a\ Pt) = 3503$ Hz, $J(P_a\ P_b) = 54.4$ Hz], 108.4 [P_b; $J(P_b\ Pt) = 3292$ Hz]; MS: m/e = 262, 183, 154, 122, 93, 80 (100%), 79, 78, and (10× amplified) 841 (M^+), 719, 457.

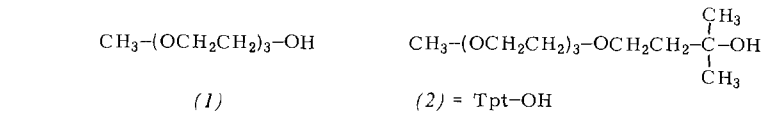
Solubilizing Acid-Labile Peptide Protecting Groups

By *Hermann Anzinger, Manfred Mutter*, and *Ernst Bayer*[*]

A central problem in the synthesis of polypeptides is the sparing solubility of larger peptides[1,2]. Particularly valuable as solubilizing protecting groups[2-5] are, *e.g.*, polyethylene glycol residues, which increase the solubility both in organic as well as in aqueous media[3,5].

For general application as amino acid protecting groups these solubilizing residues must be so modified that they can be cleaved off under the normal conditions of peptide synthesis. We describe here the first *O*-hydroxyalkylation of a primary alcohol to a tertiary alcohol [*(2)*] using triethyleneglycol monomethyl ether *(1)* as example. Acid-labile solubilizing protecting groups of the *tert*-butylcarboxyl and *tert*-butyloxycarbonyl type thus become accessible.

We synthesized *(2)* by addition of *(1)* to methyl vinyl ketone and subsequent Grignard reaction with CH_3MgI[6]. Direct reaction of *(1)* with epoxides[3,6] was unsatisfactory.

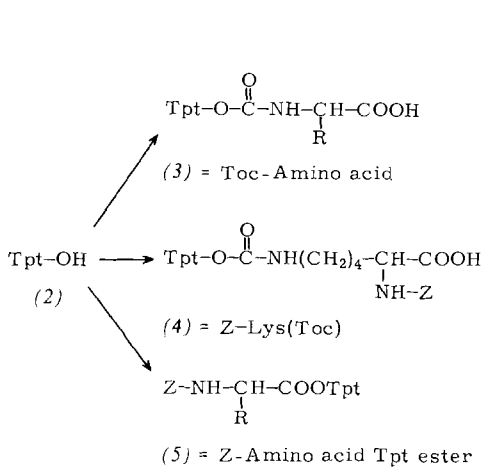


(1) *(2)* = Tpt–OH

The introduction of the Tpt–O–CO group ("Toc" group)[7] as acid-labile α-amino protecting group as in *(3)* or ε-amino protecting group of lysine as in *(4)* was achieved in high yields *via* the mixed carbonates[8]. The reaction of *N*-protected amino acids with *(2)* leading to the acid-labile Tpt esters *(5)* was accompanied by considerable racemization.

Investigations on model peptides showed that the Toc and Tpt groups are just about as acid-labile as the Boc and *t*-Bu groups, respectively. The new protecting group has already proven useful, especially in conformational studies[9].

[*] Prof. Dr. M. Mutter [+], Dipl.-Chem. H. Anzinger, Prof. Dr. E. Bayer
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)
[+] Author to whom correspondence should be addressed.



Procedure

Synthesis of *(2)*: *(1)* (8.2 g, 50 mmol) is treated with $NaOCH_3$ (81 mg, 1.5 mmol) and, after warming to 35 °C, methyl vinyl ketone (3.5 g, 50 mmol) is added dropwise to the stirred mixture such that the temperature remains constant. Stirring is continued for a further 2 h at 35 °C and the mixture neutralized with glacial acetic acid. The ketone is purified by column chromatography (silica gel); yield 4.8 g (41%) as colorless oil (characterization: ^{1}H-NMR).—A solution of the ketone (4.7 g, 20 mmol) in ether (40 ml) is treated with 40 mmol CH_3MgI. The resulting precipitate is filtered off and hydrolyzed with ice/NH_4Cl. The aqueous solution is washed with ether and then evaporated to dryness. The residue is digested with CH_2Cl_2/acetone (1/1) and filtered; the filtrate is dried over K_2CO_3, concentrated by evaporation, and purified by column chromatography (silica gel). 2.6 g (52%) of *(2)* is obtained as a colorless oil (characterization: ^{1}H-NMR).

Synthesis of *(3)*, R = CH_3: L-alanine (360 mg, 4.05 mmol) is dissolved in a 40% alcoholic solution of Triton B. After removal of solvent by evaporation the residue is stripped of water by azeotropic distillation with 2 × 10 ml dimethylformamide. The residue is taken up in 12 ml dimethylformamide, treated with 1.5 g Tpt-phenyl carbonate (4.05 mmol) and stirred for 3 h at 50 °C. The mixture is added to ice-water and washed three times with ether. The temperature is kept at 0 °C and the pH is adjusted to 2—3 with citric acid. The mixture is then saturated with NaCl, exhaustively extracted with CH_2Cl_2, and the combined extracts washed with NaCl solution, dried and evaporated down. The oil thus obtained is thin-layer chromatographically pure; yield 1.09 g (74%). Racemization test: <1% D-component (characterization: ^{1}H-NMR, elemental analysis).

Synthesis of *(5)*, R = H: 636 mg (3.04 mmol) of *Z*-glycine, 760 mg (3.04 mmol) of *(2)*, and 37 mg of 4-dimethylaminopyridine are dissolved in 5 ml of CH_2Cl_2. The solution is cooled to 0 °C and 3 mmol of dicyclohexylcarbodiimide (DCC) is added dropwise with stirring. After continued stirring for 0.5 h at 0 °C and 4 h at 25 °C, the mixture is filtered, the filtrate diluted with CH_2Cl_2, washed with dilute acetic acid (saturated with NaCl) and 5% $NaHCO_3$ solution (saturated with NaCl), dried, and evaporated down. Subsequent column chromatography (silica gel) affords 360 mg (27%) of *(5)*, R = H, as a colorless oil (characterization: ^{1}H-NMR, elemental analysis).

Received: April 9, 1979 [Z 279 IE]
German version: Angew. Chem. *91*, 747 (1979)

[1] *E. Wünsch*, Angew. Chem. *83*, 773 (1971); Angew. Chem. Int. Ed. Engl. *10*, 786 (1971).

[2] *A. Hubbuch, W. Danko, H. Zahn* in *M. Goodman, J. Meienhofer*: Peptides. Proceedings of the 5th American Peptide Symp. Wiley, New York 1977, p. 540.

[3] *Th. Wieland*, Acta Chim. Acad. Sci. Hung. *44*, 5 (1965).
[4] *I. G. Tesser, I. C. Balvert-Geers*, Int. J. Pept. Protein Res. *7*, 295 (1975); *H. Kunz*, Chem. Ber. *109*, 2670 (1976).
[5] *M. Mutter, E. Bayer*, Angew. Chem. *86*, 101 (1974); Angew. Chem. Int. Ed. Engl. *13*, 88 (1974).
[6] *H. Anzinger*, Diplomarbeit, Universität Tübingen 1978.
[7] Tpt is derived from *tert*-pentyl and triethylene glycol; Toc was formed in analogy to Boc.
[8] *P. Sieber, B. Iselin*, Helv. Chim. Acta *51*, 622 (1968).
[9] *H. Anzinger, M. Mutter*, Tetrahedron, in press.

Stereoselective Synthesis of *Z*-α,β-Unsaturated Aldehydes

By *Hans Jürgen Bestmann, Kurt Roth*, and *Manfred Ettlinger*[*]

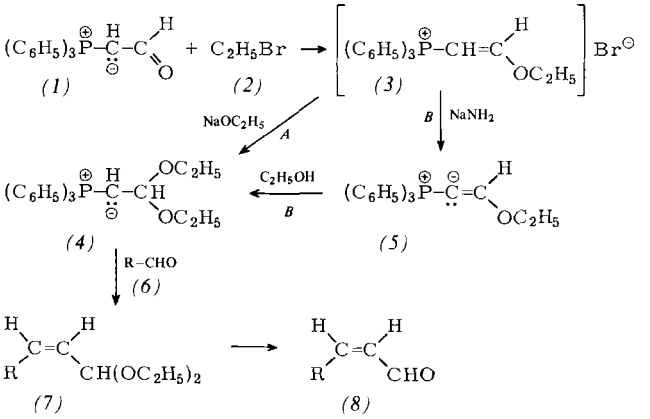
Dedicated to Professor Ernst Ruch on the occasion of his 60th birthday

Despite the variety of methods available for the synthesis of α,β-unsaturated carbonyl compounds[1], only limited success has been achieved with the preparation of the *Z*-α,β-unsaturated aldehydes *(8)*[2]. We describe here a generally applicable and extensively stereoselective method for the synthesis of compounds *(8)*.

Formylmethylenetriphenylphosphorane *(1)*[3] reacts with ethyl bromide *(2)* to give the vinylphosphonium salt *(3)*. Reaction of compound *(3)* with equimolar amounts of sodium ethoxide in anhydrous tetrahydrofuran affords the previously inaccessible[3,4] ylide *(4)*, which reacts with aldehydes *(6)* in a *Z*-stereoselective Wittig reaction to give the diethyl acetals *(7)* of the *Z*-α,β-unsaturated aldehydes (Method *A*); phosphorane *(1)*, on the other hand, reacts with *(6)* *E*-stereoselectively[3,5] (for an explanation of the different stereoselectivity see [6]).

The following variant often gives better yields of *(7)*:*(3)* is treated with sodium amide in liquid ammonia to give the phosphaallenylide *(5)* which is converted with an equimolar amount of anhydrous ethanol in ether into *(4)* and finally subjected to the Wittig reaction with aldehyde *(6)* (Method *B*).

Acetal-cleavage of *(7)* with catalytic amounts of *p*-toluenesulfonic acid in acetone/water (15 min at 0 °C; Method *C*) or with moist silica gel (2 days at room temperature; Method *D*)[7] affords the *Z*-α,β-unsaturated aldehyde *(8)*; the *Z*/*E* ratio was determined ^{1}H-NMR spectroscopically (cf. Table 1). The isomeric composition of *(7)* could not be determined, either by gas chromatography or by nuclear magnetic resonance.



Received: May 28, 1979 [Z 280 IE]
German version: Angew. Chem. *91*, 748 (1979)

CAS Registry numbers:
(1) (uncharged form), 2136-75-6; *(1)* (charged form), 71276-92-1; *(2)*, 74-96-4; *(3)*, 71276-93-2; *(4)* (uncharged form), 71276-94-3; *(4)* (charged form), 71276-95-4; *(5)* (uncharged form), 71276-96-5; *(5)* (charged form), 71276-97-6; *(6)* (R = *t*-C_4H_9), 630-19-3; *(6)* (R = CH_3 $(CH_2)_4$), 66-25-1; *(6)* (R = CH_3 $(CH_2)_7$), 124-19-6; *(6)* (R = CH_3 $(CH_2)_9$), 112-44-7; *(6)* (R = CH_2=CH $(CH_2)_8$), 112-45-8; *(6)* (R = CH_3 CO O $(CH_2)_8$), 29541-97-7; *(6)* (R = C_6H_5), 100-52-7; *(6)* (R = *p*-CH_3 C_6H_4), 104-87-0; *(6)* (R = *p*-CH_3 O C_6H_4), 123-11-5; *(6)* (R = 3,4,5-$(CH_3O)_3$ C_6H_2), 86-81-7; *(6)* (R = 2-furyl), 98-01-1; *(7)* (R = *t*-C_4H_9), 71276-98-7; *(7)* (R = CH_3 $(CH_2)_4$), 16387-56-7; *(7)* (R = CH_3 $(CH_2)_7$), 71276-99-8; *(7)* (R = $CH_3(CH_2)_9$), 13043-66-8; *(7)* (R = CH_2 CH $(CH_2)_8$), 71277-00-4; *(7)* (R = CH_3 CO O $(CH_2)_8$), 71307-94-3; *(7)* (R = C_6H_5), 7148-78-9; *(7)* (R = *p*-CH_3 C_6H_4), 71277-01-5; *(7)* (R = *p*-CH_3 O C_6H_4), 71277-02-6; *(7)* (R = 3,4,5-$(CH_3O)_3$ C_6H_2), 71277-03-7; *(7)* (R = 2-furyl), 71277-04-8; *(Z)-(7)* (R = *t*-C_4H_9), 22597-47-3; *(E)-(7)* (R = *t*-C_4H_9), 22597-46-2; *(Z)-(7)* (R = CH_3 $(CH_2)_4$), 20664-46-4; *(E)-(7)* (R = CH_3 $(CH_2)_4$), 2548-87-0; *(Z)-(7)* (R = CH_3 $(CH_2)_7$), 71277-05-9; *(E)-(7)* (R = CH_3 $(CH_2)_7$), 53448-07-0; *(Z)-(7)* (R = CH_3 $(CH_2)_9$), 71277-06-0; *(E)-(7)* (R = CH_3 $(CH_2)_9$), 7069-41-2; *(Z)-(7)* (R = CH_2 CH $(CH_2)_8$), 71277-07-1; *(E)-(7)* (R = CH_2=CH $(CH_2)_8$), 71277-08-2; *(Z)-(7)* (R = CH_3 CO O $(CH_2)_8$), 71277-09-3; *(E)-(7)* (R = CH_3 CO O $(CH_2)_8$), 63024-89-5; *(Z)-(7)* (R = C_6H_5), 57194-69-1; *(E)-(7)* (R = C_6H_5), 14371-10-9; *(Z)-(7)* (R = *p*-CH_3 C_6H_4), 71277-10-6; *(E)-(7)* (R = *p*-CH_3 C_6H_4), 56578-35-9; *(Z)-(7)* (R = *p*-CH_3O C_6H_4), 71277-11-7; *(E)-(7)* (R = *p*-CH_3O C_6H_4), 24680-50-0; *(Z)-(7)* (R = 3,4,5-$(CH_3O)_3C_6H_2$), 71277-12-8; *(E)-(7)* R = 3,4,5-$(CH_3O)_3$ C_6H_2), 71277-13-9; *(Z)-(7)* (R = 2-furyl), 71277-14-0; *(E)-(7)* (R = 2-furyl), 39511-08-5

[1] Novel methods for the synthesis of α,β-unsaturated aldehydes: *A. I. Meyers et al.*, J. Org. Chem. *38*, 36 (1973); *E. J. Corey, D. Enders, M. G. Bock*, Tetrahedron Lett. *1976*, 7; *V. Reutrakul, W. Kanghae, ibid. 1977*, 1377; *R. H. Wollenberg, K. F. Albizati, R. Peries*, J. Am. Chem. Soc. *99*, 7365 (1977), and references cited therein.
[2] *R. A. Raphael, F. Sondheimer*, J. Chem. Soc. *1951*, 2693; *G. Gamboni, V. Theus, H. Schinz*, Helv. Chim. Acta *38*, 255 (1955); *D. A. Thomas, W. K. Warburton*, J. Chem. Soc. *1965*, 2988; *N. Ya. Grigorieva, A. V. Semenovskii*, Izv. Akad. Nauk SSSR, Ser. Khim. *1976*, 2644.
[3] *S. Trippett, D. M. Walker*, J. Chem. Soc. *1961*, 1266.
[4] *T. M. Cresp, M. V. Sargent, P. Vogel*, J. Chem. Soc. *1974*, 37.
[5] *H. J. Bestmann, O. Vostrowsky, H. Paulus, W. Billmann, W. Stransky*, Tetrahedron Lett. *1977*, 121.

Table 1. Acetals *(7)* and *Z*-α,β-unsaturated aldehydes *(8)* (Methods *A*—*D*, see text).

R	*(7)* Yield [%]		B.p. [°C/torr]	*(8)* Yield [%]	B.p. [°C/torr]	*Z*:*E*
t-C_4H_9		77 *B*	84—85/21	47 *D*	86—89/78	96:4
CH_3 $(CH_2)_4$	62 *A*	72 *B*	104/14	60 *C*	81—82/14	92:8
CH_3 $(CH_2)_7$	53 *A*	64 *B*	79—81/0.04	68 *C*	129—131/18	86:14
CH_3 $(CH_2)_9$		77 *B*	111/0.2	91 *C*	90—92/0.3	94:6
CH_2=CH $(CH_2)_8$		67 *B*	102—104/0.15	88 *C*	88/0.2	90:10
CH_3 COO $(CH_2)_8$	70 *A*		137—141/0.2	87 *C*	127—130/0.1	97:3
C_6H_5	65 *A*	86 *B*	140—142/20	94 *C*	49—51/0.1	95:5
p-CH_3 C_6H_4		57 *B*	156—158/20	87 *C*	88/0.5	92:8
p-CH_3O C_6H_4		79 *B*	107/0.3	98 *C*	97/0.15	95:5
3,4,5-$(CH_3O)_3C_6H_2$	45 *A*	71 *B*	140/0.2	88 *C*	[a]	87:13 [b]
2-Furyl	61 *A*	76 *B*	63/0.2	98 *C*	58/0.1	97:3

[a] M.p. 59—60 °C. [b] *Z*-isomer separable as forerunning zone by column chromatography on silica gel (ether), and obtainable in pure form after recrystallization from ligroin.

[*] Prof. Dr. H. J. Bestmann, Dipl.-Chem. K. Roth, Dr. Manfred Ettlinger
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestr. 42, D-8520 Erlangen (Germany)

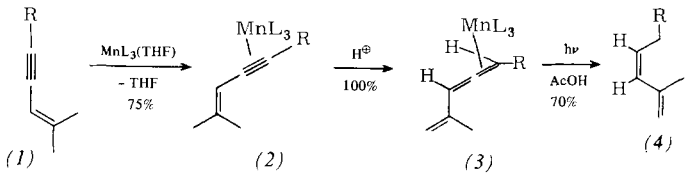
[6] *H. J. Bestmann* in: Actes du 1er congrès international sur les composés phosphorés. Oct. 1977, Rabat (Marocco) p. 519ff.; J. Pure Appl. Chem. *51*, 515 (1979).
[7] *F. Huet, A. Lechevallier, M. Pellet, J. M. Conia*, Synthesis *1978*, 63.

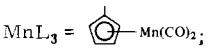
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0909-0687 $ 02.50/0*

Synthesis of Allenes from Electrophilic Acetylenes *via* Novel Allenemanganese Complexes[**]

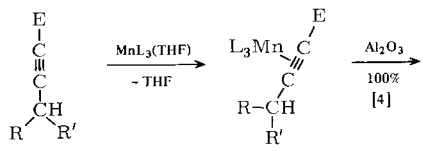
By *Michel Franck-Neumann* and *Francis Brion*[*]

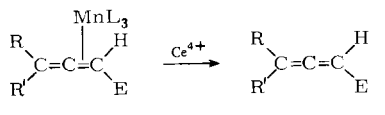
The hydrogenating photocleavage of organic ligands from their tricarbonyliron complexes[1] is already well-known. We have now found that dicarbonyl(methylcyclopentadienyl)manganese complexes of electrophilic acetylenes can very easily isomerize to allene complexes under the conditions of this reaction. Thus, *e.g.*, the manganese complex *(2)*, which is formed selectively from the enyne ester *(1)* and an irradiated tricarbonyl(methylcyclopentadienyl)manganese solution in tetrahydrofuran (THF), gives the isoprene derivative *(4)* [*Z*-isomer: NMR $J_{HH} = 11.0$ Hz; IR δ=CH 770 cm^{-1}] on irradiation in acetic acid. Compound *(4)* is formed *via* a primary isomerization of the vinylacetylene complex *(2)* to the (isolable) vinylallene complex *(3)*.

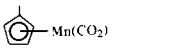


MnL_3 =  ; R = CO_2Me

The rearrangement *(2)*→*(3)* is formally a [1,5] hydrogen shift. The simpler [1,3] isomerization, *i.e.* the direct acetylene-allene rearrangement, proceeds just as readily; in this case most readily in the presence of basic aluminum oxide. Manganese complexes *(6)* of functionalized acetylenes *(5)*—esters, aldehydes, or ketones—are converted quantitatively into the allene complexes *(7)* in this way. Since their oxidative cleavage with iron(III) chloride, or better cerium(IV) ammonium nitrate, usually proceeds in excellent yields[2], this rearrangement constitutes a preparatively useful and novel method for the synthesis of allenes[3]. Table 1 lists some examples for the synthesis of mono-, di-, and trisubstituted allene derivatives *(8)* from the readily accessible electrophilic acetylenes *(5)*.





MnL_3 = 

[*] Prof. Dr. M. Franck-Neumann, F. Brion
Equipe de Recherche Associée au CNRS n° 687
Institut de Chimie de l'Université Louis Pasteur
1, rue Blaise Pascal, F-67008 Strasbourg (France)

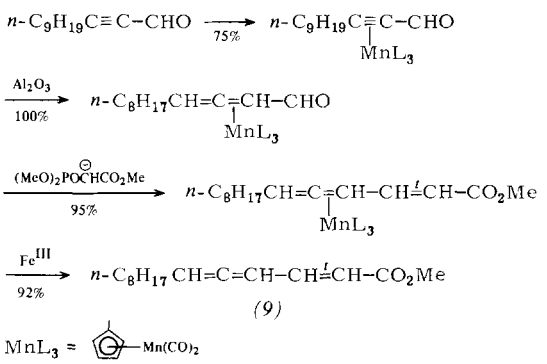
[**] This work was supported by the Délégation Générale à la Recherche Scientifique et Technique (Aide DGRST n° 77.7.0760).

Table 1. Acetylenemanganese complexes *(6)*, allenemanganese complexes *(7)* and allenes *(8)*.

	R	R'	E	*(6)* yield [%] [5]	*(8)* yield [%]	*(7)*, ^{1}H-NMR δ, *J* [b]
a	H	H	CO_2Et	70	81	2.66, t, 3 Hz
b [a]	*n*-C_4H_9	H	CO_2Me	75	95	2.67, d, 3 Hz
c [a]	*n*-C_5H_{11}	H	CHO	75	[2]	2.86, br. s
d	$(CH_2)_5$		$COCH_3$	70	72	2.71, br. s
e	$(CH_2)_5$		CHO	65	71	2.73, br. s

[a] *(7b)* and *(7c)* occur as chromatographically easily separable isomers.
[b] 90 MHz, C_6D_6, TMS; δ-values for the H atom α to E.

Special importance attaches to the complexes *(7)*, in which the allene is present as protected group. With these complexes reactions can be carried out successfully which with free allenes give only low yields. One example is the facile synthesis of the insect pheromone *(9)*, which contains a vinylallenyl moiety.



MnL_3 =

In contrast, with the free, less stable allenecarbaldehyde, which was accessible from nonanal (pelargonaldehyde) *via* a tedious method involving five steps[6], the Horner-Emmons reaction proceeded only with great difficulty (no yields quoted).

With exception of dicarbonyl(η-cyclopentadienyl)(6-methylene)manganese[7] the allenemanganese complexes *(7)* have not to our knowledge been previously reported. In the IR region of 1500—2500 cm^{-1} they show besides the absorptions of the carbonyl ligands (1992 and 1935 cm^{-1}) only bands which are due to the carbonyl groups of the substituents E (ester 1700 cm^{-1}, aldehyde 1665 cm^{-1}, ketone 1660 cm^{-1}). The ^{1}H-NMR spectra (90 MHz, C_6D_6, TMS) show in addition to the signals for the methylcyclopentadienyl group [1 singlet at δ = 1.40 (3 H) and 1 singlet (4 H) or 2 broad singlets (each 2H) between 3.86 and 4.08] and for the protons of the E, R and R' groups, a characteristic signal for the proton in the α-position to the substituent E whose chemical shift confirms the coordination at this double bond (Table 1).

Procedure

Synthesis of *(6)*: To a solution of 6.4 mmol $CH_3C_5H_4Mn(CO)_2(THF)$, prepared by UV irradiation of 1.40 g $CH_3C_5H_4Mn(CO)_3$ in 100 ml THF[8], is added 0.84 g (5.4 mmol) of methyl 2-octynoate *(5b)*. After 12 hours' stirring at room temperature and removal of solvent (water-pump vacuum), unreacted $CH_3C_5H_4Mn(CO)_3$ (0.30 g) and *(5b)* (0.15 g) are distilled off at 50 °C/10^{-2} torr. The residue is filtered through 10 g of silica gel. The orange zone of *(6b)* is eluted with petroleum ether/ether (6:1): yield 1.07 g (70%) [^{1}H-NMR (C_6H_6): δ = 2.79 (t, *J* = 7 Hz, CH_2 C≡C)].

Synthesis of *(7b)*: To a stirred solution of *(6b)* (1.0 g, 2.9 mmol) in diethyl ether (100 ml) under inert gas is added 50 g

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0909-0688 $ 02.50/0

of basic aluminum oxide (activity I, Merck). After 6 hours' stirring at room temperature the aluminum oxide is filtered off and extracted several times with chloroform. After removal of the solvents the isomeric mixture *(7b)* is obtained quantitatively as a yellow oil, which can be separated by chromatography on silica gel [^{1}H-NMR (C_6D_6): $\delta = 6.09$ for the one isomer and 6.83 for the other (t, $J = 7$ Hz; d, $J = 3$ Hz; 4H)], though this is not necessary for the next step, *i.e.* for the synthesis of *(8b)*.

Synthesis of *(8b)*: A solution of cerium(IV) ammonium nitrate (9.0 g) in acetone (120 ml) is added dropwise (*ca.* 1 h) to a solution of *(7b)* (1.0 g) in acetone (50 ml) at 0 °C. The mixture is stirred for 0.5 h, treated with 200 g of ice and extracted twice with ether. The extracts are evaporated down and the residue taken up in ether again, washed with water and dried over $MgSO_4$. After removal of solvent the residue is dissolved in hexane and filtered through a small amount of Florisil: yield 0.42 g (95%) pure *(8b)*.

Received: June 5, 1979 [Z 281 IE]
German version: Angew. Chem. *91*, 736 (1979)

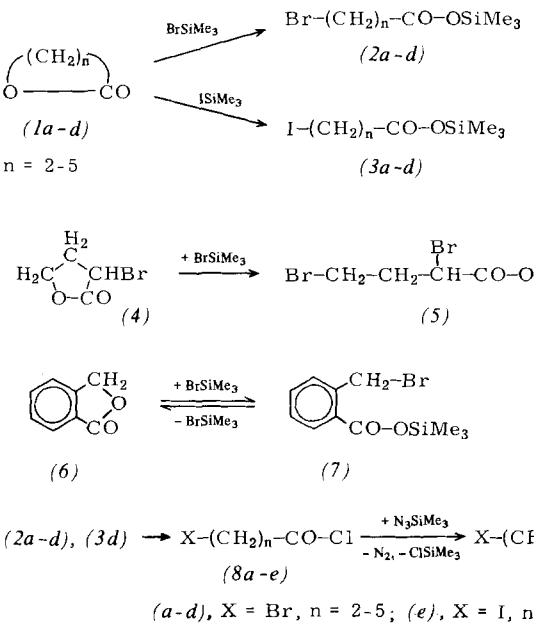
CAS Registry numbers:
(5a), 4341-76-8; *(5b)*, 111-12-6; *(5c)*, 1846-69-1; *(5d)*, 10564-83-7; *(6a)*, 71250-41-4; *(6b)*, 71276-88-5; *(6c)*, 71250-40-3; *(6d)*, 71250-39-0; *(7a)*, 71250-38-9; *(7b)*, 71250-37-8; *(7c)*, 71250-36-7; *(7d)*, 71250-35-6; *(8a)*, 14369-81-4; *(8b)*, 71277-73-1; *(8c)*, 71250-11-8; *(8d)*, 71250-12-9; *(9)*, 50320-90-6; *n*-$C_9H_{19}C{\equiv}C{-}CHO$, 71250-13-0; MnL_3(*n*-$C_9H_{19}C{\equiv}C{-}CHO$), 71250-34-5; MnL_3(*n*-$C_8H_{17}CH{-}C{-}CH\ CHO$), 71276-86-3; MnI_3(*n*-$C_8H_{17}CH{=}C{=}CH\ CH{=}CH\ CO_2Me$), 71250-33-4; $CH_3C_5H_4Mn(CO)_3$, 12108-13-3; $CH_3C_5H_4Mn(CO)_2(THF)$, 51922-84-0

[1] *M. Franck-Neumann, D. Martina, F. Brion*, Angew. Chem. *90*, 736 (1978); Angew. Chem. Int. Ed. Engl. *17*, 690 (1978).
[2] Esters are cleaved almost quantitatively with iron(III) chloride, while in the case of ketones the use of cerium(IV) ammonium nitrate, which is more gentle, is necessary. Allenealdehydes can be isolated only when they are highly substituted: *M. Bertrand, G. Gil, J. Viala*, Tetrahedron Lett. *1979*, 1595; *J. C. Clinet, G. Linstrumelle*, Nouv. J. Chim. *1*, 373 (1977), and references cited therein.
[3] Direct acetylene-allene isomerization by bases is usually only of preparative importance in the case of electrophilic, homoconjugated derivatives; these are transformed into conjugated allenecarbonyl compounds. Even in this case the yields are often poor; see *R. J. Bushby*, Q. Rev. Chem. Soc. *24*, 585 (1970).
[4] The rate of isomerization strongly depends upon substituents E; thus, the isomerization at a weight to weight ratio of 1:50 (complex *(6)*: Al_2O_3) is complete in 15 min (E = CHO), 45 min (E = $COCH_3$) and 5—6 h (E = CO_2R).
[5] In the case of acetylene esters or ketones a 20% excess of $MeC_5H_4Mn(CO)_2(THF)$ is suitable, whereas in the case of acetylene aldehydes substoichiometric quantities of this reagent are necessary.
[6] *P. D. Landor, S. R. Landor, S. Mukasa*, Chem. Commun. *1971*, 1638.
[7] This compound was obtained by direct reaction of the ligand with $C_5H_5Mn(CO)_2(THF)$: *F. Edelmann, U. Behrens*, J. Organomet. Chem. *128*, 131 (1977).
[8] Pyrex glass apparatus; 15 °C; mercury high-pressure lamp (Philips HPK 125); under argon; *ca.* 2 h.

Ring-Opening of Lactones and Cyclic Carbonates with Bromo- or Iodotrimethylsilane

By *Hans R. Kricheldorf*[*]

It is known that iodotrimethylsilane is capable of cleaving acyclic, aliphatic esters[1,2], whereas bromotrimethylsilane fails to react. We have now found that the lactones *(1a—d)* and *(4)* undergo complete ring-opening on treatment with bromotrimethylsilane, while in the case of *(6)* only equilibrium with *ca.* 30% *(7)* is achieved. Iodotrimethylsilane also cleaves the lactones *(1a—d)*. The silyl esters of ω-bromo- and ω-iodocarboxylic acids *(2a—d)*, *(3a—d)*, and *(5)* are useful alkylating reagents, affording access to a wide range of compounds including ω-hydroxy-, ω-mercapto-, and ω-amino acid derivatives. Moreover, the esters of type *(2)*, *(3)*, and *(5)* can be converted with thionyl chloride directly into ω-halocarbonyl chlorides, *e.g.* *(8a—e)*. Of the numerous possible reactions of these acid chlorides we mention here the reaction with trimethylsilyl azide, which leads to the otherwise scarcely accessible ω-haloalkyl isocyanates *(9a—e)*. Table 1 lists the physical data of some of these compounds. The acid chlorides *(8a—c)* and the isocyanates *(9a—e)* are of interest not only for preparative organic chemistry but also for the synthesis and modification of polymers.



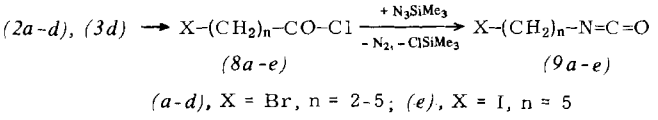


Table 1. Yield and physical data of ω-halocarboxylic acid derivatives, ω-bromoalkyl isocyanates, and ω-bromoalkoxysilanes.

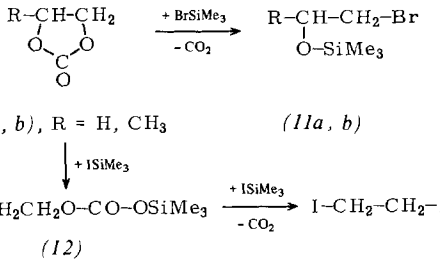
Cpd.	Yield [%]	n_D^{20}	B.p. [°C/mbar]
(2a)	79	1.4453	75—76/12
(2b)	86	1.4489	87—89/11 45—47/0.1
(2c)	90	1.4522	54—56/0.03
(2d)	96	1.4541	75—77/0.07
(8a)	92	1.4939	49—51/12
(8b)	95	1.4896	70—71/12
(8c)	87	1.4913	43—45/0.2
(8d)	98	1.4877	60—62—0.3
(9a)	82	1.4838	44—46/12
(9b)	87	1.4840	65—66/12
(9c)	81	1.4842	84—86/12
(9d)	91	1.4861	56—58/0.1
(3a)	81	1.4799	39—41/0.2
(5)	84	1.4816	68—70/0.07
(11a)	84	1.4362	34—36/12
(11b)	79	1.4431	35—37/12

Cyclic carbonates can also be opened by bromotrimethylethylsilane, but the intermediary silyl carbonates immediately decarboxylate. In the case of *(10b)* ring-opening to *(11b)* is more than 95% regioselective. Since cyclic carbonates can readily be obtained from 1,2- and 1,3-diols, 1,2- and 1,3-disubstituted compounds containing two different reactive functions are accessible from them *via* this route. Iodotrimethylsilane reacts with cyclic and acyclic carbonates to give alkyl iodides. If ethylene carbonate is allowed to react with double the molar amount of iodotrimethylsilane in the cold, the initially formed carbonate *(12)* is attacked by the excess of $ISiMe_3$ before it decarboxylates; 1,2-diiodoethane is

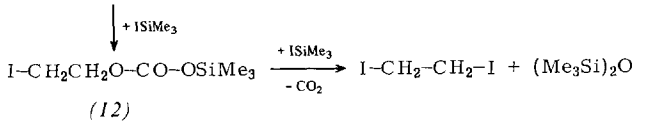
[*] Dr. H. R. Kricheldorf
Institut für makromolekulare Chemie der Universität
Stefan-Maier-Strasse 31, D-7800 Freiburg (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0909-0689 $ 02.50/0*

formed as main product. This reaction course and the strongly exothermic reaction with lactones indicate that iodotrimethylsilane is considerably more reactive than bromotrimethylsilane.

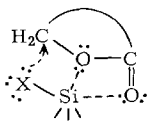


(10a, b), R = H, CH_3 *(11a, b)*



(12)

Sultones react neither with bromo- nor with iodotrimethylsilane, even though they are better alkylating reagents than lactones or carbonates. Since, however, the sulfonyl oxygen atoms are poorer nucleophiles than carbonyl oxygen atoms, we believe that the ring-opening of lactones and carbonates proceeds *via* a cyclic transition state *(13)*, in which the carbonyl oxygen is complexed by silicon *via* the vacant d-orbitals.



(13)

Procedure

Synthesis of trimethylsilyl 6-bromohexanoate *(2d)*: A mixture of 1 mol ε-caprolactone and 1.2 mol bromotrimethylsilane[3] is heated for *ca.* 10 h at 100 °C and *ca.* 30 h at 120 °C (or after addition of 20 ml CCl_4 heated under reflux for 30 h). *(2d)* is then isolated by distillation.—In the case of α-bromo-γ-butyrolactone *(4)* the reaction time must be prolonged; with β-propiolactone *(1a)* *ca.* 8 h suffices.

Synthesis of 6-bromohexanoyl chloride *(8d)*: A mixture of 1 mol *(2d)* and 1.1 mol distilled thionyl chloride in 250 ml anhydrous chloroform is heated to boiling until evolution of SO_2 ceases (*ca.* 4 h); *(8d)* is then isolated by distillation.—The reaction of *(8d)* with trimethylsilyl azide is carried out in chloroform or benzene[4].

Received: May 30, 1979 [Z 282 IE]
German version: Angew. Chem. *91*, 749 (1979)

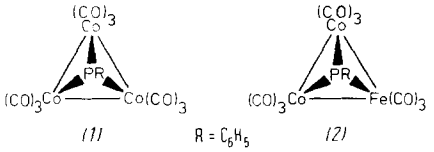
[1] *T.-L. Ho, G. Olah*, Angew. Chem. *88*, 847 (1976); Angew. Chem. Int. Ed. Engl. *15*, 774 (1976); cf. also *G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra, ibid. 91*, 648 (1979) and *18*, 612 (1979), respectively.
[2] *M. E. Jung, M. Lyster*, J. Am. Chem. Soc. *99*, 968 (1977).
[3] *P. A. Mccuskey, E. L. Reilly*, J. Am. Chem. Soc. *75*, 1503 (1953).
[4] *H. R. Kricheldorf*, Synthesis *1972*, 551.

Experiments on the HOMO-LUMO Nature of Metal-Metal Bonds[**]

By *Harald Beurich, Thomas Madach, Felix Richter,* and *Heinrich Vahrenkamp*[*]

Dedicated to Professor Lawrence F. Dahl

The results of theoretical studies on metal-metal interactions range from the prediction of maximum bond energies[1] to the ascertainment of the absence of a direct bond[2]. Verification of such predictions is often just as difficult as the critical evaluation of the calculational procedures employed[3]. Experimental investigations are usually limited to isolated measurements on individual compounds[3]. Synthesis of the phosphorus-bridged trinuclear cluster *(2)*[4] has now made it possible to compare the results of *different* experimental methods for *(1)*[5] and *(2)*.



(1) R = C_6H_5 *(2)*

The cluster *(1)* contains one more electron than required by the 18-electron rule. On replacement of a cobalt atom by iron, however, all the metal atoms in *(2)* have closed electron shells. The nature of the excess unpaired electron in the HOMO of *(1)* becomes clear in a crystallographic comparison of *(1)* and *(2)*[6]: it is antibonding with respect to the metal-metal interaction. For, as in the corresponding complexes with sulfur atoms as bridging ligands[7], the metal-metal distances in *(2)* are shorter by *ca.* 10 pm than in *(1)* with essentially the same molecular geometry (cf. Fig. 1).

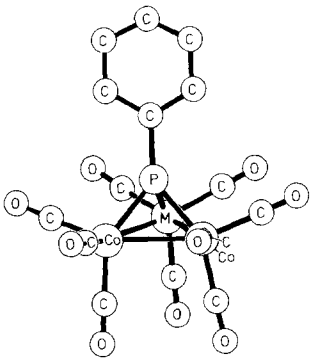


Fig. 1. Molecular structure of the clusters *(1)* (M = Co) and *(2)* (M = Fe). Principal bond lengths in *(1)*: Co Co = 271.2(3), 271.4(3), and 272.5(2); CO P = 212.3(4), 212.7(4), and 213.4(3); in *(2)*: Co Co = 263.2(2); Fe Co = 262.1(2) and 261.6(2); Co P = 212.0(2) and 212.2(2); Fe P = 216.2(3) pm.

This result is supplemented by the redox behavior of the two clusters. Only the oxidation of *(1)* to the monocation and the reduction of *(2)* to the monoanion can be observed as chemically and electrochemically reversible processes. Attempts at further oxidation led to destruction of the complexes. This means that occupation of the first antibonding orbital (*i.e.* the HOMO in *(1)* and the LUMO in *(2)*) does not effect decomposition but that this is brought about by an emptying of the highest bonding orbital (*i.e.* the HOMO in $(1)^{\oplus}$ and *(2)*). Since metal-metal single bonds number among the weakest bonds[3], it appears reasonable to assign essentially bonding metal-metal interactions to the HOMOs in $(1)^{\oplus}$ and *(2)*.

The ESR spectra (Fig. 2) supply further information about the first antibonding MOs of *(1)* and *(2)*. The 22-line pattern recorded for *(1)* demonstrates the interaction of the unpaired electron with all three cobalt atoms, and the 15-line pattern obtained for $(2)^{\ominus}$ reveals the corresponding interactions with the two cobalt atoms[8]. The good agreement of the HFS constants confirms the similarity of the two HOMOs. The most important result in both cases, however, is the absence of coupling with the phosphorus atom. The resolution of the ESR spectra is such that this coupling constant must be smaller than 1—2 gauss to escape detection. We have thus ob-

[*] Prof. Dr. H. Vahrenkamp, Dipl.-Chem. H. Beurich, Dipl.-Chem. T. Madach, Dipl.-Chem. F. Richter
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Rechenzentrum der Universität Freiburg. We are grateful to the Physical Chemistry Institute of this University for the possibility of conducting ESR measurements.

tained experimental proof that the HOMO of *(1)* and the LUMO of *(2)* are practically exclusively combinations of metal d-orbitals. This conclusion was also reached by *Dahl et al.* for $SCo_3(CO)_9$[9] but could not be verified because the normal sulfur atom does not have a nuclear spin.

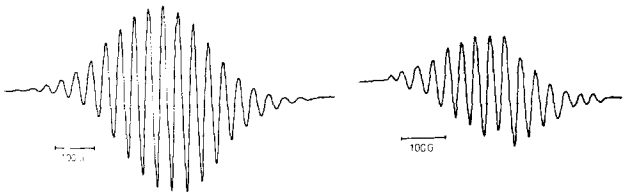


Fig. 2. ESR spectra of *(1)* and the anion of *(2)* in heptane/tetrahydrofuran. HFS constants 32.8(2) G for *(1)* and 29.1(2) G for $(2)^{\ominus}$.

The results of the crystallographic, electrochemical, and ESR measurements are consistent. They support the qualitative concept of significant energetic separation of metal-metal and metal-ligand bonding. The proven HOMO-LUMO nature of metal-metal interactions should be the starting point of an extensive and readily accessible chemistry of complexes having metal-metal bonds which has hardly been studied up to now.

Received: April 17, 1979 [Z 283 IE]
German version: Angew. Chem. *91*, 751 (1979)

[1] *F. A. Cotton, C. B. Harris,* Inorg. Chem. *6*, 924 (1967).
[2] *M. Bénard,* J. Am. Chem. Soc. *100*, 7740 (1978).
[3] Cf. *H. Vahrenkamp,* Angew. Chem. *90*, 403 (1978); Angew. Chem. Int. Ed. Engl. *17*, 379 (1978).
[4] *F. Richter, H. Beurich, H. Vahrenkamp,* J. Organomet. Chem. *166*, C 5 (1979); *J. C. Burt, G. Schmid,* J. Chem. Soc. Dalton Trans. *1978*, 1385.
[5] *L. Markó, B. Markó,* Inorg. Chim. Acta *14*, L 39 (1975).
[6] *(1):* monoclinic C2/c, $Z=8$, $a=1408.8(3)$, $b=813.2(1)$, $c=3377.3(6)$ pm, $\beta=96.42(2)°$; 2841 reflections, $R=0.073$.—*(2):* monoclinic, $P2_1/c$, $Z=4$, $a=804.6(2)$, $b=3373.6(5)$, $c=809.5(1)$ pm, $\beta=119.91(2)°$; 2566 reflections, $R=0.058$.
[7] *D. L. Stevenson, C. H. Wei, L. F. Dahl,* J. Am. Chem. Soc. *93*, 6027 (1971).
[8] Interaction with the iron atom, which has no nuclear spin, does not become evident in this measurement.
[9] *C. E. Strouse, L. F. Dahl,* Discuss. Faraday Soc. *47*, 93 (1969).

A New Synthesis of Carbonyl Selenide

By *Kiyoshi Kondo, Satoshi Yokoyama, Noritaka Miyoshi, Shinji Murai,* and *Noboru Sonoda*[*]

We wish to describe a novel, convenient, and high yield synthesis of carbonyl selenide (Se=C=O) by the low-temperature reaction of ammonium selenolcarbamates *(1)* with acids. Carbonyl selenide has previously been prepared by the reaction[1] of selenium with carbon monoxide at 500—700 °C or by the reaction[2] of aluminum selenide with phosgene at 210 °C. Both these known methods require complicated apparatus and suffer from low yields; the former leads to blockage of the apparatus with selenium. Hence the chemistry of carbonyl selenide[3] has hardly been studied in contrast to that of carbonyl sulfide[4].

We have already reported[5] that amines react with carbon monoxide in the presence of selenium under atmospheric pressure at room temperature to give ammonium selenolcarbamate *(1)* quantitatively:

$$2\,RR'NH + CO + Se \rightarrow \underset{(1)}{[RR'NH_2]^+[RR'N{-}C(O){-}Se]^-} \qquad (a)$$

[*] Dr. K. Kondo [†], S. Yokoyama, N. Miyoshi, Prof. Dr. S. Murai, Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University
Suita, Osaka 565 (Japan)
[†] Author to whom correspondence should be addressed.

Cautious addition of this intermediate salt *(1)* to a tetrahydrofuran (THF) solution of strong acid at −78 °C (see Experimental) gives carbonyl selenide[6]:

$$H^+ (\text{excess}) + (1) \rightarrow SeCO + 2\,RR'NH_2^+ \qquad (b)$$

The results of the synthesis of carbonyl selenide from various ammonium selenolcarbamates *(1)* prepared *in situ* using different acids are given in the Table 1.

Table 1. Synthesis of SeCO according to eq. (b). Compound *(1)* (5 mmol) is added at −78 °C to an excess of acid (50 mmol).

$[RR'NH_2]^+[RR'N\ C(O)\ Se]^-$	$RR'N$	Acid	Se=C=O Yield [%]
(1a)	Et_2N	H_2SO_4	98
		p-$CH_3\ C_6H_4\ SO_3H$	96
		H_3PO_4	88
		HCl	97
		C_6H_5COOH	11
		CH_3COOH	0
(1b)	n-Bu_2N	H_2SO_4	83
(1c)	Piperidino	H_2SO_4	90
(1d)	n-BuNH	H_2SO_4	98

Viewed experimentally, the reaction of *(1a)* with sulfuric acid represents the best choice. The low solubility of p-toluenesulfonic acid precludes its use for large scale syntheses; the high viscosity of phosphoric acid at low temperature might cause difficulty in stirring; the vapor of hydrochloric acid could contaminate the sample of carbonyl selenide.

Experimental

Synthesis of SeCO from *(1a)* produced *in situ:* Metallic selenium (0.4 g, 5 mmol), diethylamine (1.2 ml, 12 mmol), and THF (20 ml) are placed in a 50-ml flask and CO (30 ml/min) is passed through the resultant solution at room temperature with vigorous stirring over a period of one hour. A colorless, homogeneous THF solution of *(1a)* is obtained. This solution is then cautiously added dropwise to a mixture of sulfuric acid (2.5 ml) and THF (20 ml) at −78 °C in a nitrogen atmosphere. A white precipitate, probably diethylammonium sulfate, is formed. Subsequent distillation from the reaction vessel at −50 °C/5 torr directly into a tube cooled to −196 °C gives essentially pure carbonyl selenide containing a little THF. Trap-to-trap distillation affords pure SeCO. The yield (98%) was determined by reaction with n-butylamine (1.2 ml, 12 mmol) in THF (20 ml) at −78 °C and subsequent oxidation with oxygen at room temperature to give selenium (0.392 g, 4.9 mmol) and 1,3-di-n-butylurea (0.843 g, 4.9 mmol)[7]. Other combinations of salts *(1)* and acids were subjected to reaction under identical conditions.

Received: April 6, 1979 [Z 284a IE]
German version: Angew. Chem. *91*, 760 (1979)

[1] *T. G. Pearson, P. L. Robinson,* J. Chem. Soc. *1932*, 652.
[2] *O. Glemser, T. Risler,* Z. Naturforsch. *B 3*, 1 (1948).
[3] a) *A. B. Callear, W. J. R. Tyerman,* Proc. Chem. Soc. (London) *1964*, 296; b) *D. A. Stiles, W. J. R. Tyerman, O. P. Strausz, H. E. Gunning,* Can. J. Chem. *44*, 1677 (1966).
[4] a) *R. J. Ferm,* Chem. Rev. *57*, 621 (1957); b) *M. Shimizu,* Chem. Econ. Eng. Rev. *8*, 41 (1976).
[5] a) *N. Sonoda, T. Yasuhara, K. Kondo, T. Ikeda, S. Tsutsumi,* J. Am. Chem. Soc. *93*, 6344 (1971); b) *K. Kondo, N. Sonoda, S. Tsutsumi,* J. Chem. Soc. Chem. Commun. *1972*, 307; c) *K. Kondo, N. Sonoda, K. Yoshida, M. Koishi, S. Tsutsumi,* Chem. Lett. *1972*, 401.
[6] a) SeCO, IR: 2020 cm^{-1} (cf. [6b]); MS: $m/e=102$ (2.7%), 104 (20.3), 105 (17.0), 106 (49.8), 107 (4.6), 108 (100), 109 (3.7), 110 (18.6); b) *M. Bavia, G. D. Lonardo, G. Galloni, A. Trombetti,* J. Chem. Soc. Faraday Trans. II *68*, 615 (1972).
[7] *K. Kondo, S. Yokoyama, N. Miyoshi, S. Murai, N. Sonoda,* Angew. Chem. *91*, 761 (1979); Angew. Chem. Int. Ed. Engl. *18*, 692 (1979).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0909-0691 $ 02.50/0*

Reactions of Carbonyl Selenide with Amines and Aminoalcohols to Produce Ureas and Carbamates

By *Kiyoshi Kondo, Satoshi Yokoyama, Noritaka Miyoshi, Shinji Murai,* and *Noboru Sonoda*[*]

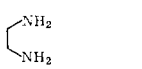
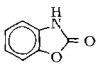
Carbonyl selenide (Se=C=O) has now become readily available by a new synthesis[1]. We have found that it is highly reactive towards nucleophiles such as amines and aminoalcohols, even at low temperature. The carbonylations described below are the first reported reactions of SeCO with organic compounds.

The reaction of carbonyl selenide with amines *(1)* proceeds even at $-78\,^{\circ}C$; subsequent oxidation gives urea derivatives *(2)* as well as selenium and water:

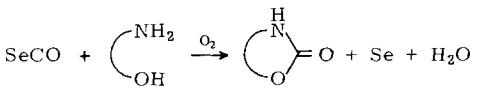
$$SeCO + 2\,RR'NH \xrightarrow{O_2} (RR'N)_2CO + Se + H_2O$$

(1) *(2)*

Table 1. Synthesis of ureas *(2)* by reaction of SeCO (5 mmol) with amines *(1)* (12 mmol) and synthesis of cyclic carbamates *(4)* by reaction of SeCO (5 mmol) with aminoalcohols *(3)* (12 mmol); each in tetrahydrofuran (THF) (5 ml) at $-78\,^{\circ}C$ and subsequent oxidation at room temperature. The yields are based on SeCO.

	Reactant		Product	Yield [%]
(1a)	*n*-$BuNH_2$	*(2a)*	$(n\text{-BuNH})_2CO$	100
(1b)	*c*-$C_6H_{11}NH_2$	*(2b)*	$(c\text{-}C_6H_{11}NH)_2CO$	98
(1c)	Me_2NH	*(2c)*	$(Me_2N)_2CO$	100
(1d)	$PhCH_2NH_2$	*(2d)*	$(PhCH_2NH)_2CO$	80
(1e)		*(2e)*		86
(1f)	NH_3	*(2f)*	$(NH_2)_2CO$	80
(1g)	$PhNH_2$	*(2g)*	$(PhNH)_2CO$	4
(3a)		*(4a)*		70
(3b)		*(4b)*		72
(3c)		*(4c)*		57

Results are shown in Table 1. Alkylamines and ammonia give excellent yields, while aromatic amines do not. The reaction of SeCO with *n*-butylamine could be used for quantitative determination of SeCO[1].



(3) *(4)*

The reaction of SeCO with aminoalcohols *(3)* under the same reaction conditions gives cyclic carbamates *(4)*. Selected results are shown in Table 1.

Experimental

Synthesis of *(2b):* A solution of cyclohexylamine (12 mmol, 1.19 g) in THF (5 ml) is added dropwise at $-78\,^{\circ}C$ to vigorously stirred SeCO (5 mmol) prepared as previously reported[1]. After warming the reaction mixture to room temperature and passage of air, precipitated selenium is filtered off. Evaporation of the filtrate gives essentially pure *(2b)* (1.1 g, 4.9 mmol; corresponding to 98% yield).—Liquified ammonia (1 ml) is treated with SeCO at $-78\,^{\circ}C$. All ureas except *(2c)* (liquid) are obtained as solids at room temperature.—Cyclic carbamates are synthesized under identical conditions. All the carbamates except *(4b)* (oil) are solids.—The ureas and carbamates were identified by spectroscopic comparison with authentic samples.

Received: April 30, 1979 [Z 284b IE]
German version: Angew. Chem. *91*, 761 (1979)

[1] *K. Kondo, S. Yokoyama, N. Miyoshi, S. Murai, N. Sonoda,* Angew. Chem. *91*, 760 (1979); Angew. Chem. Int. Ed. Engl. *18*, 691 (1979).

Existence of 1,2,3-Benzoxadiazole in the Gas Phase[**]

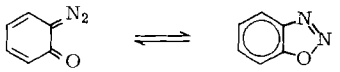
By *Reinhard Schulz* and *Armin Schweig*[*]

1,2,3-Oxadiazoles *(1a)*—in contrast to their thia- and aza-analogs *(1b)* and *(1c)*—are still unknown; so far only the valence isomeric dicarbonyl form has been described[1].



(1a) *(2)* *(1b)* *(1c)*

UV and IR investigations have given no indication of the existence of the 1,2,3-benzoxadiazole *(4)*[2], either in the solid state or in solution. We have now been able to show by UV photoelectron spectroscopy that 6-diazo-2,4-cyclohexadienone *(3)*[3] is formed in equilibrium with the benzoxadiazole *(4)* in the gas phase.



(3) *(4)*

The PE spectrum of *(3)* at $40 \pm 10\,^{\circ}C$ (Fig. 1) shows a weak band at 8.20 eV, which beyond doubt is to be assigned to the $^2A''$ (π) ionic state of the diazocarbonyl form. This follows from the comparison of the findings with a) the band position for the corresponding ionization in the isostructural and isoelectronic ketoketene *(5)* (8.43 eV)[4], b) earlier mass spec-

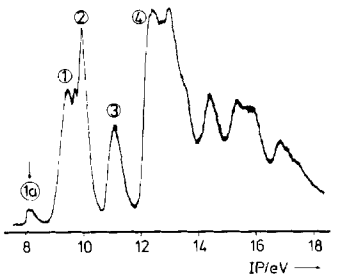


Fig. 1. He-I photoelectron spectrum of a mixture of 1,2,3-benzoxadiazole *(4)* and 6-diazo-2,4-cyclohexadienone *(3)* (80—90 and 10—20%, resp.) at $40 \pm 10\,^{\circ}C$. *(4)* predominates when crystalline *(3)* undergoes transition to the gas phase.

[*] Dr. K. Kondo [†], S. Yokoyama, N. Miyoshi, Prof. Dr. S. Murai, Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering, Osaka University
Suita, Osaka 565 (Japan)
[†] Author to whom correspondence should be addressed.

[*] Prof. Dr. A. Schweig, R. Schulz
Fachbereich Physikalische Chemie der Universität
Auf den Lahnbergen, D-3550 Marburg 1 (Germany)

[**] Part 83 of "Theory and Application of Photoelectron Spectroscopy". This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 82: *A. Schweig, N. Thon,* to be published.

troscopic measurements (8.26 eV)[5], and c) the results of CNDO/S-[6] and MNDO-[7] PERTCI[8] calculations (Fig. 2).

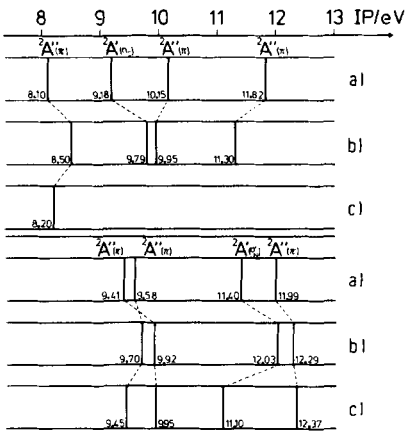


Fig. 2. Calculated CNDO/S- (a) and MNDO-PERTCI- (b) and measured (c) vertical ionization potentials of the valence isomers *(3)* (top) and *(4)* (bottom).

In the spectrum, a series of very much more intense bands starts at 9.45, 9.95, 11.10, 12.37 eV. On the basis of PERTCI calculations with MNDO-optimized molecular geometries (Fig. 2) we assign these bands to the benzoxadiazole *(4)*. The calculations fairly accurately reproduce the measured spectrum (exception: MNDO-$^2A'(\sigma_N)$ ionic state at 11.10 eV, which is about 0.9 eV too high in energy). The measured first ionization energy (9.45 eV), moreover, is in exceptionally good agreement with an estimated value (9.50 eV) quoted by other authors[5].



(5)

(6)

On heating the sample gas to 320 °C elimination of N_2 takes place with exclusive formation of 6-fulvenone *(6)*, whose spectrum contains no bands between 10 and 12 eV[4]. This finding proves that the intense bands observed above 9.45 eV in the spectrum shown in Figure 1 are not caused by a decomposition product of *(3)*.

From the relative band intensities of the ionization of diazocyclohexadienone (band 1a at 8.20 eV) and of benzoxadiazole (band 1 and successive bands)—assuming similar ionization cross-sections—it follows that in the gas phase at 40 ± 10 °C the product mixture consists of 80—90% *(4)* and only 10—20% *(3)*. This corresponds to a greater stability of the benzenoid structure of about 1 kcal/mol over that of the quinonoid structure.

Received: April 19, 1979 [Z 285 IE]
German version: Angew. Chem. *91*, 737 (1979)

[1] *M. Regitz:* Diazoalkane. Thieme, Stuttgart 1977.
[2] *L. A. Kazitsyna, B. S. Kikot, A. V. Upadysheva,* Russ. Chem. Rev. *35*, 388 (1966).
[3] *B. S. Kikot,* J. Gen. Chem. USSR *33*, 221 (1963).
[4] *R. Schulz, A. Schweig,* Tetrahedron Lett. *1979*, 59.
[5] *O. Thorstad, K. Undheim,* Chem. Scr. *6*, 222 (1974).
[6] *K.-W. Schulte, A. Schweig,* Theor. Chim. Acta *33*, 19 (1974).
[7] *M. J. S. Dewar, W. Thiel,* J. Am. Chem. Soc. *99*, 4899 (1977); *M. J. S. Dewar, M. L. McKee, H. S. Rzepa, ibid. 100*, 3607 (1978).
[8] *H. L. Hase, G. Lauer, K.-W. Schulte, A. Schweig,* Theor. Chim. Acta *48*, 47 (1978).

Tris(trichlorophosphoranediylamino)carbenium Hexachloroantimonate, $[C(N{=}PCl_3)_3]^+SbCl_6^-$

By *Ulrich Müller, Inge Lorenz,* and *Fritjof Schmock*[*]

The Staudinger reaction of organic azides with phosphanes leads to iminophosphoranes. We have utilized the corresponding reaction of triazidocarbenium hexachloroantimonate[1] with phosphorus trichloride to synthesize the title compound *(1)*; UV radiation was necessary for activation:

$$[C(N_3)_3]^+SbCl_6^- + 3\,PCl_3 \xrightarrow{h\nu} [C(N{=}PCl_3)_3]^+SbCl_6^- + 3\,N_2$$

(1)

(1) forms colorless crystals which are sensitive to hydrolysis; they are soluble in polar solvents such as acetonitrile. We have characterized *(1)* by elemental analysis, by IR and Raman spectra, and by X-ray structure analysis.

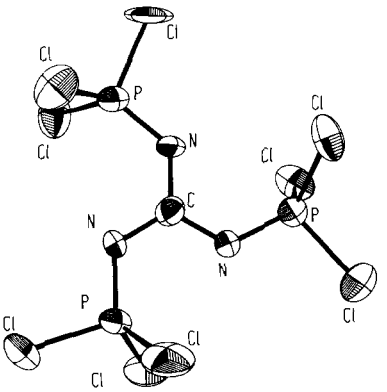


Fig. 1. Structure of the $[C(NPCl_3)_3]^+$ ion showing ellipsoids of thermal vibration (at 21 °C; 50% probability distribution).

The crystals of *(1)* are triclinic[2]. Neither the cation nor the anion is located in crystallographically defined symmetry positions. Nevertheless, a higher symmetry applies to both species to a good approximation: the $SbCl_6^-$ ion is octahedral, and the $[C(NPCl_3)_3]^+$ ion has almost C_{3h} symmetry (cf. Fig. 1). Mutually equivalent bonds are practically equal. The (averaged) C—N distance is 135 pm as in the guanidinium ion and comparable ions, corresponding to a 1⅓ bond. The P—N distance of 155 pm lies at the lower limit of the values found for λ^5-phosphazenes such as $(PNCl_2)_x$; it corresponds roughly to a P=N double bond. The averaged bond angles are: N—C—N 120°, C—N—P 123°, Cl—P—Cl 106°, N—P—Cl 116 and 106° (latter value for Cl in the plane of the molecule). Mean P—Cl distances: 196 pm.

In addition to the known bands of the $SbCl_6^-$ ion (IR: 335; Raman: 330, 285, 172 cm^{-1}), the vibrational spectrum contains the following bands: 1385 ($\nu_{as}C(N)_3$), 1016 and 1004 (νP—N), 750 (Raman, δNCN), 744 (IR, $\gamma C(N)_3$), nine bands between 647 and 450 (νP—Cl), further bands below 350 cm^{-1} (deformation modes); the bands are observed in the Raman and the IR spectra unless stated otherwise. The frequency of the P=N stretching vibrations (around 1000 cm^{-1}) suggests a weakened double bond.

Procedure

A solution of $[SbCl_4N_3]_2$ (*ca.* 3 g)[3] in CH_2Cl_2 (30 ml) is heated under reflux with CCl_4 (*ca.* 5 ml); $[C(N_3)_3]SbCl_6$ precipitates. The precipitate is filtered off after 12 h, washed

[*] Prof. Dr. U. Müller, I. Lorenz, F. Schmock
Fachbereich Chemie der Universität
Hans-Meerwein-Strasse, D-3550 Marburg 1 (Germany)

with CCl_4 (1—2 ×), and dissolved in 1,2-dichloroethane (80 ml) at 50 °C. Freshly distilled PCl_3 (5 ml) (previously freed from HCl by Fe powder) is added and the mixture irradiated at 40—50 °C with an immersed Hg lamp. After *ca.* 2 h, evolution of N_2 has ceased and the solution is evaporated down to ¼ of its volume. Addition of a small volume of acetonitrile and heptane leads to crystallization of *(1)*.—All operations must be conducted with exclusion of moisture and precautions usual for azides.

Received: April 20, 1979 [Z 286 IE]
German version: Angew. Chem. *91*, 735 (1979)

CAS Registry numbers:
(1), 21934-76-9; $[C(N_3)_3]^+ SbCl_6^-$, 12069-93-1; PCl_3, 7719-12-2

[1] *U. Müller, K. Dehnicke*, Angew. Chem. *78*, 825 (1966); Angew. Chem. Int. Ed. Engl. *5*, 841 (1966).

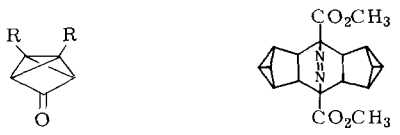
[2] Crystal data: space group $P\bar{1}$, $Z=2$, $a=904$, $b=1046$, $c=1307$ pm, $\alpha=94.8$, $\beta=88.3$, $\gamma=103.8°$; 1631 reflections, measured with $Mo_{K\alpha}$ radiation on a four-circle diffractometer, refined to $R=2.7\%$.

[3] *U. Müller*, Z. Anorg. Allg. Chem. *396*, 187 (1973).

Bonding in Bicyclo[1.1.0]butane Derivatives[**]

By *Hermann Irngartinger* and *Karl Ludwig Lukas*[*]

The bond between the two bridgehead atoms in bicyclo[1.1.0]butane exhibits properties of a CC multiple bond, though formally it is a single bond[1]. In order to investigate the dependence of the length of this bond on the interplanar angle δ between the two three-membered rings and its relationship to the hybridization state of the bridgehead atoms, we have determined the crystal and molecular structures of 1,5-diphenyltricyclo[2.1.0.$0^{2,5}$]pentan-3-one *(1)*[2] and of the analogous 1,5-dimethyl compound *(2)*[3], in whose bicyclobutane skeleton a smallest possible δ-angle ought to be reached by the short bridging of a carbonyl group. For comparison, we have also determined the structure of dimethyl 15,16-diazaoctacyclo[6.6.2.$0^{2,7}$.$0^{3,5}$.$0^{4,6}$.$0^{9,14}$.$0^{10,12}$.$0^{11,13}$]hexadeca-15-ene-1,8-dicarboxylate *(3)*[4], in which the bridging of the bicyclobutane skeleton is extended by one carbon atom. The crystallographic data are given in Table 1[5].



(1), R = C_6H_5
(2), R = CH_3

(3)

Table 1. Crystallographic constants.

	(1)	*(2)*	*(3)*
a	563.4(3) pm	1095.3(7) pm	1570.3(2) pm
b	865.3(2) pm	691.5(2) pm	548.2(1(pm
c	2584.6(5) pm	854.8(7) pm	1783.2(1) pm
β	100.85(2)°	111.16(8)°	99.65(1)°
	$P2_1/c$; $Z=4$	C2/c; $Z=4$	C2/c; $Z=4$

The molecules *(2)* and *(3)* each lie on a crystallographic twofold axis. The bond between the bridgehead atoms has pronounced π-character[1]. The orientation of the corresponding π-orbitals, above and below the C C bond line, is defined by the plane bisecting the interplanar angle δ. The two phenyl rings in *(1)* are arranged almost perpendicular to this plane (93.6 and 89.9°), so that there is optimal possible conjugation between the two phenyl groups *via* the π-population of the bridge bond. The conjugation effects lead to a lengthening of the bridge bond in *(1)* to 1.444 Å as compared to the corresponding bond length of 1.408 Å in the dimethyl compound *(2)*. The bridge bonds of all three bicyclobutane derivatives are considerably shorter than the standard value of 1.54 Å for a $C(sp^3)$ $C(sp^3)$ single bond. As can be seen from Figure 2, in which the values are plotted for molecules which are not influenced by conjugation effects, *the distance between the bridgehead atoms increases with increasing interplanar angle* δ.

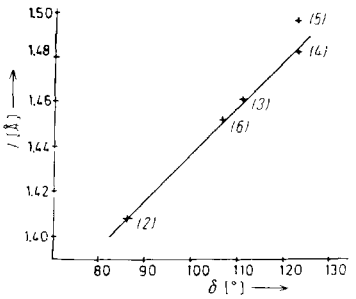


Fig. 2. Relation between the length of the bridgehead bond *l* of bicyclo[1.1.0]butane derivatives and the interplanar angle δ. The diagram contains the values for *(2)*, *(3)*, a bicyclobutane *(4)* bridged by the C=C S group [6], the parent compound *(5)* [7], and benzvalene *(6)* [8].

Received: April 23, 1979 [Z 287 IE]
German version: Angew. Chem. *91*, 750 (1979)

[1] *M. Pomerantz, E. W. Abrahamson*, J. Am. Chem. Soc. *88*, 3970 (1966); *M. D. Newton, J. M. Schulman, ibid. 94*, 767 (1972); *H. Finkelmeier, W. Lüttke, ibid. 100*, 6261 (1978).

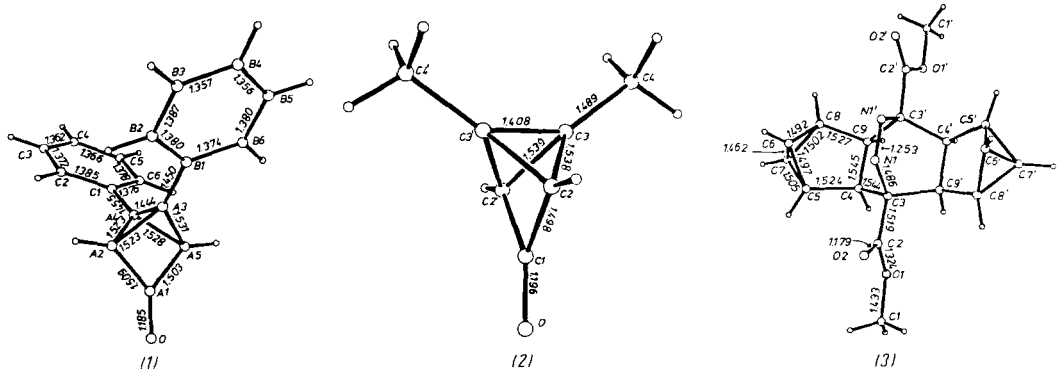


Fig. 1. Molecular structure of *(1)*, *(2)*, and *(3)* with bond lengths in Å; the mean standard deviation is 0.002—0.003 Å.

[*] Prof. Dr. H. Irngartinger, Dipl.-Chem. K. L. Lukas
Organisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

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

[2] Synthesized according to *J. Trotter, C. S. Gibbons, N. Nakatsuka, S. Masamune*, J. Am. Chem. Soc. *89*, 2792 (1967).

[3] *W. v. E. Doering, M. Pomerantz*, Tetrahedron Lett. *1964*, 961; *G. Maier, H. P. Reisenauer, H.-A. Freitag, ibid. 1978*, 121. We thank Prof. *G. Maier* for a sample of *(2)*.

[4] *M. Christl, H.-J. Lüddeke, A. Nagyrevi-Neppel, G. Freitag*, Chem. Ber. *110*, 3745 (1977). We thank Dr. *M. Christl* for kindly supplying us with a sample of *(3)*.

[5] Measurement and refinement conditions: room temperature, $Mo_{K\alpha}$ radiation, graphite monochromator, $\sin\theta/\lambda \leq 0.664$ Å^{-1}, *R*-value for *(1)* 0.052, *(2)* 0.046, *(3)* 0.049.

[6] The value for 6-thiatetracyclo[5.4.0.0^{2,4}.0^{3,5}]undeca-1(7),8,10-triene *(4)* was determined by X-ray structure analysis: *C. Kabuto, T. Tatuoka, I. Murata, Y. Kitahara*, Angew. Chem. *86*, 738 (1974); Angew. Chem. Int. Ed. Engl. *13*, 669 (1974).

[7] The value for bicyclo[1.1.0]butane *(5)* was determined by microwave spectroscopy: *K. W. Cox, M. D. Harmony, G. Nelson, K. B. Wiberg*, J. Chem. Phys. *50*, 1976 (1969).

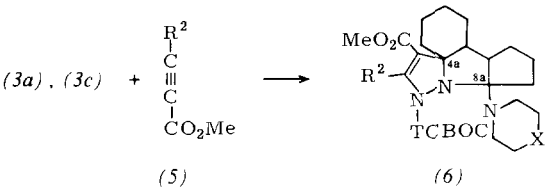
[8] The structure of benzvalene *(6)* was determined by microwave spectroscopy: *R. D. Suenram, M. D. Harmony*, J. Am. Chem. Soc. *95*, 4506 (1973).

[3+2]-Cycloadditions of Azoalkenes to Enamines—Criss-Cross Cycloadditions to Azoalkenes[**]

By *Sven Sommer*[*]

Cycloadditions of multiple bond systems to 1,3-dienes usually take place at the 1,4-, but also at the 1,2-(or 3,4-)position. Cycloadditions at the 1,3-(or 2,4-)position, on the other hand, are a rarity, and to our knowledge have only been observed in the open-chain azines (2,3-diaza-1,3-butadienes)[1,8]. That this mode of reaction is not limited to azines is demonstrated by the [3+2]-cycloadditions of azoalkenes *(1)* (1,2-diaza-1,3-butadienes) to enamines *(2)*[2]: In the reaction of the azoalkenes[3] *(1a)* and *(1b)* with the enamines *(2a)* or *(2b)* analytically pure [3+2]-cycloadducts of the type *(3)* crystallize from the reaction solution after a few minutes (Table 1). On heating above the melting point (very slowly in solution at room temperature) they immediately form the *N*-aminopyrroles *(4)* (Table 1).

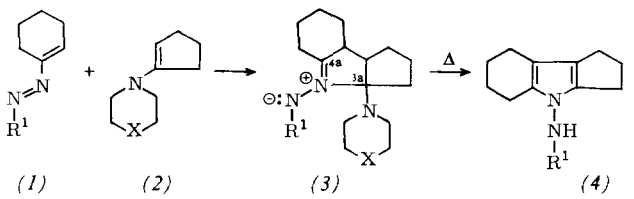
The azomethineimine structure *(3)* follows from the downfield position of the ^{13}C-NMR signals for C-4a [$\delta = 173.6$ *(3a)*, 179.5 *(3b)*] and C-3a [$\delta = 109.2$ *(3a)*, 110.4 *(3b)*, $CDCl_3$/TMS] and from the shift to lower wave numbers of the IR absorptions of the C=O group of *(3a)* [ν(C=O) = 1635 cm^{-1}, KBr and $CHCl_3$] and *(3c)* [ν(C=O) = 1640 cm^{-1}, KBr], and of the SO_2 group of *(3b)* [$\nu(S{=}O)_{antisym} = 1135$ cm^{-1}, $\nu(S{=}O)_{sym} = 1285$ cm^{-1}, KBr][4].



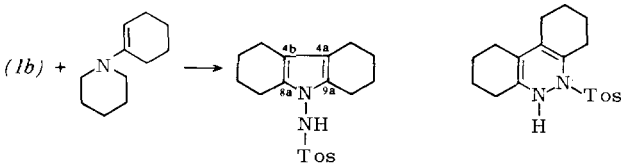
(5) (6)

Further evidence for the azomethineimine structure *(3)* is provided by the ability of *(3a)* and *(3c)* to undergo 1,3-dipolar cycloaddition with acetylenecarboxylates *(5)*[5] to give the compounds *(6)* (Table 2). The cycloaddition to *(6a)* and *(6b)* proceeds regiospecifically.

(6a)—*(6c)* are formed *via* a sequence of two [2+3]-cycloadditions to the 1,3- and 2,4-positions of the 1,2-diaza-1,3-butadiene skeleton of *(3a)* and *(3c)*. Such criss-cross cycloadditions have previously only been observed in the case of the azines[1a,6,8]. In many of the reactions of enamines with azoalkenes the [2+3]-cycloadducts *(3)* presumed to be formed initially cannot be isolated, but only compounds which can be regarded as their secondary products. Thus, on reaction of *(1b)* and *(2c)* the *N*-aminopyrrole *(4c)* is obtained (see Table 1).



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



(2c) (4c) (7)

Table 1. [3+2]-cycloadditions of azoalkenes *(1)* to enamines *(2)* (1:1 at room temperature) to give azomethineimines *(3)*, and their thermal decomposition to *N*-aminopyrroles *(4)*.

Reactants *(1)*,	R^1	*(2)*,	X	Solvent	Product *(3)* Yield [%]	M.p. (dec.) [°C]	Product *(4)* Yield [%]	M.p. (dec.) [°C]	IR [a] ν [cm^{-1}]
(1a),	TCBOC [b]	*(2a)*,	CH_2	pentane	*(3a)* 64	102—103	*(4a)* 98	175—178	3320
(1b),	Tos	*(2a)*,	CH_2	ether	*(3b)* 82	102—103	*(4b)* 44	205—206	3195
(1a),	TCBOC [b]	*(2b)*,	O	ether	*(3c)* 56	114—115	*(4a)* 98	175—178	3320
(1b),	Tos	*(2c)*	[c]	ether	—		*(4c)* [c] 70	232—233	3200
(1c)	[c]	*(2b)*,	O	ether	[d]		*(4d)* [c] 81	154—155	3220

[a] In KBr, ν(NH). [b] TCBOC = C(O)—O—C(CH$_3$)$_2$—CCl$_3$. [c] See under formula indicated. [d] The product isolated was *(8a)*.

Table 2. "Criss-cross" cycloadducts *(6)* of acetylenecarboxylic esters *(5)* and azomethineimines *(3)*.

Reactants *(3)*,	X	*(5)*,	R^2	Conditions	Product *(6)* Yield [%]	M.p. [°C]
(3a),	CH_2	*(5a)*,	H	excess of *(5a)*, CH_2Cl_2, 1 h	*(6a)* 75	152—153
(3c),	O	*(5a)*,	H	excess of *(5a)*, CH_2Cl_2, 1 h	*(6b)* [a] 85	179—180
(3c),	O	*(5b)*,	CO_2Me		*(6c)* 71	139—140

[a] ^{13}C-NMR ($CDCl_3$/TMS): δ(C-4a, C-8a) = 75.9, 99.0; IR (KBr): ν(C=O) 1705, 1760 cm^{-1}; ν(C=C) 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$/TMS): δ(CH=) = 7.53.

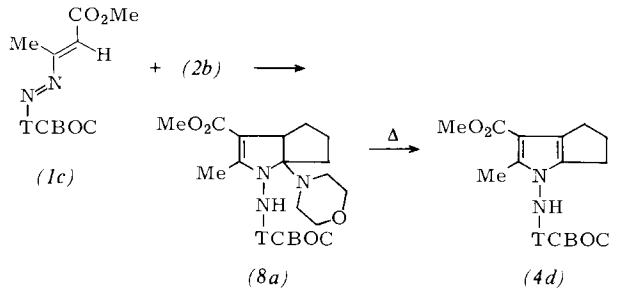
[*] Dr. S. Sommer
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Reactions with Azo Compounds, Part 6.—Part 5: [2].

The pyridazine structure *(7)*, which cannot be disregarded *a priori*, is ruled out on the grounds of the ^{13}C-NMR spectrum: it shows only two signals for the four pyrrole C-atoms

[δ(C-4a, C-4b) = 112.8, δ(C-8a, C-9a) = 126.4, [D$_6$]-DMSO/TMS].

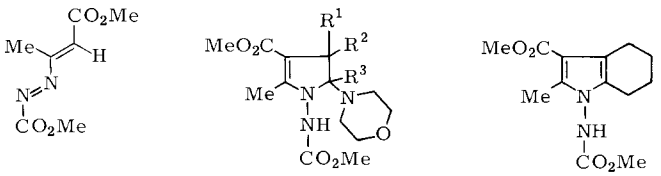
Reaction of *(1c)*[3] with *(2b)* leads to the *N*-amino-2-pyrroline *(8a)* [95%, m.p. 123—124 °C, IR (KBr): ν(NH) = 3220 cm^{-1}]. It is plausible to assume that compounds of type *(8)*



(1c) *(8a)* *(4d)*

are formed as intermediates in the conversion of *(3)* into *(4)*. Like *(3)*, on heating above the melting point *(8a)* forms an *N*-aminopyrrole *(4d)* (Table 1).

On the basis of these results the enamine adducts of *(1d)* obtained previously, which were described as pyridazine derivatives[2], should be regarded as *N*-amino-2-pyrrole derivatives *(8b)* [86%, m.p. 127 °C] and *(8c)* [70%, m.p. 140 °C] and as the *N*-aminopyrrole derivative *(4e)* [32% referred to *N*-morpholino-1-cyclohexene *(2d)* for *(1d)*:*(2d)* in the ratio 1:2, m.p. 125 °C].



(1d) *(8b)*, R^1 = H, R^2–R^3 = –(CH$_2$)$_3$– *(4e)*
(8c), R^1 = R^2 = Me, R^3 = H

The compounds *(3)*, *(4)*, *(6)* and *(8)* gave correct CHN analyses, and IR, ^{1}H-NMR, ^{13}C-NMR and mass spectra in accord with the given structures[7].

Received: April 17, 1979 [Z 288a IE]
German version: Angew. Chem. *91*, 756 (1979)

[1] a) Review: *T. Wagner-Jauregg*, Synthesis *1976*, 349; b) *K. Burger, F. Hein*, Chem.-Ztg. *102*, 152 (1978), and references cited therein.

[2] In addition to [3+2]-cycloadditions, [4+2]-cycloadditions were also observed: *S. Sommer*, Chem. Lett. *1977*, 583, and unpublished results.

[3] Synthesis of *(1a)* [89%, m.p. 74—75 °C (dec.)] and *(1c)* [60%, m.p. 77—78 °C (dec.)] by 1,4 elimination of HCl from the corresponding α-chlorohydrazones with the aid of 1 N aqueous Na_2CO_3 solution in ether: *S. Sommer*, unpublished.

[4] Cf. *H.-J. Timpe*, Z. Chem. *12*, 250 (1972), see p. 254.

[5] Reactions of azomethineimines with acetylenic dipolarophiles, see *E. Eckell, R. Huisgen*, Chem. Ber. *110*, 559 (1977).

[6] a) *K. Burger, W. Thenn, R. Rauh, H. Schickaneder, A. Gieren*, Chem. Ber. *108*, 1460 (1975); b) *K. Burger, H. Schickaneder, W. Thenn, G. Ebner, C. Zettl*, Justus Liebigs Ann. Chem. *1976*, 2156; c) *K. Burger, F. Hein, ibid. 1979*, 133; formal criss-cross cycloaddition of sulfur trioxide to cyanogen see: *H. W. Roesky, N. Amin, G. Remmers, A. Gieren, V. Riemann, B. Dederer*, Angew. Chem. *91*, 243 (1979); Angew. Chem. Int. Ed. Engl. *18*, 223 (1979).

[7] *S. Sommer*, unpublished work.

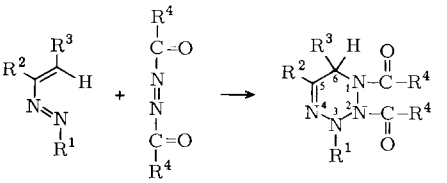
[8] *Note added in proof:* A further example of 1,3- and "criss-cross" cycloaddition to hetero-1,3-dienes is the addition of ketenes to the N—N C O system of azodicarbonyl compounds: *J. Markert, E. Fahr*, Tetrahedron Lett. *1970*, 769; *E. Büttner*, Dissertation, Universität Würzburg 1976.

[4+2]-Cycloadditions of Azoalkenes to Azodicarbonyl Compounds. A Novel Facile Route to the 1,2,3,4-Tetrazine System[**]

By *Sven Sommer* and *Ulrich Schubert*[*]

Aromatic 1,2,3,4-tetrazines have so far not been synthesized. This also applies in the case of nine of the total of ten possible partially or completely hydrogenated forms[1]. All previously known routes to this system lead exclusively to derivatives of 1,4,5,6-tetrahydro-1,2,3,4-tetrazine[1c,2]. Only in a few cases have yields of up to 50% been reported.

The ability of azoalkenes (1,2-diaza-1,3-butadienes) *(1)* to form [4+2]-cycloadducts with electron-deficient double bond systems[3] now opens up a novel simple entry to the 1,2,3,4-tetrazine system. Azoalkenes *(1)* react with the azodicarbonyl compounds *(2)*[4] (1:1 in benzene or tetrahydrofuran at room temperature) to give derivatives of the 1,2,3,6-tetrahydro-1,2,3,4-tetrazine *(3)* in good yields (Tables 1 and 2). The duration of reaction lies between *ca.* three hours and four days; acceptor substituents on *(1)* decrease the rate of reaction.



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

Table 1. 1,2,3,6-Tetrahydro-1,2,3,4-tetrazines *(3)* from azoalkenes *(1)* [a] and azodicarbonyl compounds *(2)* [a]. The yields refer to pure isolated compounds.

	R^1	R^2	R^3	R^4	Yield [%]	M.p. [°C]
(a)	Ph	(CH$_2$)$_4$		OMe	77	132 [b]
(b)	4-Br C$_6$H$_4$	(CH$_2$)$_4$		OMe	79	162—163 [c]
(c)	Ph	(CH$_2$)$_4$		OPh	90	161—162 [d, h]
(d)	Me	(CH$_2$)$_4$		OCH$_2$CCl$_3$	81	95—96 [e]
(e)	Me	Me	H	OCH$_2$CCl$_3$	80	68—69 [e]
(f)	Me	Me	PhNHCO	OMe	79	131—133 [f, h]
(g)	Me	Me	PhNHCO	OC(CH$_3$)$_2$CCl$_3$	72	176—177 [g, h]
(h)	Me	Me	H	Ph	34	133—134 [e]

[a] With the exception of *(1f)*, all the azoalkenes used have been described in the literature. Synthesis of *(1f)* [m.p. 131—133 °C (dec.), yield 44%]: *S. Sommer et al.*, unpublished.—With the exception of *(2g)*, all compounds *(2)* have been described in the literature. *(2g)* m.p. 173—174 °C (petroleum ether 60—90 °C), yield 85% was prepared from the corresponding *N,N'*-hydrazine dicarboxylate [m.p. 145—146 °C (ethanol/H$_2$O), yield 96%] by oxidation with HOCl following the method of *N. Rabjohn* (Org. Synth. Coll. Vol. III, 1955, 375). *(2g)*: ^{1}H-NMR (CDCl$_3$) 2.13 (s, C(CH$_3$)$_2$CCl$_3$); IR (KBr): ν(C=O) = 1784 cm^{-1}. [b] Ethyl acetate/petroleum ether 40—80 °C. [c] CHCl$_3$/petroleum ether 40—80 °C. [d] Benzene/petroleum ether 40—80 °C. [e] CH$_3$OH. [f] Tetrahydrofuran (THF). [g] THF/ether. [h] Decomposition.

Proof of the structure of adducts *(3)* is based on correct CHN analyses (within 0.3%), spectral data and an X-ray structure analysis. Except in the case of *(3f)* and *(3g)* (CO NHPh), no NH bands appear in the IR spectra. The weak C N band is comparable with the C N band of 1,4,5,6-tetrahydropyridazines[5]. The ^{13}C-NMR signal observed between δ = 147 and 157—in the region of the ^{13}C N

[*] Dr. S. Sommer
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)
Dr. U. Schubert
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] Reactions of Azo Compounds, Part 7.—Part 6: [7].

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0909-0696 $ 02.50/0

Table 2. Some spectroscopic data of compounds *(3)*. ^{1}H- and ^{13}C-NMR spectra in $CDCl_3$ with TMS as internal standard, δ values, coupling constants [Hz]. IR spectra in KBr, ν [cm^{-1}].

(3a), ^{1}H-NMR: 3.72 (s, OCH_3), 3.79 (s, OCH_3), 4.35 (br. dd, $J \approx 5$ and 11, CHN); ^{13}C-NMR: 53.4, 54.5 (2 OCH_3), 54.9 (CHN), 153.8, 154.6, 156.1 (2 C=O, C=N); IR: 1630 (C=N), 1725, 1755 (C=O)

(3b), ^{1}H-NMR: 3.79 (s, OCH_3), 3.85 (s, OCH_3), 4.4 (br. dd, $J = 5.0$ and 11.0, CHN); ^{13}C-NMR: 53.6, 54.8 (2 OCH_3), 54.8 (CHN), 154.1, 154.6, 155.9 (2 C=O, C=N); IR: 1630 (C=N), 1742, 1760 (C=O)

(3c), ^{1}H-NMR: 4.53 (br. dd, $J = 5.0$ and 11.5, CHN); ^{13}C-NMR: 55.2 (CHN), 152.5, 153.7 (2 C=O, C=N); IR: 1630 (C=N), 1750 (C=O)

(3d), ^{1}H-NMR: 3.01 (s, NCH_3), 4.41 (m, CHN), 4.58, 5.09 (AB spectrum, $J_{AB} = 12.0$, CH_2CCl_3), 4.75, 4.98 (AB spectrum, $J_{AB} = 12.0$, CH_2CCl_3); ^{13}C-NMR: 43.6 (NCH_3), 54.1 (CHN), 75.4, 75.8 (2 CH_2CCl_3), 94.8 (2 CCl_3), 152.3, 156.8 (2 C=O, C=N); IR: 1628 (C=N), 1720, 1750 (C=O)

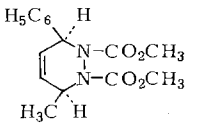
(3e), ^{1}H-NMR: 1.99 (s, CH_3C=N), 3.07 (s, NCH_3), 3.99, 4.40 (AB spectrum, $J_{AB} = 18.5$, CH_2N), 4.65, 5.05 (AB spectrum br., $J_{AB} = 12.0$, CH_2CCl_3), 4.73, 5.02 (AB spectrum, $J_{AB} = 12.0$, CH_2CCl_3); ^{13}C-NMR: 21.3 (CH_3C=N), 43.2 (CH_2N), 44.5 (NCH_3), 75.5, 75.9 (2 CH_2CCl_3), 94.6 (2 CCl_3), 148.6, 152.5, 153.2 (2 C=O, C=N); IR: 1635 (C=N), 1740 (C=O)

(3f), ^{1}H-NMR: 2.29 (s, CH_3C=N); 3.03 (s, NCH_3), 3.88 (s, 2 OCH_3); 5.22 (s, CHN), 9.82 (s, NH); ^{13}C-NMR: 23.1 (CH_3C=N); 44.1 (NCH_3), 54.7, 54.9 (2 OCH_3), 59.2 (CHN), 147.0, 155.2 (2 C=O, C=N), 163.3 (CONH); IR: 1620 (C=N); 1689 (O–C–NHPh), 1719, 1735 (sh) (C=O)? 3320 (NH)

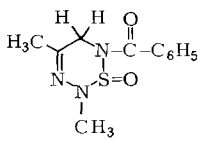
(3g), ^{1}H-NMR: 1.91 (s, 1 CH_3, ester), 2.02 (s, 3 CH_3, ester), 2.32 (s, CH_3C=N), 3.11 (s, NCH_3), 5.25 (s, CHN), 9.83 (s, NH); ^{13}C-NMR: 21.3 (1 CH_3, ester), 21.6 (3 CH_3, ester), 23.3 (CH_3C=N), 44.7 (NCH_3), 58.5 (CHN), 91.4 (2 $C(CH_3)_2CCl_3$), 105.3 (2 CCl_3), 144.7, 151.8 (2 C=O, C=N), 163.0 (CONH); IR: 1620 (C=N), 1690 (O–C–NHPh), 1722, 1740 (sh) (C=O), 3340 (NH)

(3h), ^{1}H-NMR: 1.90 (s, CH_3C=N), 2.79 (s, NCH_3), 4.20, 4.80 (AB spectrum, $J_{AB} = 18.5$, CH_2N); ^{13}C-NMR: 22.0 (CH_3C=N), 42.0 (CH_2N), 43.9 (NCH_3), 152.9 (C=N); 172.1, 173.6 (2 C=O); IR: 1637 (C=N), 1665, 1685 (C=O)

signals of hydrazones[6]—together with the signals of the two CO groups confirms the presence of a C=N group. Since the C=O signals appear further downfield in the spectrum of *(3h)* the assignment of δ(^{13}C=N) is unequivocal in this case.



(4)



(5)

The positions of these signals also rule out [3+2]-cycloadducts[7]. The strong IR bands between $\nu = 1720$ and 1760 cm^{-1} for the ester CO-groups of *(3a–g)* lie in the C=O absorption region of cyclic *N,N'*-hydrazinedicarboxylates [ν(CO) = 1710–1760 cm^{-1}][8a]; an example is *(4)* [ν(KBr) = 1718 and 1739 cm^{-1}]. The positions of the ^{1}H-NMR signals of the methoxycarbonyl protons of *(3a, b, f)* ($\delta = 3.7$–3.9) are also in good agreement with the corresponding δ-values of dimethyl esters[8b] such as *(4)*. Essential evidence for the six-membered ring and 1,2,3,4-tetrazine structure is provided by the fact that the geminal coupling constants of the ring protons in *(3h)* and *(5)* are of the same magnitude[3c].

For final proof of the structure, an X-ray structural analysis was carried out on *(3a)* (Fig. 1). This confirmed the proposed structure and showed that the 1,2,3,4-tetrazine ring in the crystal assumes a slightly distorted half chair conformation: N(3) lies 41 pm below, and N(4) 17 pm above the C(2) C(1)–N(1)–N(2) plane. 1,4-Dimethyl-1,4,5,6-tetrahydro-1,2,3,4-tetrazine 2-oxide[2f], on the other hand, has a distorted pyramidal conformation. While N(2) and N(3) are pyramidally configurated, N(4) is coplanar with the atoms to which it is bound, thus indicating conjugation of N(4) with the methoxycarbonyl group. This is confirmed by the significantly shorter N(4)–C(9) bond as compared with the N(3)–C(7) bond, as well as by the finding that the plane of the atoms around C(9) is rotated through an angle of only 9.4° from the plane of the atoms around N(4) (at N(3): 33.9°). The NN bond lengths are of the usual order, if one takes into consideration the nature of the substituents and the state of hybridization of the nitrogen atoms[9].

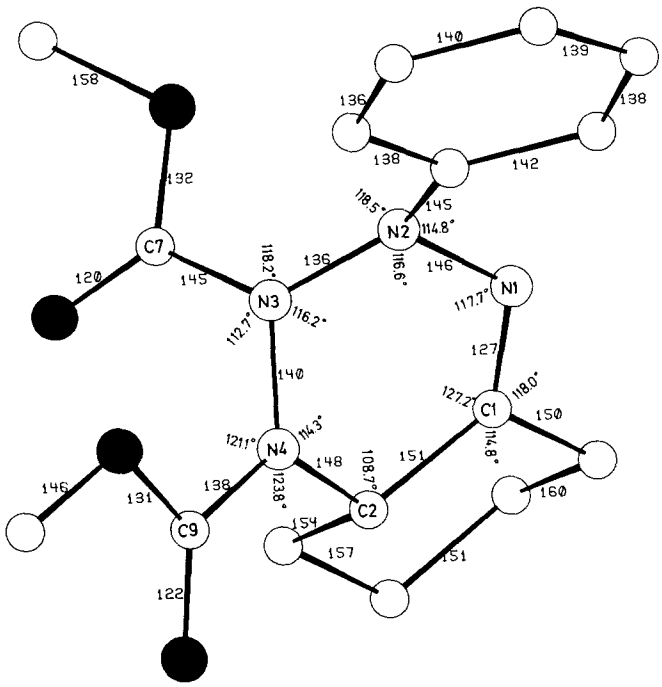


Fig. 1. Molecular structure of *(3a)*. The standard deviations are 1 pm for the bond lengths and 0.7° for the angles. 1487 structure factors ($F_o \geq 5.0\sigma(F_o)$). Syntex $P2_1/XTL$, $Mo_{K\alpha}$ radiation ($\lambda = 71.069$ pm), $2° \leq 2\theta \leq 40°$; $R = 0.109$. Triclinic, space group $P\bar{1}$, $a = 837(1)$, $b = 1092(1)$, $c = 1234(1)$, $\alpha = 100.29(8)$, $\beta = 91.04(7)$, $\gamma = 80.43(8)$, $Z = 2$, $V = 1095 \times 10^6$ pm^3, ρ(calc.) = 1.37 g/cm^3. The unit cell contains two molecules of $CDCl_3$ (not shown), which are strongly disordered.—A list of the atomic coordinates and structural factors are obtainable on request *(U. Sch.)*.

Received: June 7, 1979 [Z 288b IE]
German version: Angew. Chem. *91*, 757 (1979)

[1] Reviews: a) *V. P. Wystrach*, Chem. Heterocycl. Compds. *10*, 138 (1956); b) Heterocycl. Compds. *8*, 107 (1967); c) *P. F. Wiley*, Chem. Heterocycl. Compds. *33*, 1287 (1978).

[2] a) *S. F. Nelsen, R. Fibiger*, J. Am. Chem. Soc. *94*, 8497 (1972); b) *S. Mataka, J.-P. Anselme*, Chem. Lett. *1973*, 51; c) *D. Seebach, D. Enders, B. Renger, W. Brügel*, Angew. Chem. *85*, 504 (1973); Angew. Chem. Int. Ed. Engl. *12*, 495 (1973); d) *R. Kreher, H. Wissmann*, Chem. Ber. *106*, 3097 (1973); e) *D. Seebach, D. Enders*, Angew. Chem. *87*, 1 (1975); Angew. Chem. Int. Ed. Engl. *14*, 15 (1975); f) *D. Seebach, R. Dach, D. Enders, B. Renger, M. Jansen, G. Brachtel*, Helv. Chim. Acta *61*, 1622 (1978).

[3] a) *L. Caglioti, G. Rosini, P. Tundo, A. Vigevani*, Tetrahedron Lett. *1970*, 2349; b) *K. N. Zelenin, V. A. Nikitin, N. M. Anodina, Z. M. Matveeva*, Zh. Org. Kim. *8*, 1438 (1972); c) *S. Sommer*, Synthesis *1977*, 305.

[4] Review: *H. Wollweber:* Diels-Alder-Reaktion. Thieme, Stuttgart 1972, p. 191.

[5] a) *K. N. Zelenin, L. M. Korzhikova, O. V. Sverdlova*, Zh. Prikl. Spektrosk. *11*, 1080 (1969); b) *S. Sommer*, Tetrahedron Lett. *1977*, 117; c) Chem. Lett. *1977*, 583.

[6] *N. Naulet, M. L. Filleux, G. J. Martin, J. Pornet*, Org. Magn. Reson. *7*, 326 (1975).

[7] Cf. *S. Sommer*, Angew. Chem. *91*, 756 (1979); Angew. Chem. Int. Ed. Engl. *18*, 695 (1979).

[8] a) *J. Firl*, unpublished results; *S. Sommer*, Dissertation, Technische Universität München 1971; b) *J. Firl*, Chem. Ber. *102*, 2169, 2177 (1969).

[9] *M. Veith*, Acta Crystallogr. *B 31*, 678 (1975).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/0909-0697 $ 02.50/0*

Abietospiran, the Triterpene from the Bark of the White Fir *(Abies alba)*

By *Wolfgang Steglich, Manfred Klaar, Lothar Zechlin,* and *Hans Jürgen Hecht*[*]

Dedicated to Professor Alfred Treibs on the occasion of his 80th birthday

On work-up of fruiting bodies of the fungus *Hymenochaete mougeotii* we recently isolated a triterpene, $C_{31}H_{48}O_4$, characterized by an IR band (KBr) at 1785 cm^{-1}[1]. A re-investigation showed that the compound arises from adhering particles of bark of the white fir (*Abies alba* Mill.) on which it forms a crystalline coating responsible for the silver-gray color of the bark.

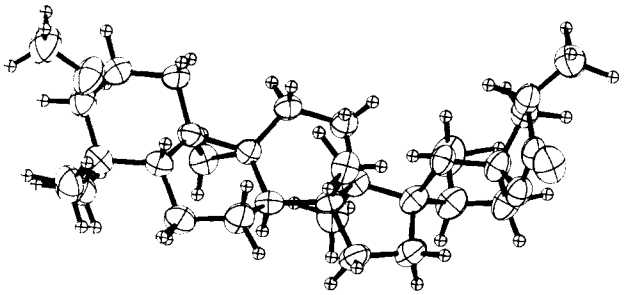
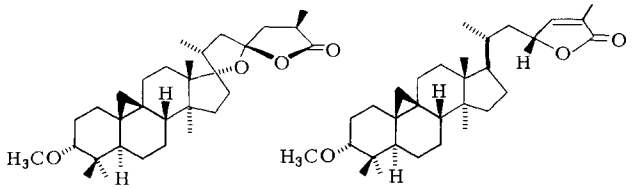


Fig. 1. Molecular structure of abietospiran (for the sake of clarity the enantiomer of formula *(1)* is shown).

The triterpene *(1)*, which we call abietospiran, can be readily obtained in a pure state by extraction of the topmost layer of the bark with light petroleum and recrystallization from ethyl acetate (*ca.* 0.14 g/g of bark). Its structure was determined by single-crystal X-ray structure analysis[2] (Fig. 1).



(1) *(2)*

(1) is closely related to cyclograndisolide *(2)* from the bark of *Abies grandis*[3]; hence we assign *(1)* the same absolute configuration. A 9(11)-dehydrolanostane derivative was recently isolated from needles of the white fir[4].

Isolation procedure

On Soxhlet extraction with light petroleum (40—60 °C, 2 d), a sample of the topmost layer of bark of *Abies alba*[5] (34.4 g) afforded 6.3 g of a crude substance, which yielded 4.9 g of *(1)* on recrystallization from ethyl acetate; m. p. 219—221 °C, $[\alpha]_{589}^{22}$ −16.8° (*c* = 0.68 in $CHCl_3$); IR (KBr): 1785 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 0.34, 0.47 (AB system, *J* = 4 Hz, cyclopropyl H), 0.86, 0.92, 1.03, 1.17 (each s, C—CH_3), 1.01, 1.24 (each d, *J* = 7 Hz, CH—CH_3), 2.84 (br. s, half-width 5 Hz, 3-H), 3.33 (s, OCH_3).

[*] Prof. W. Steglich, Dr. M. Klaar, Dr. L. Zechlin
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)
Dr. H. J. Hecht
Forschergruppe Röntgenstrukturanalyse Biologischer Makromoleküle der Universität
Am Hubland, D-8700 Würzburg (Germany)

Received: June 27, 1979 [Z 289 IE]
German version: Angew. Chem. *91*, 751 (1979)

[1] *M. Klaar, W. Steglich,* Chem. Ber. *110*, 1063 (1977).
[2] *(1)* crystallizes in the orthorhombic space group $P2_12_12_1$ with *a* = 3006.7(8), *b* = 712.2(4), *c* = 1293.4(5) pm, *Z* = 4. 2485 independent reflections were recorded in the range $2.5 \leq \theta \leq 65.0°$ on a STOE single crystal diffractometer with Ni-filtered $Cu_{K\alpha}$ radiation; *R* = 3.9% for 2410 reflections with $I \leq 2\sigma$. For details of X-ray structure analysis, see *H. J. Hecht et al.*, to be published.
[3] *F. H. Allen, J. P. Kutney, J. Trotter, N. D. Westcott,* Tetrahedron Lett. *1971*, 283.
[4] *J.-C. Muller, G. Ourisson,* Phytochemistry *13*, 1615 (1974).
[5] Dead fir tree from Sinzing (nr. Regensburg, Germany). *(1)* could also be isolated from living fir trees. We thank Prof. Dr. *A. Bresinsky* for providing the bark.

Crystal Structure of Na_3NO_4[**]

By *Martin Jansen*[*]

The Raman spectra of Na_3NO_4 and K_3NO_4 were interpreted assuming the presence of NO_4^{3-} groups[1]; in contrast to Na_3NO_3[2], therefore, those compounds can be regarded as "ortho salts". This is the first deviation from the pronounced tendency of oxoanions of first-row nonmetals to achieve low coordination numbers by forming multiple bonds, in contrast to their higher homologs. It thus appeared appropriate to confirm the results of vibrational spectroscopy by X-ray structure analysis, especially since no precise information was available about the dimensions of the NO_4^{3-} ion.

Growth of crystals was made difficult by the high reactivity and the thermal sensitivity of Na_3NO_4: addition of fluxes or solvents effected decomposition; temperatures above 500 °C led to attack of the crucible material owing to the basic and oxidizing properties of the orthonitrates. Long-term experiments at a maximum temperature of 415 °C finally proved successful. Several silver crucibles were filled with microcrystalline Na_3NO_4[1], closed with stoppers, and individually sealed into glass ampoules under argon. They were placed together in a crucible furnace and heated to 415 °C (heat-up rate 10 °C/h). The changes in degree of crystallization of the samples were examined by removal of one crucible at a time at intervals of 60 d. After 240 d, a size adaquate for single-crystal studies has been reached (diam. ≈ 0.1 mm); the slowly cooled samples (2.5 °C/h) contained crystals that appear free from defects on examination by optical and X-ray methods.

Structural analysis[3] proves the existence of tetrahedral orthoanions in solid Na_3NO_4. In view of the site symmetry 1,

Table 1. Distances [pm] in Na_3NO_4.

				corr.	
N	O(1)	138.4(3)		139.2	
N	O(2)	138.9(3)		139.3	
N	O(3)	138.1(3)		138.7	
N	O(4)	138.2(3)		138.9	
$\bar{d}$		138.4		139.0	
O(1)	O(2)	226.2(3)	Na(1)	[O(1); O(2); O(3); O(3); O(4)]:	
O(1)	O(3)	225.0(3)		[238.9; 231.5; 231.8; 240.9; 226.9]	
O(1)	O(4)	225.7(3)	Na(2)	[O(1); O(2); O(3); O(4)]:	
O(2)	O(3)	226.4(3)		[237.7; 238.1; 237.4; 247.1]	
O(2)	O(4)	227.1(3)	Na(3)	[O(1); O(2); O(2); O(4); O(4)]:	
O(3)	O(4)	225.8(3)		[230.8; 233.6; 246.0; 234.2; 253.0]	

[*] Dr. M. Jansen
Institut für Anorganische und Analytische Chemie der Universität
Heinrich-Buff-Ring 58, D-6300 Giessen (Germany)

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

the dimensions of the NO_4^{3-} group are remarkably regular: T_d symmetry is present within the limits of error (cf. Table 1). The coefficients of the anisotropic temperature factors can be reasonably interpreted assuming librational motion of rigid NO_4^{3-} ions[4]; correspondingly corrected distances are also listed in Table 1.

The N—O distances are unexpectedly small; they lead to the shortest known contacts (226 pm) between oxygen particles not directly linked together. Considering the coordination number of N, a length of *ca.* 150 pm would be estimated for the N—O single bond. A value calculated approximately for the equilibrium distance by the EHMO method is of the same order of magnitude (151 pm)[5]. The only possible reason for the significant shortening to 139 pm lies in polar interactions superimposed on the single bond. This result emphatically demonstrates that pd-π bonding contributions[6] need not be invoked in explaining the bond lengths in oxoanions such as PO_4^{3-}, SO_4^{2-}, or ClO_4^-!

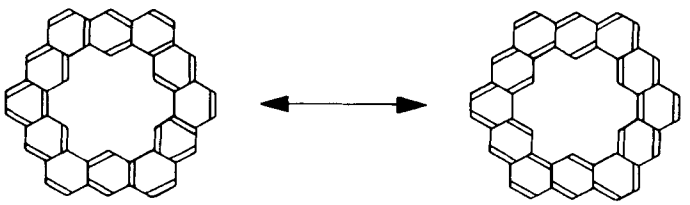
Received: May 10, 1979 [Z 292 IE]
German version: Angew. Chem. *91*, 762 (1979)

[1] *M. Jansen*, Angew. Chem. *89*, 567 (1977); Angew. Chem. Int. Ed. Engl. *16*, 534 (1977); Habilitationsschrift, Universität Giessen 1978.
[2] *M. Jansen*, Angew. Chem. *88*, 410 (1976); Angew. Chem. Int. Ed. Engl. *15*, 376 (1976); Z. Anorg. Allg. Chem. *435*, 13 (1977).
[3] $a=863.2(2)$, $b=973.1(2)$, $c=904.2(2)$ pm, space group Pbca, $Z=8$; 1073 observed intensities (diffractometer data), $R=0.05$.
[4] *V. Schomaker, K. N. Trueblood*, Acta Crystallogr. *B 24*, 63 (1968).
[5] *D. K. Johnson, J. R. Wasson*, Inorg. Nucl. Chem. Lett. *10*, 891 (1974).
[6] Cf. *D. W. J. Cruickshank*, J. Chem. Soc. *1961*, 5486; *L. Pauling*: The Nature of the Chemical Bond, Cornell University Press, Ithaca; Die Natur der chemischen Bindung. Verlag Chemie, Weinheim 1968.

Molecular Structure and Spectroscopic Properties of Kekulene[1]

By *Claus Krieger, Francois Diederich, Dieter Schweitzer,* and *Heinz A. Staab*[*]

Kekulene *(1)*, the synthesis of which was recently reported[2], is the first example of a new class of aromatic compounds in which the annellation of six-membered rings leads to a cyclic system enclosing a cavity lined with hydrogen atoms. Compound *(1)*, for which 200 Kekulé structures with different arrangements of double and single bonds can be formulated[3], was of interest with regard to π-electron delocalization and the related problem of the diatropicity in the macrocyclic system for which, as long ago as 1951, different theoretical approaches were shown to lead to contradictory predictions in the specific case of *(1)*[4]. Experimentally, the ^{1}H-NMR absorption of the internal hydrogens did not show any evidence for a diatropicity in the macrocyclic system[2], in qualitative agreement with MO calculations of chemical shifts[4, 5]. In this context, and in connection with some spectroscopic properties of *(1)*, the determination of the molecular structure of kekulene by X-ray analysis was of special interest.



(1)

(1) crystallized from pyrene (purified by zone-melting) in a tube sealed under high-vacuum on slow cooling from 450 to 350 °C. Removal of pyrene by high-vacuum sublimation and washing the crystals with chloroform yielded yellow monoclinic needles suitable for a structure analysis [crystal size $0.05\times0.08\times0.4$ mm; space group C2/c; $a=2799(3)$, $b=458.7(5)$, $c=2271(2)$ pm, $\beta=109.6(1)°$, $Z=4$, $\rho_{calc.}=1.45$ g·cm^{-3}; $Mo_{K\alpha}$ radiation, 1596 observed reflections, $R=0.056$].

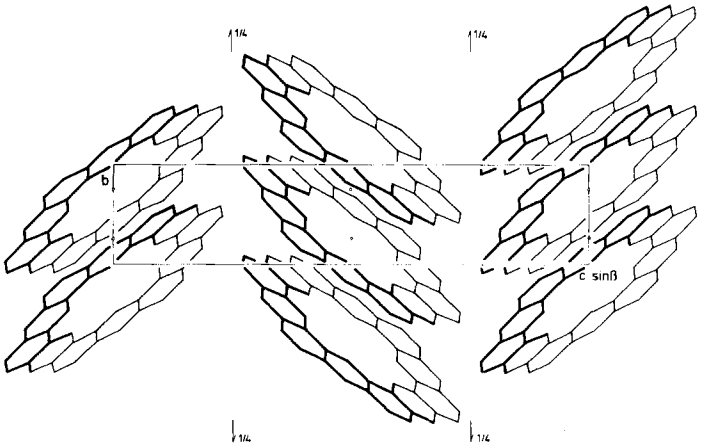


Fig. 1. Lattice structure of *(1)* as projected along the *a* axis (the rear half of the unit cell is not drawn).

In the crystal lattice of *(1)* the molecules are stacked along the *b* axis with the stacking axis forming an angle of 42.9° with the molecular planes. Neighboring molecules in such a stack have an interplanar distance of 336 pm and are parallel-shifted by 312 pm. The molecular planes of adjacent stacks are inclined by 86° to each other, resulting in the "herringbone pattern" shown in Figure 1 as a side view along the *a* axis.

With a mean deviation of carbon atoms from the mean plane through the 48 carbon atoms of only 3 pm and a maximum deviation of 7 pm, *(1)* has an almost perfectly planar structure. This includes, with deviations of 5 and 10 pm, respectively, even the six internal hydrogens, although the non-bonding distances of 196(2) pm between adjacent hydrogen atoms are unusually short.

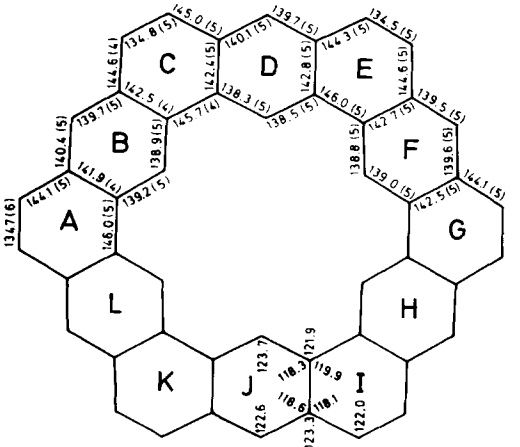
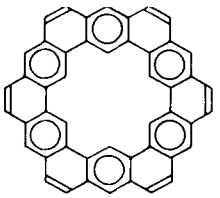


Fig. 2. Bond lengths of *(1)* in pm (standard deviations in units of the last figure given in brackets) and valence angles (as mean values of equivalent angles).

[*] Prof. Dr. H. A. Staab, C. Krieger, Dr. F. Diederich
Abteilung Organische Chemie
Dr. D. Schweitzer
Abteilung Molekulare Physik
Max-Planck-Institut für medizinische Forschung
Jahnstrasse 29, D-6900 Heidelberg 1 (Germany)

Figure 2 shows clearly that there is a remarkable difference between the bond lengths in the two groups of six-membered rings A, C, E, G, I, K and B, D, F, H, J, L. Only in the last-mentioned group, with mean values of 138.8 pm for the bonds of the internal *(1)*-perimeter and of 139.8 pm for the bonds of the external perimeter, are "normal" arene bond lengths observed; even here, all six radial bonds, having a mean value of 142.3 pm, are significantly stretched. Drastic deviations from the bond lengths of these "aromatic rings" (B, D,...), however, are found for the second group of six equivalent six-membered rings (A, C,...): The six peripheral CH—CH bonds of these rings have a mean value of 134.6 pm, *i.e.* almost the length of a normal C=C double bond; correspondingly, a mean length of 144.5 pm for the bonds between these "double bonds" and the "aromatic rings" (B, D,...) indicates a relatively high single bond character. An even stronger extension is found for the bonds (about 146 pm) which link the "aromatic rings" in the inner perimeter; they accordingly approach single bonds of the type found in polyphenyl systems.

Considering the number of 200 possible Kekulé structures of *(1)*, the considerable bond localization evident from the bond lengths might seem surprising. The observed variation in bond lengths was, however, predicted in its qualitative trend—though not in the extent actually found—by MO-SCF calculations[6]. Excellent agreement with the experimental bond lengths was found on evaluation of the Kekulé structures with regard to Pauling bond orders of the individual bonds in *(1)*[7]. On the basis of the structure analysis, a formulation employing *Clar*'s sextet notation *(1a)* is undoubtedly the best representation of the actual bonding situation in kekulene.



(1a)

Some spectroscopic properties of kekulene also agree well with the sextet formulation *(1a)*: The electronic spectrum of *(1)* shows an absorption at remarkably short wavelength as is generally observed, according to *Clar*[8], for arenes of the "condensed polyaryl type", such as hexabenzocoronene (Fig. 3).

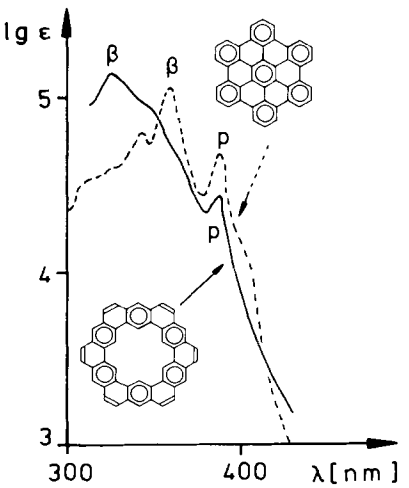


Fig. 3. Absorption spectra of *(1)* and hexabenzocoronene (in 1,2,4-trichlorobenzene).

3). The symmetry-forbidden α-band of *(1)* is obviously hidden under the long-wavelength part of the p-band; however, the strongly vibrationally structured fluorescence band at 453 nm evidently has to be assigned to this α-transition (Fig. 4a).

Just as hexabenzocoronene shows a strong phosphorescence at 575 nm (in 1,2,4-trichlorobenzene) at low temperatures[8], compound *(1)* in a [D_2]-1,2,4,5-tetrachlorobenzene matrix at 1.3 K exhibits a strong phosphorescence emission in the range 585—595 nm with several narrowly spaced "site"-dependent maxima and a vibrational structure resulting from combination with molecular vibrations in the range 1280—1630 cm^{-1} (Fig. 4b).

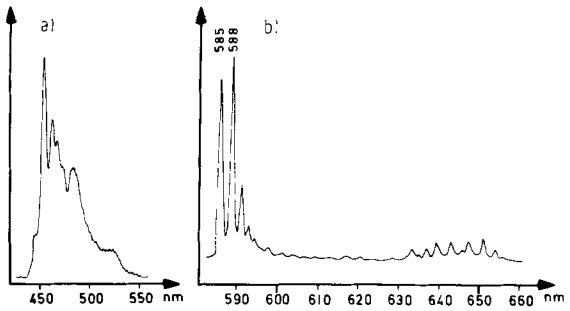


Fig. 4. a) Fluorescence spectrum of *(1)* (in 1,2,4-trichlorobenzene, 298 K, excitation 326 nm); b) phosphorescence spectrum of *(1)* (in [D_2]-1,2,4,5-tetrachlorobenzene, 1.3 K, excitation 365 nm); intensities in arbitrary units.

The strong phosphorescence of *(1)* permits application of the ODMR method for the determination of zero field splitting parameters |E| and |D| of the excited triplet state[9]. For *(1)* in a [D_2]-1,2,4,5-tetrachlorobenzene matrix, an |E| value of 0.001935 cm^{-1} was obtained which, as expected from the D_{6h} symmetry of *(1)*, is very low (benzene: $|E| = 0.0064$ cm^{-1}). However, the |D| value—which measures the dipolar coupling of the triplet electrons and, therefore, is inversely proportional to the third power of the average distance between these electrons—found for kekulene [$|D| = 0.10622$ cm^{-1}] is only slightly lower than for benzene and even greater than |D| for naphthalene and anthracene (cf. benzene 0.1581, naphthalene 0.0994, anthracene 0.0694 cm^{-1}). This unexpectedly small reduction of |D| in *(1)*[10] is very striking at first sight, considering the wide spatial extension of the π-electron system in kekulene. We seek to explain this result qualitatively as an effect of the partial compartmentization of the π-electron system in *(1)* as suggested by the X-ray structure analysis[11].

Received: July 31, 1979 [Z 293 IE]
German version: Angew. Chem. *91*, 733 (1979)

[1] Conjugation in Macrocyclic Systems, Part 30.—Part 29: *H. A. Staab, U. E. Meissner, A. Gensler*, Chem. Ber., in press.

[2] *F. Diederich, H. A. Staab*, Angew. Chem. *90*, 383 (1978); Angew. Chem. Int. Ed. Engl. *17*, 372 (1978).—*W. Jenny, P. Baumgartner, R. Paoni* (ISNA-Proc., Sendai/Japan, August 1970) claimed, without giving any details, to have prepared kekulene *(1)*—which they named "[12]coronaphene"—as long ago as 1970. Since other authors (cf., for example, [3]) refer to this claim we are compelled to make the following statement: The authors named have until now published neither a synthesis of *(1)* nor any account of its properties in the chemical literature. Although they have not repeated their claim to the synthesis of *(1)* in later topically related publications, they have failed so far to withdraw this claim.

[3] *J. Aihara*, Bull. Chem. Soc. Jpn. *49*, 1429 (1976).

[4] *R. McWeeny*, Proc. Phys. Soc. London *A 64*, 261, 921 (1951), and references given therein.

[5] *G. Ege, H. Vogler*, Theor. Chim. Acta *26*, 55 (1972); *H. Vogler*, Tetrahedron Lett. *1979*, 229; *C. Wilcox*, personal communication.

[6] *G. Ege, H. Fischer*, Tetrahedron *23*, 149 (1967).

[7] We thank Prof. *W. C. Herndon*, University of Texas at El Paso, for stimulating discussions.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/0909-0700 $ 02.50/0

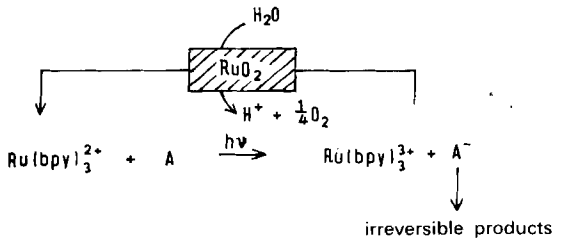
[8] *E. Clar:* Polycyclic Hydrocarbons, Vol. 2. Academic Press, New York/Springer-Verlag, Berlin 1964, p. 97.
[9] Concerning the ODMR method, see references in *D. Schweitzer, K. H. Hausser, V. Taglieber, H. A. Staab*, Chem. Phys. *14*, 183 (1976).
[10] Regarding these results with *(1)* it is interesting that similar ODMR results have been obtained recently with hexabenzocoronene and related aromatic hydrocarbons of the "polyaryl type" with high molecular symmetry: *J. Voitländer*, personal communication.
[11] Attempted theoretical treatment of this hypothesis: *H. Vogler*, Symposium on Aromaticity, Dubrovnik, September 1979.

Cyclic Cleavage of Water into H_2 and O_2 by Visible Light with Coupled Redox Catalysts[**]

By *Kuppuswamy Kalyanasundaram* and *Michael Grätzel*[*]

Hydrogen evolution from water can be catalyzed by suitable noble metal (oxide) dispersions[1]. Recently, we succeeded in developing redox catalysts which are capable of mediating oxygen production from water[2]. RuO_2 proved to be a judicious choice of material since it has an extremely low overpotential for O_2 evolution[3]. This paper reports on a system of two coupled redox catalysts permitting cyclic cleavage of water by light.

The water contained $Ru(bpy)_3^{2+}$ as a sensitizer, which after light excitation reduces an electron acceptor (A). Initially we added only RuO_2 to the solution and chose the acceptor such that it undergoes rapid subsequent reaction once it has been reduced. Such a system is suitable for separate investigation of the light-induced evolution of oxygen from water (Scheme 1).



Scheme 1

Table 1. Light induced evolution of O_2 from water with $Ru(bpy)_3^{2+}$ as sensitizer and RuO_2 as catalyst. t = irradiation time. Variant A: 50 ml of solution with 20 mg of RuO_2 powder or 0.3 mg of RuO_2 colloid. Variant B: 150 ml of solution with 50 mg of RuO_2 powder or 1.0 mg of RuO_2 colloid.

Acceptor Formula	c [mol/l]	pH	RuO_2 form	Variant	t [h]	O_2 [ml]
$TlCl_3$	8×10^{-3}	1.6	Powder	A	0.5	0.3
			Colloid	A	0.33	0.4
$[Co(NH_3)_5Cl]^{2+}$	10^{-2}	4.8 [a]	Powder	A	1.5	1.2
			Colloid	B	3	12
$[Co(NH_3)_5Br]^{2+}$	10^{-2}	4.8	Powder	B	9	3
			Colloid	B	9	3.2
$Co(C_2O_4)_3$	10^{-2}	4.8	Powder	A	1.5	0.3
			Colloid	A	1.5	0.4

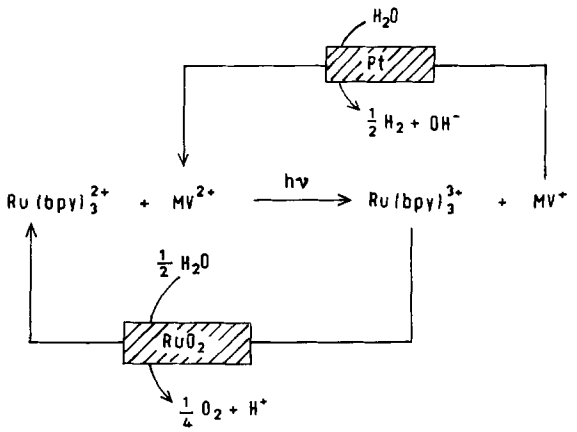
[a] The pH value of the solutions with cobalt complexes increases during irradiation, leading to formation of a brown precipitate. Precipitation can be avoided by buffering with acetate; cf. also [9].

Results are shown in Table 1. Oxygen is obtained with all the acceptors employed. The pathway of decomposition of the cobalt(III) complexes[4] and the irreversible photooxidation of $Ru(bpy)_3^{2+}$ by Tl^{3+} have been described in the literature[5]. An advantage of the Tl^{3+} system is the high quantum yield of $Ru(bpy)_3^{2+}$ oxidation ($\phi = 2$); however, the pH of the solution has to be kept below 1.7 to avoid precipitation of hydroxide complexes. Higher O_2 yields are obtained at pH between 4 and 5. It is noteworthy that even after long irradiation periods there is practically no depletion in sensitizer, indicating that the reverse reaction of $Ru(bpy)_3^{3+}$ to $Ru(bpy)_3^{2+}$ (Scheme 2) occurs faster than thermal decomposition[6]. (The turnover number of the sensitizer must be at least 100.) Table 1 also shows that colloidal RuO_2 is much more effective in mediating O_2 evolution than the powdered compound, since almost the same yields are obtained at 50–100 times smaller concentrations. The colloidal dispersion also has the advantage of being completely transparent.

The experiments for the simultaneous light-induced production of H_2 and O_2 were performed with dimethylviologen (*N,N'*-dimethylbipyridine dication, MV^{2+}) as an acceptor. MV^{2+} is reduced by photo-excited $Ru(bpy)_3^{2+}$ in a diffusion-controlled process[1e,7]. The reaction products, *i.e.* $Ru(bpy)_3^{3+}$ and MV^+, have the thermodynamic ability to produce oxygen and hydrogen from water. However, to mediate these processes, very active redox catalysts have to be employed since the back reaction can occur with a rate constant of $k = 2.4\times10^9$ l mol^{-1} s^{-1}[1c]. We recently found that a finely dispersed, centrifuged Pt sol (10^{-3} mol/l) reoxidizes MV^+ within microseconds[8]. This is therefore used to catalyze H_2 formation: RuO_2, on the other hand, can mediate efficiently the O_2 evolution step. When illuminating a solution containing 10^{-4} mol/l of $Ru(bpy)_3^{2+}$ and 2×10^{-3} mol/l of MV^{2+} at a pH of 4.7 in the presence of RuO_2 powder (50 mg/150 ml) or colloidal RuO_2 (1 mg/150 ml) *and* colloidal Pt (4.5 mg/150 ml), *simultaneous evolution of H_2 and O_2* is indeed observed. Typically, we obtained 0.3 ml of O_2 and 0.6 ml of H_2 after 3 hours' illumination of 150 ml of solution with a 250-W projector lamp. Blank experiments showed that the presence of both redox catalysts is mandatory for production of both gases. The depletion of $Ru(bpy)_3^{2+}$ during 3 hours' irradiation is less than 5%, illustrating the cyclic nature of this cleavage of water. The two catalysts seem to be sufficiently specific to avoid short-circuiting of the back reaction. Also, it appears that charge transfer from MV^+ to Pt can compete efficiently with O_2 reduction according to

$$MV^+ + O_2 \rightarrow O_2^- + MV^{2+}$$

From these findings we deduce the following reaction sequence shown in Scheme 2.



Scheme 2

According to these findings, the cleavage of water by visible light is undoubtedly possible in a four-quantum process.

[*] Prof. Dr. M. Grätzel, Dr. K. Kalyanasundaram
Institut de chimie physique, Ecole Polytechnique Fédérale
CH-1015 Lausanne (Switzerland)

[**] Acknowledgment is made to the Swiss National Foundation for supporting this work under grant No. 4.061.076.04, and to Ciba-Geigy Ltd., Basel, Switzerland.

In the development of such systems we see a possibility of achieving solar energy conversion by use of homogeneous or microheterogeneous aqueous solutions.

Experimental

The RuO_2 catalysts used were $RuO_2 \cdot H_2O$, (Alfa Inorganics) and a colloidal suspension stabilized by a copolymer of styrene and maleic anhydride[10]. The colloid was prepared by treating a neutral solution of RuO_4 in water (50 mg) with a 0.5% aqueous solution (25 ml) of the copolymer. The pH is adjusted to 8 and the solution stirred for one hour. A RuO_2 sol is formed spontaneously with a mean particle radius of 300 Å.

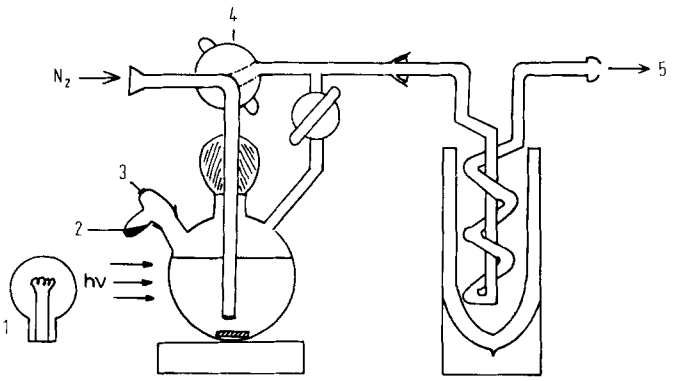


Fig. 1. Schematic illustration of the instrumental set-up used for light-induced cleavage of water. 1, 250-W lamp; 2, catalyst; 3, septum; 4, three-way stopcock; 5, to oxygen measuring instrument.

The solution is placed in a flask containing the solid catalyst in a side arm. This is also fitted with a septum allowing for injection of colloidal catalyst and removal of gas samples. The flask is connected to a trap and an End-O-Mess oxygen meter (Friedrichsfeld GmbH, Mannheim, Germany) (Fig. 1).

Prior to illumination, the whole system is carefully deaerated by flushing with nitrogen. The two stopcocks are then closed and the flask illuminated by a 250-W slide projector lamp. After irradiation the gas evolved in the solution is flushed out and transferred to the oxygen meter by a stream of nitrogen. In order to check hydrogen production a sample of gas is taken through the septum by an air-tight syringe and subjected to gas chromatography.

A test run was first made with a 8×10^{-3} M Ce^{4+} solution in 1 N H_2SO_4 which, on contact with the hydrated RuO_2 powder, gave oxygen in the dark[2] under simultaneous reduction of Ce^{4+} to Ce^{3+}. This reaction produces O_2 with a >80% efficiency. Unhydrated RuO_2 failed to give oxygen.

Received: July 13, 1979 [Z 291 IE]
German version: Angew. Chem. *91*, 759 (1979)

[1] a) *B. V. Koryakin, T. S. Dzhabiev, A. E. Shilov,* Dokl. Akad. Nauk SSSR *238*, 620 (1977); b) *J. M. Lehn, J. P. Sauvage,* Nouveau J. Chim. *1*, 449 (1977); c) *K. Kalyanasundaram, J. Kiwi, M. Grätzel,* Helv. Chim. Acta *61*, 2720 (1978); d) *A. Moradpour, E. Amouyal, P. Keller, H. Kagan,* Nouveau J. Chim. *2*, 547 (1978); e) *B. O. Durham, W. J. Dressick, T. J. Meyer,* J. Chem. Soc. Chem. Commun. *1979*, 381.
[2] *J. Kiwi, M. Grätzel,* Angew. Chem. *90*, 900 (1978); *91*, 659 (1979); Angew. Chem. Int. Ed. Engl. *17*, 860 (1978); *18*, 624 (1979); Chimia *33*, 289 (1979).
[3] *H. H. Miles,* J. Electroanal. Chem. Interfacial Electrochem. *60*, 84 (1975).
[4] *H. D. Gafney, A. W. Adamson,* J. Am. Chem. Soc. *94*, 8238 (1972); *G. Navon, N. Sutin,* Inorg. Chem. *13*, 2159 (1974); *J. N. Demas, A. W. Adamson,* J. Am. Chem. Soc. *95*, 5159 (1973).
[5] *G. S. Laurence, V. Balzani,* Inorg. Chem. *13*, 2976 (1974).
[6] *C. Creutz, N. Sutin,* Proc. Nat. Acad. Sci. USA *72*, 2858 (1975).
[7] *R. C. Young, T. J. Meyer, D. G. Whitten,* J. Am. Chem. Soc. *98*, 286 (1976).
[8] *J. Kiwi, M. Grätzel,* J. Am. Chem. Soc., in press.
[9] We thank Prof. *Lehn,* for providing us with a manuscript in which evidence for O_2 evolution with the same system was presented.— Note added in proof: cf. *J.-M. Lehn, J.-P. Sauvage, R. Ziessel,* Nouveau J. Chim. *3*, 423 (1979).
[10] We thank Unilever, Port Sunlight (England), for the gift of the copolymer.

BOOK REVIEWS

Hummel/Scholl: Atlas of Polymer and Plastics Analysis. 2nd, revised edition. Vol. 1. Polymers: Structures and Spectra. By *D. O. Hummel.* Verlag Chemie, Weinheim/Carl Hanser Verlag, München 1978. xxxii, 671 pp., 1903 IR spectra, DM 475.00.

IR spectroscopists working with polymers will welcome publication of this new edition of "Hummel"—ten years after the appearance of the first edition. Subdivision and aim of the compilation of spectra have changed: Volume 1 now bears the title "Structures and Spectra", and the subsequent Volumes 2 (Plastics, Fibres, Rubbers, Resins) and 3 (Additives and Processing Acid) are subtitled "Spectra and Methods of Identification". The textual volume has been dropped. New features include the use of an improved decimal classification system, adoption of names recommended by IUPAC, and consistent use of a linear wave number scale.

The 1903 spectra depict a cross-section through the polymer chemistry of the past decade, ranging from materials of construction to polymers newly developed, *e.g.*, as ion exchangers, semiconductors, or carriers for enzymes. Most of the polymers have been described in the literature; the respective samples reached the author from laboratories throughout the world.

A problem attending such a work is always that of the purity of the substances concerned. Thus, a glance at page 2 of the book already shows absorption bands of ubiquitous silicone oil (spectrum no. 4) or gives an indication of oxidative degradation (spectra nos. 5 and 6). Whenever recognized, any impurities are mentioned in the accompanying text.

Searches are greatly facilitated by a list of contents, decimal classification, subject index, molecular formula index, and author index.

The spectra cover the range of 4000 to 400 cm^{-1}. The scale of the two formats adopted agree in the region between 2000 and 400 cm^{-1}. Comparison and reading off of wave numbers is often made difficult by the failure to emphasize the round hundreds on the wave number grid. There is no wavelength scale for those still accustomed thereto. (Perhaps a transparent foil bearing a wave number and wavelength grid could be supplied with futures volumes.)

In spite of its high price, the book can be recommended as a valuable tool to all concerned with the IR spectroscopy of polymers.

Hans H. Suhr [NB 474 IE]

Correlation Analysis in Chemistry. Recent Advances. Edited by *N. B. Chapman* and *J. Shorter*. Plenum Press, New York 1978. xiii, 546 pp., bound, $ 59.40.

Six years after the publication of "Advances in Linear Free Energy Relationships", *N. B. Chapman* and *J. Shorter* have produced a sequel, "Correlation Analysis in Chemistry". Specific aspects of linear free energy relationships are presented in great detail in ten chapters authored by specialists in the fields concerned.

Two contributions (*S. Wold* and *M. Sjöström; M. Godfrey*) are concerned with the fundamental question of the conditions under which linear correlations are to be expected between the characteristic properties of an ensemble of processes and systems (molecules). Since not only free energies (thermal and kinetic quantities) are correlated with one another, a somewhat less specific title was chosen for the book. It was then also possible to report about attempted correlations in biochemistry *(C. Hansch)*.

The topic of four surveys is the best known linear free energy relationship, the Hammett equation. *J. Shorter* reviews Hammett relationships which require more than a single σ parameter. *D. F. Ewring* summarizes correlations between σ values and NMR data. Linear correlations in polycyclic and heterocyclic aromatic compounds are described by *M. Charton*, and *O. Exner* provides a critical survey of the σ values of over 500 substituents.

Two further contributions consider the effects of substituents on alkenes *(G. P. Ford, A. R. Katritzky, R. D. Topsom)* and on nucleophiles *(C. Duboc)*. In conclusion, *R. P. Bell* retraces the first 50 years of the oldest known linear free energy relationship, *viz.* the Brønstedt equation.

The individual sections are broad in their coverage and each contains up to 400 literature references. The main emphasis is not placed on presentation of the very latest results; instead, an attempt is made to give a general description of the field covered.

This book is intended for chemists engaged in research and/or teaching in the area of reaction mechanisms. Apart from the value of the other contributions, the enormous collection of σ values by *Exner*, which renders further searching unnecessary, recommends the purchase of this book by chemical libraries.

Bernd Giese [NB 476 IE]

The Gamma Rays of the Radionuclides. By *G. Erdtmann* and *W. Soyka*. Verlag Chemie, Weinheim 1979. xv, 862 pp., bound, DM 240.00.

Gamma ray spectrometry is by far the most important method for the identification and activity determination of radionuclides. It has become an indispensable tool for work in pure nuclear physics, in nuclear and radio-chemistry, and for applications such as nuclear technology, activation analysis, and the monitoring of environmental radioactivity. A sound knowledge of data pertaining to the emitted gamma rays and the availability of corresponding tabulated values are essential requirements for practical gamma ray spectrometry.

The first edition of the catalog "Die γ-Linien der Radionuclide", published in 1973 as a special report of the Nuclear Research Establishment at Jülich was the sole complete compilation of the γ-lines of all the radionuclides then known. In view of the advances made in this field, it is hardly surprising that the authors have now provided a revised and greatly expanded edition of that work.

The book contains two tables listing all the radionuclides known in 1977 (2055). In the first table, they are arranged in order of increasing atomic and mass numbers, and the X-rays and γ-rays emitted on their disintegration are arranged according to their energy. Absolute intensities are given as percentages in most cases. Only in those cases where the authors were unable to obtain reliable absolute values are relative intensities given on the basis of the intensity of the most frequent γ-transition. Intensity data have been omitted only for a few of the radionuclides which are far removed from the stability line, and therefore difficult to produce and of very little practical importance. The evaluation and interpretation of complex gamma ray spectra is greatly facilitated by inclusion of escape lines which are generated by interaction of high-energy gamma rays ($E_\gamma > 1.022$ MeV) with detector material (by pair production processes) but appear in the guise of photopeaks of true gamma lines in the spectrum.

Since high-resolution Si(Li), Ge(Li), and very pure germanium detectors have become available, X-ray spectrometry has joined the γ-ray method as an important measuring technique, especially in activation analysis. Therefore the enormous efforts of the authors to arrive at the absolute intensities of X-ray lines deserve special praise, for these intensities have been measured for only few radionuclides. The $K_{\alpha 2}, K_{\alpha 1}, K'_{\beta 1}$, and $K'_{\beta 2}$ lines are normally given separately, being considered together only when the energy difference is less than 100 eV. In this way the tabulated data are very well adapted to the present situation, with today's detectors having an energy resolution around 140 eV.

The first table also contains data of radionuclides which do not emit γ-rays, *i.e.* pure β- or X-ray emitters; this ensures an optimum degree of completeness. Supplementary data characterizing radionuclides, such as half-lives and generation reactions, as well as parent and daughter nuclides can often be extremely useful.

The second table is intended for assisting in the evaluation of unknown spectra; it contains X-ray and γ-ray lines in the order of increasing energy, together with the corresponding radionuclide, its half-life, up to five further X-ray or γ-ray lines, and details concerning the generation of the radionuclide.

Credit must also go to the authors for the critical approach adopted in determining the values for the γ-lines; they were obtained either by searching for the "most reliable" value or by weighting the individual results. All the more pity, then, that limitations of space precluded the inclusion of information about the accuracy of energy and intensity values.

Considering the completeness, the quality, and the presentation of the data as assessment criteria, this tabular work is a masterpiece. As the most important catalog of X-ray and γ-ray lines presently available it should have a place in the library of every laboratory in which such spectrometric techniques are used. It should be mentioned, however, that one can justifiably expect a very valuable work for this handsome price which will unfortunately prevent most people from purchasing their personal copy.

Viliam Krivan [NB 478 IE]

pH-Wert-Berechnungen. By *C. Bliefert*. Verlag Chemie, Weinheim 1978. xvi, 255 pp., bound, DM 48.00.

In keeping with its title, this book provides a survey of acid-base theories and an introduction to the calculation of pH values. Starting from relatively simple problems, such as pH calculations for monoprotic acids and bases, the book progresses to a detailed treatment of more complicated systems (acid- and base mixtures, ampholytes), and the calculation of titration curves, pH diagrams, degrees of protolysis, *etc.* is explained. In this way it becomes possible to deal quan-

titatively with a large number of acid-base equilibria using simple mathematical tools. Not only exact calculations are considered, but approximation methods are also treated wherever they are of value. It appears particularly valuable that exact and approximate calculations are compared, giving numerical data concerning the effect of neglecting certain quantities for various concentration ranges and pK_a values in the approximate methods. This enables the user to select the method suitable or adequate for his purpose without having to always use the involved formula required for exact calculation. Many graphic representations aptly illustrate the calculations. Numerous questions at the end of each chapter not only introduce the reader to the problems involved but provide him with an opportunity to test his ability, and also furnish yet more information. The solutions—and in most cases the method of solution—are given for all questions. An appendix contains flow charts for some selected calculations which can be translated into computer language.

The book is written fluently and clearly. Its aim of showing the beginner and advanced student, as well as the practical chemist, how to calculate (approximately or exactly) the pH values of aqueous systems is undoubtedly fulfilled. It can therefore be wholeheartedly recommended to all interested persons, and particularly to teachers at all levels. The reviewer has just one wish for a second edition: It would be convenient if a further section could be included comparing calculated and measured pH values in somewhat more detail, *i.e.* if the influence of factors such as concentration, ionic strength, *etc.* on the activity were to be viewed more closely. The fact that measured pH values often deviate considerably from the calculated values, which often confuses the beginner, would then be easier to understand. In spite of this wish: the book truly enriches the available chemical literature.

Hans Rudolf Christen [NB 479 IE]

Kirk-Othmer: Encyclopedia of Chemical Technology. Editorial board: *H. F. Mark, D. F. Othmer, C. G. Overberger,* and *G. T. Seaborg.* John Wiley & Sons, New York 1978, 3rd Edit. Vol. 4: Blood, Coagulants and Anticoagulants to Cardiovascular Agents. xxv, 930 pp., bound, $ 95.00.

The fourth volume of Kirk-Othmer[*] contains entries on some 30 keywords, the longest ones being: carbon (*ca.* 150 pages); boron compounds (*ca.* 130 pages); carbides (*ca.* 60 pages); cardiovascular agents (*ca.* 60 pages); carboxylic acids (*ca.* 60 pages); blood fractionation (*ca.* 40 pages). The reader notes that not only chemical technology but also biotechnological aspects are treated at considerable length.

The subdivision of the material is very balanced, as in the first volumes. In addition to production and workup, space is always given to the physical and chemical properties of products, their uses, and the principal economic data of the processes. Presentation is generally terse, and yet highly informative. Omissions in the material are very rare. Production figures could be a little more up-to-date in some cases: those given for borate do not extend beyond 1973/1975. There is no mention, in the article about carbon dioxide, of the use of supercritical CO_2 for extraction of heat-sensitive natural products (such as coffee and tobacco) although plants utilizing this technology have already come on stream. Moreover, some sections consider only English-language literature.

Nevertheless, such minor points do not detract from the excellence of this work, specifically the present Volume 4.

R. Steiner [NB 480 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Lexikon Elektronik. Edited by *H.-D. Junge.* Physik-Verlag, Weinheim 1978. 751 pp., bound, DM 34.00.—ISBN 3-87664-038-5

Advances in Heterocyclic Chemistry. Vol. 23. Edited by *A. R. Katritzky* and *A. J. Boulton.* Academic Press, New York 1978. ix, 487 pp., bound, $ 49.50.—ISBN 0-12-020623-4

Chemistry of the Environment. By *R. A. Bailey, H. M. Clarke, J. P. Ferris, S. Krause,* and *R. L. Strong.* Academic Press, New York 1978. x, 575 pp., bound, $ 26.00.—ISBN 0-12-073050-2

Polymer Stress Reactions. Vol. 2. Experiments. By *A. Casale* and *R. S. Porter.* Academic Press, New York 1979. xxi, pp. 253—594, bound, $ 32.00.—ISBN 0-12-162802-7

Grenzorbitale und Reaktionen organischer Verbindungen. By *I. Fleming.* Verlag Chemie, Weinheim 1979. x, 292 pp., sewed, DM 44.00.—ISBN 3-527-25792-6

Toxicity of Heavy Metals in the Environment. Part 2. Edited by *F. W. Oehme.* Marcel Dekker, New York 1979. x, pp. 517—970, bound, $ 45.00.—ISBN 0-8247-6719-5

Reactive Intermediates. Vol. 1. Edited by *M. Jones, Jr.* and *R. A. Moss.* John Wiley & Sons, London 1978. ix, 349 pp., bound, £ 16.50.—ISBN 0-471-01874-1

Polarized Light Microscopy. By *W. C. McCrone, L. B. McCrone,* and *J. G. Delly.* Ann Arbor Science, Ann Arbor 1978. vii, 251 pp., bound, $ 33.00.—ISBN 0-250-40262-9

Grundlagen der Histochemie. Teil I. By *H. Luppa.* Vieweg, Braunschweig 1978. 369 pp., bound, DM 34.00.—ISBN 3-528-06835-3

Energy Conservation in Biological Membranes. Edited by *G. Schäfer* and *M. Klingenberg.* Springer-Verlag, Berlin 1978. xiv, 288 pp., bound, DM 68.00.—ISBN 3-540-09079-7

The Gamma Rays of the Radionuclides. Vol. 7. By *G. Erdtmann* and *W. Soyka.* Verlag Chemie, Weinheim 1979. xv, 862 pp., bound, DM 240.00.—ISBN 3-527-25816-7

Physiologische Grundlagen von Haltung und Bewegung. By *G. Asmussen.* Verlag Chemie, Weinheim 1979. 155 pp., bound, DM 22.00.—ISBN 3-527-25830-2

Die Korrosion der Metalle. By *H. Kaesche.* Springer-Verlag, Berlin 1979. 2nd, revised and enlarged edition. 390 pp., bound, DM 148.00.—ISBN 3-540-08881-4

ANGEWANDTE CHEMIE

International Edition in English

Volume 18 · Number 10
October 1979
Pages 707–808

New Synthetic Reactions Based on the Onium Salts of Aza-Arenes

New synthetic methods (29)

By Teruaki Mukaiyama[*]

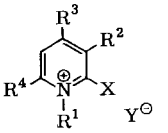
Effective syntheses employing 2-halogenated pyridinium, benzoxazolium, benzothiazolium, and pyridinium salts have been accomplished in the absence of strong acids and bases. Activation of carboxylic acids or alcohols with these onium salts leads to 2-acyloxy and 2-alkoxy intermediates which can be transformed into esters, amides, thiol esters, (macrocyclic) lactones, acid fluorides, olefins, allenes, carbodiimides, isocyanates, isothiocyanates, nitriles, and isocyanates. The possibility of performing stereospecific syntheses (involving configurational inversion) with onium salts deserves attention.

1. Introduction

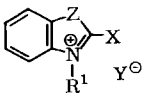
Remarkable progress has been achieved in the field of synthetic organic reactions by the use of readily available strong bases such as alkyllithium and also of acidic reagents such as $TiCl_4$[1]. However, in the synthesis of complex molecules, such as biologically active substances having base- or acid-labile functionalities, it is highly desirable to be able to work under neutral or neutralization conditions. One approach is to utilize characteristic properties of trivalent phosphorus compounds and organosulfur compounds in "oxidation-reduction condensation"[2]. For example, this method affords carboxylic thiol esters from carboxylic acids and thiols without any assistance from an acid or a base[3]:

$$R^1CO_2H + R^2SSR^2 + (C_6H_5)_3P \rightarrow R^1C(O)SR^2 + R^2SH + (C_6H_5)_3P{=}O$$

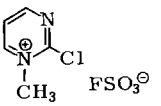
In reactions of this type, the utilization of the onium salts seems to be promising, since ionic character in the intermediate should result in the close proximity of reacting species around the onium salts, thus promoting smooth reaction under mild conditions. On the basis of this consideration, we have investigated the use of onium salts of aza-arenes, and it has become clear that the onium salts are effective for the activation of carboxyl and hydroxyl components in the presence of such weak bases as trialkylamines under neutralization condition. Table 1 lists some of the onium salts used and various abbreviations.



(1)



(33), (55)



(58)

Table 1. Onium salts used and key to abbreviations.

Onium salt	R^1	R^2	R^3	R^4	X	Y	Z
(1a)	CH_3	H	H	H	Cl	I	—
(1b)	CH_3	H	H	H	Br	I	—
(1c)	C_2H_5	H	H	H	Cl	BF_4	—
(1d)	C_2H_5	H	H	H	Br	BF_4	—
(1e)	CH_3	H	H	H	F	TsO	—
(1f)	C_6H_5	C_6H_5	H	CH_3	Cl	BF_4	—
(1g)	CH_3	CH_3	H	H	F	TsO	—
(1h)	C_2H_5	H	H	H	F	BF_4	—
(1i)	C_2H_5	H	CH_3	CH_3	F	BF_4	—
(1k)	C_2H_5	CH_3	H	H	F	BF_4	—
(33)	C_2H_5	—	—	—	Cl	BF_4	O
(55a)	CH_3	—	—	—	F	FSO_3	S
(55b)	C_2H_5	—	—	—	F	BF_4	S

Me = methyl, Et = ethyl, Bu = butyl, Ph = phenyl, Ac = acetyl, Bz = benzyl, Ts = *p*-toluenesulfonyl, THP = tetrahydropyranyl

TEBA = benzyltriethylammonium chloride, DME = dimethoxyethane, HMPA = hexamethylphosphoric triamide, THF = tetrahydrofuran

[*] Prof. Dr. T. Mukaiyama
Department of Chemistry, Faculty of Science
The University of Tokyo, Hongo, Tokyo 113 (Japan)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0707 $ 02.50/0*

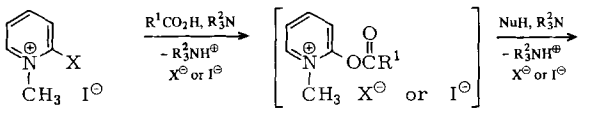
This review describes recent synthetic advances using 2-halopyridinium, 2-fluorobenzothiazolium, and 2-chlorobenzoxazolium salts with specific accounts of intermolecular and intramolecular dehydration, and syntheses of optically active substances.

2. Intermolecular Dehydration

2.1. Activation of Carboxylic Acids

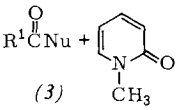
2.1.1. Synthesis of Carboxylic Esters, Amides, and Thiol Esters

The study of these reactions was prompted by the following observations: 2-Acyloxy-1-methylpyridinium iodide *(2)*, an active acylating intermediate, should be produced easily and rapidly by a nucleophilic attack of a carboxylate ion on 2-chloro- *(1a)* or 2-bromo-1-methylpyridinium iodide *(1b)*, since the 2-halogen atom of these onium salts is easily replaced by nucleophiles. The intermediate *(2)* should in turn be converted into stable neutral molecules, *i.e.* the acylated product *(3)*, 1-methyl-2-pyridone, and the ammonium salt, by the attack of a nucleophile in the presence of a tertiary amine as hydrogen iodide captor. Since all the reacting species are in close proximity to the central pyridinium ion, the condensation reaction should be entropically advantageous.



(1a), X = Cl
(1b), X = Br

(2)



(3)

On the basis of these assumptions, the formation of carboxylic esters from equimolar amounts of carboxylic acids and alcohols was investigated[4]. In the first place, effective hydrogen halide captors were examined for the condensation of equimolar amounts of phenylacetic acid and benzyl alcohol using *(1a)*. Triethylamine, tributylamine, and 2,6-lutidine gave good results (98, 99, and 97% yield, respectively); the yield of benzyl phenylacetate decreased as the basicity of the amine decreased.

Table 2. Synthesis of esters from equimolar amounts of carboxylic acid and alcohol with 2-chloro- *(1a)* or 2-bromo-1-methylpyridinium iodide *(1b)* and tri-*n*-butylamine (3 h, reflux).

$R^1CO_2H + R^2OH \rightarrow R^1CO_2R^2$

Onium salt	R^1	R^2	Yield [%] in CH_2Cl_2	in toluene
(1b)	C_6H_5	$C_6H_5CH_2$	80	
	$C_6H_5CH_2$	C_2H_5	92	
	$C_6H_5CH_2$	$C_6H_5CH_2$	97	
	$C_6H_5CH_2$	$(CH_3)_3C$	70	82
	CH_3	$C_6H_5CH_2$	80	
	CH_3	$C_6H_5CH{=}CHCH_2$	80	
(1a)	$C_6H_5CH_2$	C_6H_5	90	
	$C_6H_5CH_2$	$C_6H_5CH_2CH_2$	93	
	$C_6H_5CH_2$	$(CH_3)_3C$	81	84
	$C_6H_5CH_2$	$C_6H_5(CH_3)CH$	85	88
	CH_3	$C_6H_5CH_2CH_2$	74	
	$(CH_3)_3C$	$C_6H_5CH_2$	31	62

No significant solvent effect was observed in the reaction, benzyl phenylacetate being obtained in almost quantitative yield in diethyl ether (97%), dichloromethane (99%), acetonitrile (98%), pyridine (98%), toluene (99%), *etc.*—Examples of esterification are shown in Table 2.

The effect of changing the counterion and the halogen atom of the pyridinium salt on the yield of carboxylic esters urged us to look for more effective pyridinium salts. Thus ester formation from 3-phenylpropionic acid and benzyl alcohol (tri-*n*-butylamine, 1 h, reflux in dichloromethane) using the 2-halopyridinium salts *(1a)*—*(1d)* gave yields of 69, 61, 73, and 82%, respectively (Table 1).

Table 3. Synthesis of esters from equimolar amounts of carboxylic acid and alcohol with 2-bromo-1-ethylpyridinium tetrafluoroborate *(1d)* and tri-*n*-butylamine in CH_2Cl_2.

$R^1CO_2H + R^2OH \rightarrow R^1CO_2R^2$

R^1	R^2	Yield [%] 3 h reflux [a]	12 h 20 °C
$C_6H_5CH_2CH_2$	C_2H_5	73 (59)	
$C_6H_5CH_2CH_2$	C_6H_5	57	61
C_2H_5	$C_6H_5CH_2$	62 (39)	71
C_2H_5	$C_6H_5CH_2CH_2$	60 (48)	
$C_6H_5CH{=}CH$	$C_6H_5CH_2$	71 (62)	
$C_6H_5CH{=}CH$	C_2H_5	43 (27)	
$(CH_3)_3C$	$(CH_3)_3C$	21	54
$C_6H_5CH_2$	$(CH_3)_3C$		78
Cl_3C	$C_6H_5CH_2$	40	62
$ClCH_2$	$C_6H_5CH_2$	88	
$ClCH_2$	$C_6H_5CH_2CH_2$	80	
2-Furyl	$C_6H_5CH_2$		97
$C_6H_5C{\equiv}C$	$C_6H_5CH_2$		85
$C_6H_5COCH_2$	$C_6H_5CH_2$		87
$CH_3COCH_2CH_2$	$C_6H_5CH_2$		45
Cyclopropyl	$C_6H_5CH_2$		62
$CH_3CH{=}CH{-}CH{=}CH$	$C_6H_5CH_2$		59

[a] Values in parentheses refer to the reaction with 2-chloro-1-methylpyridinium iodide *(1a)*.

Then the reaction of several carboxylic acids, including functionalized ones, with strictly equimolar amounts of alcohols was carried out with 2-bromo-1-ethylpyridinium tetrafluoroborate *(1d)* and tri-*n*-butylamine as coupling reagents; favorable results were obtained especially at room temperature (Table 3). Particular mention should be made of the esterification of pivalic acid, trichloroacetic acid, and benzoylacetic acid, also with various sterically hindered alcohols, such as *tert*-butyl alcohol.

When alcohols were replaced by primary or secondary amines as nucleophiles, carboxamides were obtained in high yields (Table 4)[5]. The preparation of carboxamides using 2-

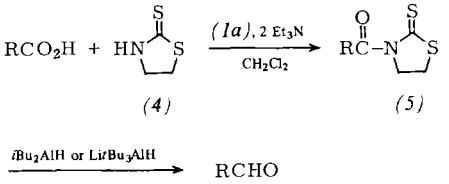
Table 4. Synthesis of carboxamides from acids and amines with the onium salt *(1a)* or *(1b)* and tri-*n*-butylamine (1 h, reflux in CH_2Cl_2).

$R^1CO_2H + R^2R^3NH \rightarrow R^1CONR^2R^3$

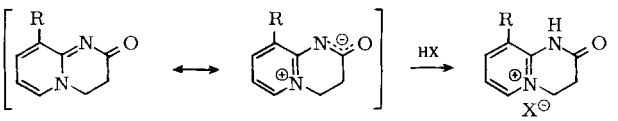
Onium salt	R^1	R^2	R^3	Yield [%]
(1a)	C_6H_5	n-C_4H_9	n-C_4H_9	quant.
	$C_6H_5CH_2$	t-C_4H_9	H	quant.
	t-C_4H_9	$C_6H_5CH_2$	H	93
(1b)	C_6H_5	C_6H_5	H	85
	$C_6H_5CH_2$	$C_6H_5CH_2$	H	quant.
	$C_6H_5CH_2$	n-C_8H_{17}	H	98

iodopyridinium salt as a coupling agent had been previously studied in detail by *Sutherland et al.*[6]. However, only modest yields were obtained. These results again indicate the significant effect of the halogen atom attached to position 2; only chlorine and bromine derivatives give favorable results.

3-Acylthiazolidine-2-thione *(5)*, obtained in high yield from a carboxylic acid and thiazolidine-2-thione *(4)* on use of a 2-chloro-1-methylpyridinium iodide *(1a)*, proved to be an interesting intermediate. When *(5)* was treated with aluminum hydride reagents, the corresponding aldehyde was produced selectively, free from alcohol. Thus the overall transformation provides a new and efficient method for the partial reduction of carboxylic acids to aldehydes[7].



In the above syntheses of carboxylic esters or amides, the use of two moles of tertiary amine per mole of acid is necessary to scavenge hydrogen halide formed during the reaction. Although at the end of the reaction, tertiary amine is completely converted into the ammonium salt, the reaction medium is initially weakly basic. Development of a less basic acid captor to replace the tertiary amine therefore appeared desirable. It was thought that dihydropyridopyrimidones *(6)* would be most promising captors since a betaine structure *(7)* can be written and, on treatment with an acid, they are converted into the onium salt *(8)*. The pyrimidone derivatives *(6a)* and *(6b)* are easily prepared from ethyl acrylate and 2-aminopyridine or 2-aminopicoline[8]. The use of *(6)* in place of a tertiary amine also gave favorable results in the preparation of carboxylic esters or amides from equimolar amounts of carboxylic acids and alcohols or amines[9].



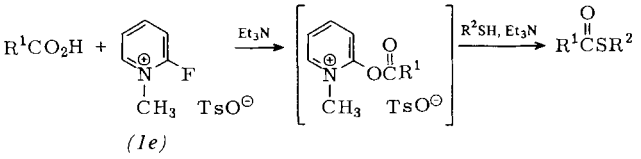
(6a), R = H
(6b), R = CH_3

(7)

(8)

The basicity of pyrimidone *(6)* is low ($pK_b = -6.5$), and the pyrimidinium salt *(8)* formed by reaction with a hydrogen halide is insoluble in almost all organic solvents and precipitates from the reaction mixture. Consequently, condensation can be performed under almost completely neutral conditions. The reaction requires 2 moles of *(6)* per mole of acid; the yields of esters and amides are 70—97 and 80—*ca.* 100%, respectively.

A similar procedure proved unsuccessful for the preparation of thiol esters from carboxylic acids and thiols, since competitive attack of thiols on the 2-chloropyridinium salts caused the reaction to become rather complex. However, this difficulty was overcome by use of a stepwise procedure and employment of a 2-fluoropyridinium salt such as *(1e)*. When a carboxylic acid is treated with a 2-fluoropyridinium salt and triethylamine in dichloromethane at low temperature, a 2-acyloxypyridinium salt is formed immediately, and subsequent addition of thiol affords the corresponding thiol ester in high yield (Table 5)[10]. Since the yield of thiol ester from the reaction of acid fluoride and thiol under similar conditions is generally low, this result affords indirect support for the intervention of 2-acyloxypyridinium salts as an intermediate. The usefulness of 2-fluoropyridinium salts will be demonstrated in Section 2.1.3.



(1e)

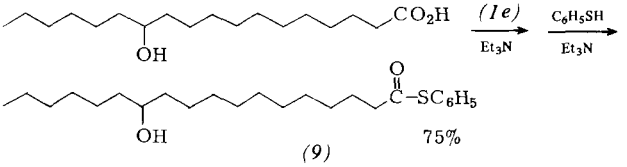
Table 5. Synthesis of thiol esters with 2-fluoro-1-methylpyridinium tosylate *(1e)* and triethylamine.

R^1	R^2	Yield [%]
C_6H_5	C_6H_5	87
$C_6H_5CH_2$	C_6H_5	96
$(CH_3)_3C$	C_6H_5	88
$CH_3COCH_2CH_2$	C_6H_5	83
$HO_2C(CH_2)_4$	C_6H_5	79 [a]
$C_6H_5CH_2$	n-C_4H_9	81 [b]
$C_6H_5CH_2$	s-C_4H_9	81
$C_6H_5CH_2$	t-C_4H_9	84
$C_6H_5CH_2$	α-Pyridyl	79

[a] Synthesis of hexanebis(*S*-phenyl thioate) from adipic acid and thiophenol in a molar ratio of 1:2. [b] With tri-*n*-butylamine as base.

Alternative methods for the direct preparation of thiol esters from free carboxylic acids include a method utilizing triphenylphosphane and diphenyldisulfane (or 2,2′-dipyridyldisulfane) which has been reported from our laboratory[2,3]. *Yamada et al.* used diethyl phosphorocyanidate or diphenyl phosphorazidate[11]. However, the present reaction provides a convenient method for the preparation of thiol esters with respect to (i) direct synthesis from equimolar amounts of free carboxylic acid and thiol and (ii) the mildness of the reaction conditions.

Furthermore, preparation of the thiol ester *(9)* derived from a hydroxy acid (12-hydroxyoctadecanoic acid) and thiophenol was successfully accomplished without protecting the hydroxyl group by adding the 2-fluoropyridinium salt *(1e)* to the carboxylic acid and triethylamine at room temperature, and treating the resulting mixture with thiophenol and triethylamine[10].



(9)

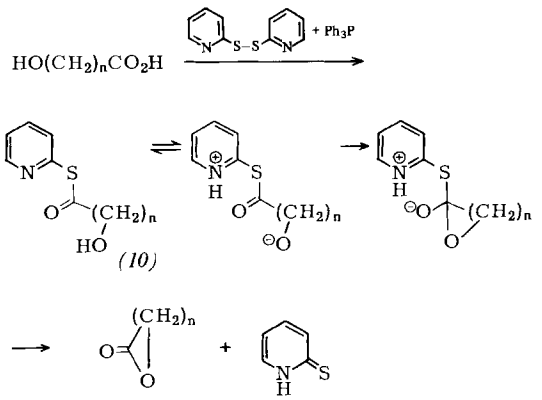
2.1.2. Synthesis of Macrocyclic Lactones[*]

The discovery of numerous macrolide antibiotics has generated a recent surge of interest in new solutions to the problem of macrocyclic lactone synthesis[12]. Since most of the

[*] Lactone synthesis will be considered in connection with intermolecular dehydration because the most favorable procedure occurs in two steps.

macrolide antibiotics have many acid- and/or base-labile functional groups in the molecule with many chiral carbons, the construction of the carbon skeleton of the hydroxy carboxylic acid, the precursor of the macrolide, is a most difficult problem which, however, can be overcome by a strategy involving properly selected reaction conditions and stereochemical control. However, the intramolecular lactonization reaction of hydroxy carboxylic acids has also remained an unsolved problem. In particular, two problems should be pointed out: i) How can macrolide formation be carried out selectively without accompanying undesirable intermolecular lactide formation?, and ii) how can the lactonization reaction be performed under neutral or neutralization conditions?

Corey et al.[13] and *Gerlach et al.*[14] found one of the effective routes for lactonizing hydroxy carboxylic acids *via* 2-pyridinethiol *(10)* or 2-imidazolethiol esters, prepared by employing the above-mentioned oxidation-reduction condensation[2].



In the above carboxylic ester synthesis utilizing 2-halopyridinium salt, the pyridinium salt participates in all reaction steps and the condensation reaction should be favored in terms of entropy. The intramolecular lactonization reaction was therefore investigated with the expectation that the reaction would proceed smoothly and effectively.

A preliminary investigation was undertaken to determine the efficacy of various bases as hydrogen halide acceptors; triethylamine was found to be the most suitable base. Further, it became clear that the lactonization could be successfully carried out in a variety of solvents; the optimum yield was obtained in refluxing acetonitrile. In this way various ω-hydroxy carboxylic acids *(11)* were lactonized to give the medium and large ring lactones *(12)* in better yields[15] than those obtained by previous methods (Table 6)[13a].

Subsequently we developed an efficient two-step method for cyclization of long chain hydroxy acids to macrocyclic lactones *via* 6-phenyl-2-pyridyl esters *(14)*[16]. This method was successfully applied to the syntheses of recifeiolide *(15)* and ricinelaidic acid lactone *(17)*[17]; however, it was feared that the cyclization of 6-phenyl-2-pyridyl ester with *p*-toluenesulfonic acid in the second step would limit its application to more complex molecules. In order to develop a more promising method for lactonization of complex molecules, the previous method[15] using 2-chloro-1-methylpyridinium salts such as *(1a)* was re-examined. The treatment of hydroxy acids with these salts and triethylamine afforded macrocyclic

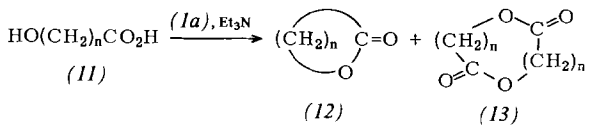
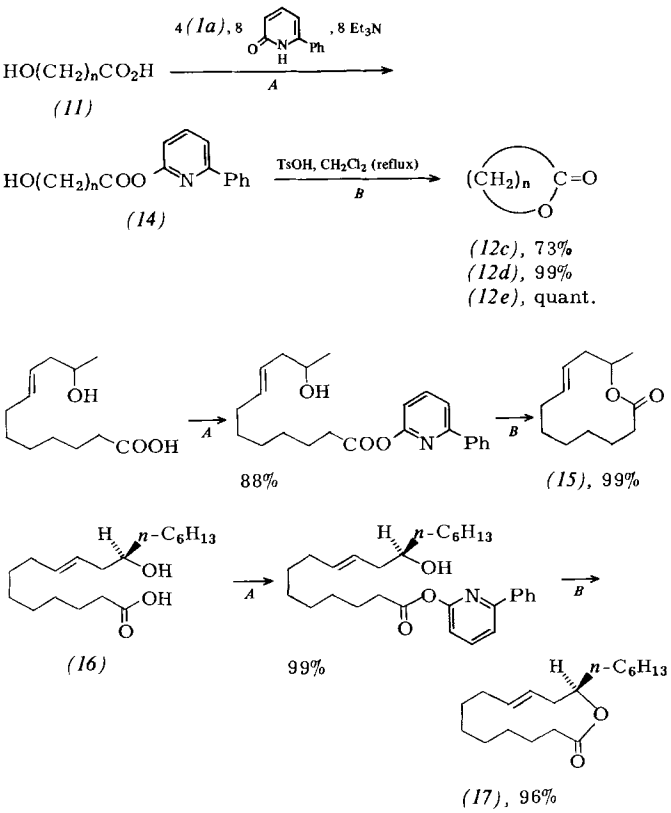


Table 6. Formation of lactones *(12)* and (undesired) lactides *(13)* from ω-hydroxy carboxylic acids *(11)* with 2-chloro-1-methylpyridinium iodide *(1a)* in boiling acetonitrile.

		Yield [%]	
	n	*(12)*	*(13)*
a	5	89	0
b	7	13	34
c	10	61	24
d	11	69	14
e	14	84	3

lactones in reasonable but not entirely satisfactory yields. This result was mainly due to the decomposition of the pyridinium salts under the cyclization conditions by the attack of triethylamine on the 1-methyl group or position 2 of the pyridinium ring to form 2-chloropyridine or 2-ammoniopyridinium salts.

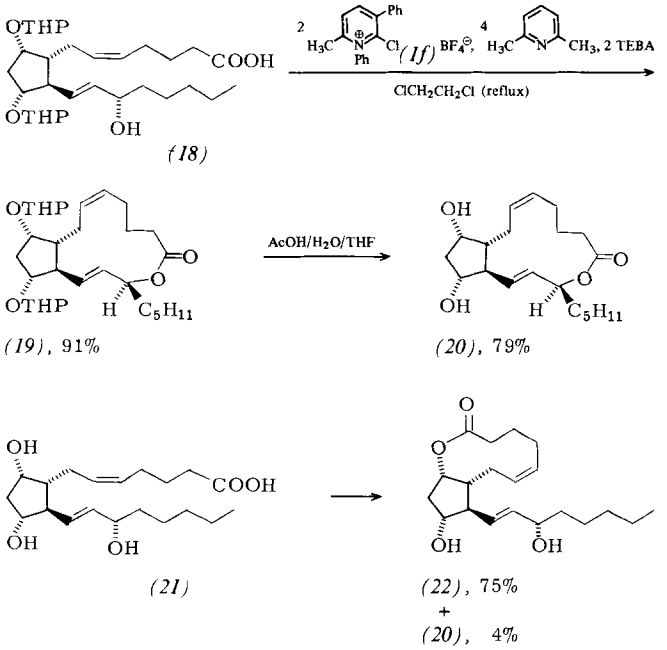
In view of the above facts, a stable pyridinium salt, 2-chloro-6-methyl-1,3-diphenylpyridinium tetrafluoroborate *(1f)*, was prepared according to the procedure developed in our laboratory[18] and tested as a reagent for the lactonization reaction[19]. When 15-hydroxypentadecanoic acid *(11e)* was treated with *(1f)* and 2,4,6-triphenylpyridine in refluxing dichloroethane by the dilution method, no pentadecanolide *(12e)* could be obtained and the hydroxy acid *(11e)* was recovered. On the other hand, the transformation of *(11e)* into *(12e)* could be achieved by addition of benzyltriethylammonium chloride (TEBA). For example, a dichloroethane (50 ml) solution of *(11e)* (0.25 mmol) and 2,4,6-triphenylpyr-



idine (1.0 mmol) was added during 7 h to a refluxing dichloroethane (30 ml) solution of *(1f)* (0.5 mmol) and TEBA (0.5 mmol) under argon. The reaction mixture was refluxed for an additional 1 h and pentadecanolide *(12e)* was isolated in 99% yield. Similarly, 12-hydroxydodecanoic acid *(11d)* was lactonized to dodecanolide *(12d)* in 85% yield.

The use of the 2-chloropyridinium salt *(1f)* for lactonization of optically active hydroxy acids is illustrated by the lactonization of (*R*)-(+)-ricinelaidic acid. (*R*)-(+)-Lactone *(17)* was obtained in 91% yield without racemization upon treatment of the hydroxy acid *(16)* with *(1f)*, 2,4,6-triphenylpyridine, and TEBA in refluxing dichloroethane. On use of 2,6-dimethylpyridine the yield was 86%.

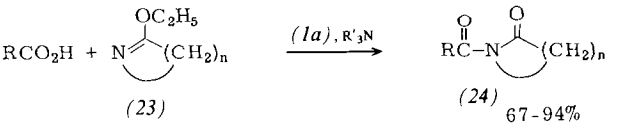
To demonstrate the applicability of this macrolactonization process to more complex hydroxy acids, the cyclization of prostaglandin $F_{2\alpha}$-9,11-bis(tetrahydropyranyl) derivative *(18)* was attempted[19]; the protected 1,15-lactone *(19)* was isolated in 91% yield. Removal of the protecting group gave prostaglandin $F_{2\alpha}$-1,15-lactone *(20)* (79%).



The lactonization of prostaglandin $F_{2\alpha}$ *(21)* under the same conditions as for *(18)*→*(19)* gave the 1,9-lactone *(22)* in 75% yield along with a small amount (4%) of the 1,15-lactone *(20)*. The successful synthesis of lactones *(16)*, *(20)*, and *(22)* described above demonstrates the utility of the present macrolactonization process.

2.1.3. Miscellaneous Acylation Reactions

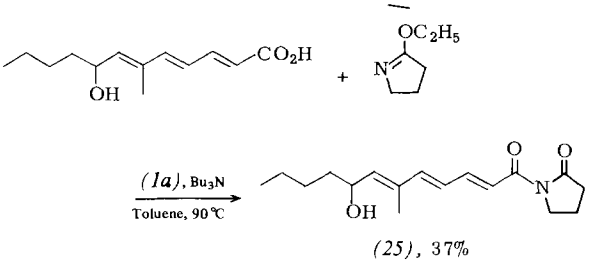
Lactim ethers *(23)* can also act as nucleophiles toward the active key intermediates, 2-acyloxypyridinium salts; *N*-acyl lactams *(24)* are obtained in good yield[20]. *N*-Acyl lactams have been most widely prepared by reaction of acyl halide with lactim ether or *N*-trimethylsilyl lactam[21]. However, little work has been reported on the preparation of *N*-acyl lactams directly from free carboxylic acids and lactim ethers. On utilization of the 2-chloropyridinium salt *(1a)*, *N*-acyl lactams *(24)* can be produced in good yields from equimolar amounts of free carboxylic acids and lactim ethers (five- or six-membered ring system).



R = *n*-C_7H_{15}, *n*-$C_8H_{17}CH{=}CH(CH_2)_6$, $CH_3O_2CCH_2CH_2$, $CH_3COCH_2CH_2$

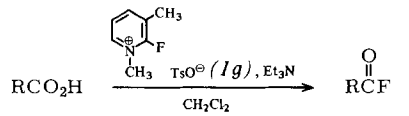
n = 2, 3

Using this method, DL-variotin *(25)*, an antifungal antibiotic, could be synthesized in simplified manner, *i.e.* without protection of the hydroxyl group[22].



In the reactions discussed so far, carboxylic acids are transformed, by treatment with a 2-chloropyridinium salt, into the active intermediate, the 2-acyloxypyridinium salt, which then reacts with various nucleophiles to produce the corresponding condensation product. In the absence of a nucleophile, competitive nucleophilic attack of chloride ion and carboxylate ion takes place, and a mixture of carboxylic anhydride and acid chloride is formed.

2-Fluoro-1,3-dimethylpyridinium tosylate *(1g)* is more reactive than 2-chloropyridinium salts such as *(1a)*. Carboxylate ion reacts with 2-fluoropyridinium salt much faster than with 2-acyloxypyridinium salt, and 2-acyloxypyridinium salt is formed exclusively. Thus it follows that, in the absence of the other nucleophiles, fluoride ion attacks the 2-acyloxypyridinium salt; this is the basis of a convenient synthesis of acid fluorides[23].

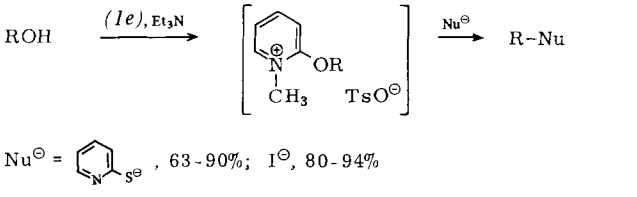


R = *n*-$C_{11}H_{23}$, quant.; $C_6H_5CH_2CH_2$, 88%; $C_6H_5CH_2$, 80%; C_6H_5, 93%; $C_6H_5CH(C_2H_5)$, 87%; $CH_3CH{=}CH$, 64%; $HO_2C(CH_2)_5$, 93%

2.2. Activation of Hydroxylic Compounds

2.2.1. Formation of 2-Alkyloxypyridinium Salts

In this section, alkylation reactions involving 2-alkyloxypyridinium salt or other onium salts of 2-alkyloxyazaarenes are discussed. At first, an unsuccessful attempt was made to produce the 2-alkyloxypyridinium salt by the reaction of 2-chloropyridinium salt and alcohol. As mentioned in Section 2.1.3, the 2-fluoropyridinium salt is more active than the 2-chloro salt; the desired 2-alkyloxypyridinium salt was readily obtained from the 2-fluoropyridinium salt *(1e)*, alcohol, and tertiary amine. Treatment of the 2-alkyloxypyridinium salt prepared *in situ* with thiolate ion or iodide ion gave the corresponding sulfide[24] or iodide[25] in good yield. In this method, 1-methyl-2-pyridone and unchanged pyridinium salts are easily removed by washing with water.



2.2.2. Olefin and Allene Synthesis by Selective Alkylation of Allylic and Acetylenic Alcohol

A Grignard reagent can also be employed as nucleophile in this reaction, and forms a carbon-carbon bond directly with the alcohol. Addition of 2-allyloxypyridinium salt to a tetrahydrofuran solution of Grignard reagent affords the corresponding coupling product in good yield. Primary and secondary alkylmagnesium bromides coupled with allyloxypyridinium salt exclusively at C-3 (S_N2' reaction). The situation is completely different in the case of phenylmagnesium bromide which attacks only C-1 (S_N2 reaction) (Table 7)[26].

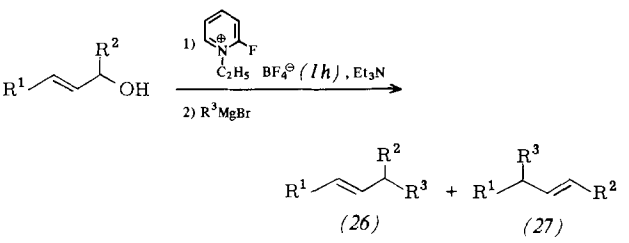


Table 7. Synthesis of olefins from allyl alcohols and Grignard compounds with 1-ethyl-2-fluoropyridinium tetrafluoroborate *(1h)*.

R^1	R^2	R^3	Yield [%] *(26)*	*(27)*
C_6H_5	H	C_6H_5	95	
		$C_6H_5CH_2CH_2$		quant.
		n-C_4H_9		84
		c-C_6H_{11}		94
		o-$CH_3C_6H_4$	92	
		o-CH_3O C_6H_4	99	
n-C_3H_7	H	C_6H_5	84	
		$C_6H_5CH_2CH_2$		85
H	CH_3	$C_6H_5CH_2CH_2$		76
C_6H_5	CH_3	C_6H_5	85 [a]	
CH_3	$C_6H_5CH_2CH_2$	C_6H_5	92 [a]	

[a] Yield of *(26)* + *(27)*.

The 2-propargyloxypyridinium salt can be also attacked at the γ-position by Grignard reagents in the presence of a catalytic amount of cuprous iodide, and the corresponding allene *(28)* was obtained in high yield (Table 8)[28].

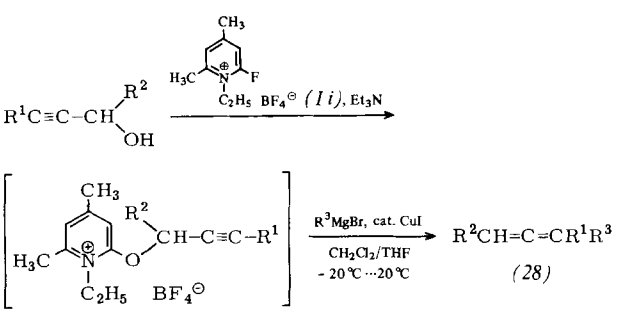


Table 8. Synthesis of allenes *(28)* from propargyl alcohols and Grignard compounds with 1-ethyl-2-fluoro-4,6-dimethylpyridinium tetrafluoroborate *(1i)*.

R^1	R^2	Yield [%] R^3 = n-C_4H_9	R^3 = c-C_6H_{11}	R^3 = t-C_4H_9
H	C_6H_5	90	82	
H	$C_6H_5CH_2$	83	89	
H	$C_6H_5CH_2CH_2$	92	99	91
H	n-C_8H_{17}	95	97	
n-C_4H_9	$C_6H_5CH_2CH_2$	77	78	94

2.2.3. Olefin Formation by Reductive β-Elimination

The reductive β-elimination of β-hydroxysulfides is also possible on use of a 2-fluoropyridinium salt. Treatment of an alkyloxypyridinium salt *(29)* derived from a β-hydroxysulfide with lithium iodide in refluxing acetone furnishes the olefin in good yield (Table 9)[29].

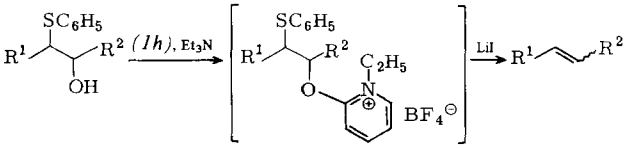
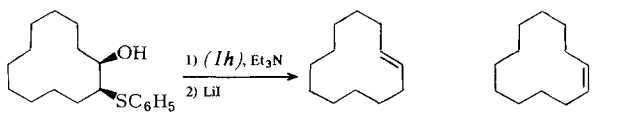


Table 9. Synthesis of olefins by reductive β-elimination from β-hydroxysulfides with 1-ethyl-2-fluoropyridinium tetrafluoroborate *(1h)* in boiling acetone.

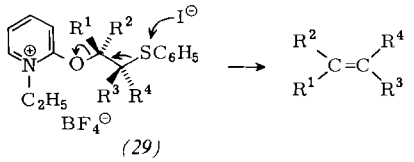
R^1	R^2	Yield [%]
C_6H_5	C_6H_5	81
C_6H_5	$C_6H_5CH_2CH_2$	91
C_6H_5	p-$(CH_3)_2NC_6H_4$	69

There are two potential pathways for attack on 2-pyridiniooxyethyl sulfides *(29)* by iodide ion: (i) attack at the sulfur atom to afford olefins with synchronous elimination of sulfenyl iodide and 1-ethyl-2-pyridone, and (ii) attack at the β-carbon to afford S_N2 displacement products. Since exclusive formation of olefins is observed (Table 9) the former reaction must be much faster than the latter. The sulfenyl iodide thus formed readily disproportionates into diphenyldisulfane and iodine. The stereospecificity of this reaction is demonstrated in the exclusive reduction of *erythro*-2-phenylthiocyclododecanol *(30)* and its *threo* isomer to *trans*- and *cis*-cyclododecene *(31)*, respectively.

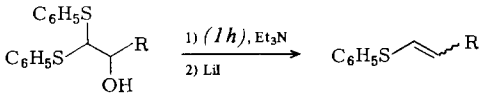


erythro-*(30)* *trans*-*(31)*, 85% *cis*-*(31)*, 76%

These results indicate that the reductive elimination proceeds with perfect stereospecificity. Thus, a *trans* elimination mechanism involving direct attack of iodide ion at sulfur atom is suggested for 2-pyridiniooxyethyl sulfides *(29)*.

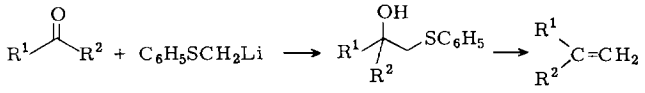


When 2-hydroxythioacetals *(32)* are used instead of β-hydroxysulfide, the corresponding vinyl sulfides are obtained in moderate yields[29].



(32) R = $C_6H_5CH_2CH_2$, 70%; n-C_7H_{15}, 71%

Since β-hydroxysulfides can be prepared from ketones or aldehydes, the reductive elimination of β-hydroxysulfides provides a useful method for the preparation of olefins starting from carbonyl compounds.—Alternative reductive elimination procedures[30] require rather drastic conditions (strong base or basic media) except when low valent titanium compounds are used as reducing agents[31].



2.2.4. Preparation of Alkyl Chlorides

2-Chlorobenzoxazolium salt *(33)* reacts with alcohols in the presence of triethylamine to afford the corresponding alkyl chlorides in good yields. Addition of tetraethylammonium chloride improves the yield[32].

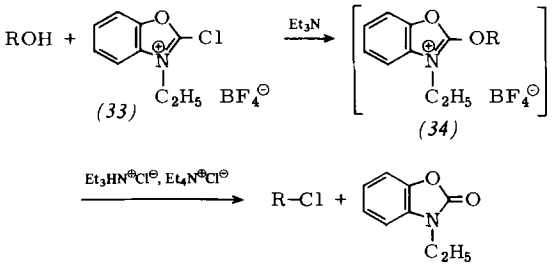
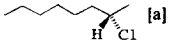
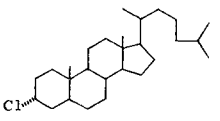


Table 10. Synthesis of alkyl chlorides from alcohols and 2-chloro-3-ethylbenzoxazolium tetrafluoroborate *(33)*.

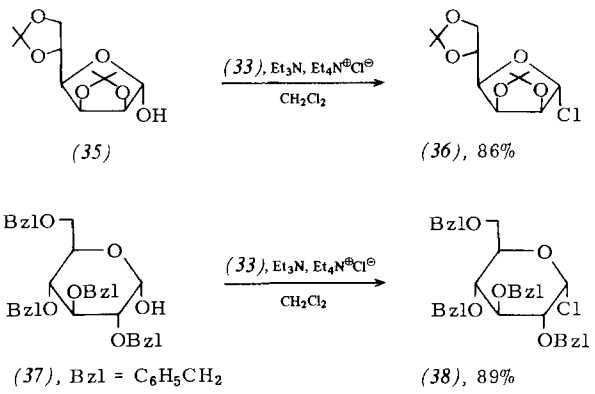
T [°C]	t [h]	Alkyl chloride	Yield [%]
20	2	$C_6H_5(CH_2)_3Cl$	97
20	2	n-$C_{18}H_{37}$	96
0	4	 [a]	76
0	4	 [b]	85

[a] Obtained from (*R*)-(−)-2-octanol with inversion of configuration. [b] Obtained from 3β-cholestanol with inversion of configuration.

As shown in Table 10, an alicyclic alcohol (3β-cholestanol) as well as acyclic alcohols (primary and secondary) are converted into the chlorides in high yields. 3β-Cholestanol and (*R*)-(−)-2-octanol react with inversion of configuration.

The reaction may be explained by assuming initial formation of the 2-alkyloxybenzoxazolium salt *(34)*, which in turn reacts with chloride ion to afford alkyl chloride and 3-ethyl-2-benzoxazolinone. The high stereospecificity in the reactions of cholestanol and 2-octanol strongly indicates that *(34)* reacts with chloride ion in an S_N2 type process.

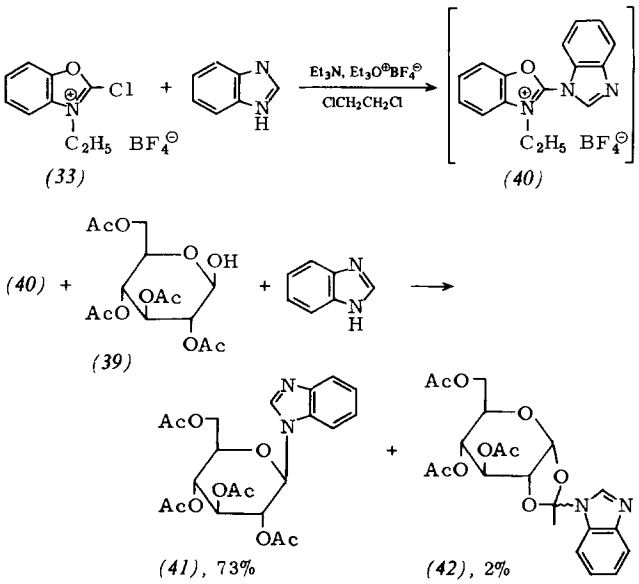
In order to examine the utility of the method, we employed two carbohydrates as substrates. When 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose *(35)* or 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose *(37)* is treated with *(33)* and tetraethylammonium chloride, one isomer [*(36)* or *(38)*], having the same configuration with the starting material, is obtained exclusively in excellent yield[32].



It is noted that the present method is suitable for the transformation of a wide variety of alcohols including alicyclic alcohols such as steroidal alcohols and carbohydrates. Thus, the benzoxazolium salt *(33)* is a promising reagent for the preparation of various optically active chlorides (see Section 4).

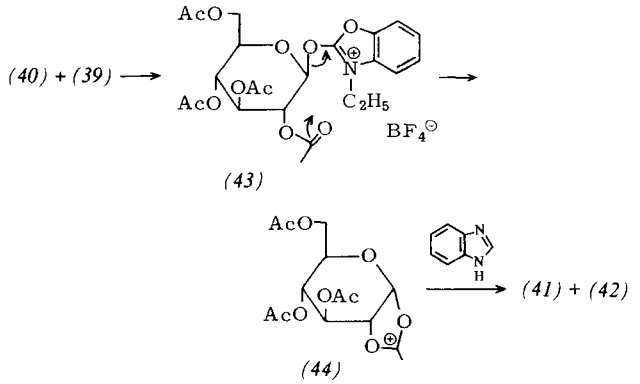
2.2.5. Nucleoside Synthesis

Nucleosides have also been prepared[33] from 1-hydroxy sugars and heterocycles utilizing the benzoxazolium salt *(33)*. The following procedure was adopted: To a stirred suspension of *(33)* and benzimidazole in 1,2-dichloroethane was added triethylamine in the same solvent at −23 °C, and the resulting mixture was heated for 5 h at 60 °C. The cooled reaction mixture was treated with triethyloxonium tetrafluoroborate in order to remove the resulting chloride ion as ethyl chloride. To this mixture was added a 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose *(39)* and benzimidazole in 1,2-dichloroethane and 1,2-dimethoxyethane, and the resulting mixture was heated for 10 h at 60 °C. Thus the desired 2,3,4,6-tetra-

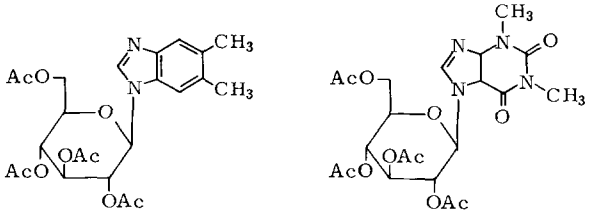


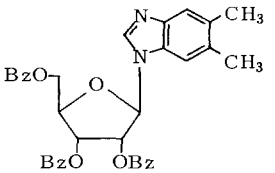
O-acetyl-β-D-glucopyranosylbenzimidazole *(41)* was obtained in 73% yield along with a trace of substituted glucopyranose *(42)*.

In the first stage of this reaction, a considerable amount of glucopyranose *(42)* was formed along with the desired nucleoside *(41)* (*ca.* 2:1). This may be explained as follows; the transient 2-(1-benzimidazolyl)benzoxazolium tetrafluoroborate *(40)* reacts with acetyl glucose *(39)* to give the intermediate *(43)*. With the assistance of the 2-acetoxy group of the sugar moiety, the elimination of 3-ethyl-2-benzoxazolinone from *(43)* takes place easily to give the acetoxonium ion *(44)*. This ion is then converted into the glucopyranose *(42)* or the *trans* nucleoside *(41)* by the nucleophilic attack of benzimidazole either on the electrophilic C atom or on the glycosidic center.



On heating *(42)* is converted into the thermodynamically more stable *(41)*. This transformation is assumed to proceed in a similar manner to the rearrangement of orthoesters of sugars to *trans* glycosides[34]. In a similar manner, the *trans* nucleosides *(41a–c)* were prepared in high yields.

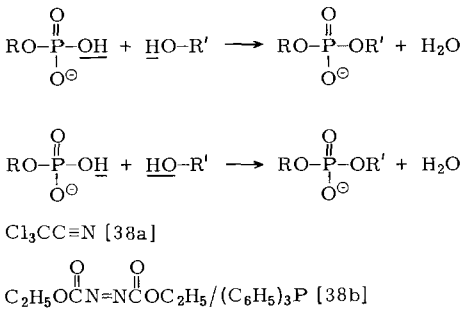




There are two general methods for the preparation of nucleosides: (i) the reaction of heavy metal salts of heterocycles and glycosyl chlorides[35], and (ii) the fusion of heterocycles with acylated sugars in the presence of acidic catalysts[36]. The striking feature of our onium salt method is that *trans* nucleosides are produced in good yields under mild conditions without any assistance from heavy metals or acidic catalysts.

2.2.6. Phosphorylation

The concept of the activation of alcohols by the onium salt method was further extended to the phosphorylation of alcohols involving 2-alkyloxybenzoxazoles as intermediates[37]. It was hoped that the *N*-protonation of the 2-alkyloxybenzoxazole by certain phosphoric acid derivatives would result in an active intermediate, similar to 2-alkyloxybenzoxazolium salts, which would attack the phosphate anion formed at the same time. Many methods are known for the phosphorylation of alcohols, most of them involving activation of the phosphoryl group; methods based on activation of the alcohol have scarcely been reported[38]. Nevertheless the latter type of phosphorylation has the advantage of avoiding pyrophosphate formation.



When 2-alkyloxybenzoxazoles *(45)*, easily prepared from alcohols and 2-fluorobenzoxazole (Table 11), are treated with diphenyl hydrogen phosphate in refluxing benzene, the corresponding alkyl diphenyl phosphates *(46)* are obtained in good yields (Table 11). This method is seen to be superior in terms of reaction time, yields, and amount of the alcohols used when compared with former methods.

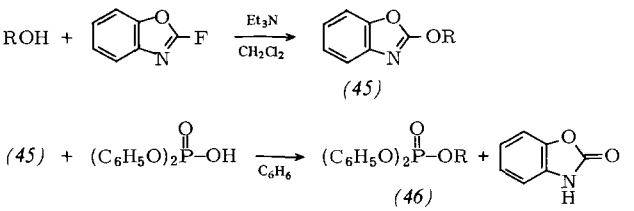


Table 11. Synthesis of 2-alkoxybenzoxazoles *(45)* from alcohols and 2-fluorobenzoxazole at room temperature and transformation of *(45)* into alkyl diphenyl phosphate *(46)*.

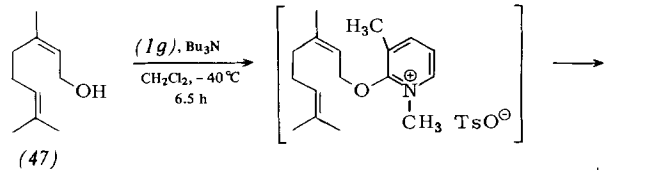
R	*(45)* *t* [h]	*(45)* Yield [%]	*T* [a]	*(46)* *t* [h]	*(46)* Yield [%]
$C_6H_5CH_2CH_2$	14	75	RT	69	74
			R	4	89
n-C_8H_{17}	20	66	RT	48	71
			R	6	93
$(CH_3)_2CHCH_2$			R	8	64
HC≡CCH_2	30	81	RT	68	67
$CH_3OCH_2CH_2$			R	7	74
$C_6H_5SCH_2CH_2CO_2CH_2CH_2$	13.5	88	R	5	68
n-$C_{17}H_{35}CO_2CH_2CH_2$	20	90	R	6.5	68
2,2-Dimethyl-1,3-dioxolan-4-ylmethyl	13	89			

[a] RT = room temp., R = reflux.

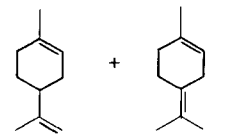
3. Intramolecular Dehydration

3.1. Biogenetic-Like Cyclization

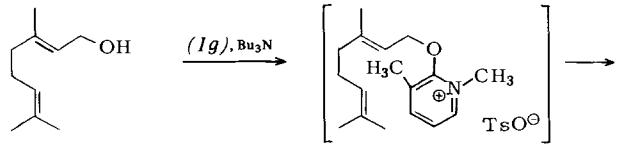
During the course of further investigation on the reaction of 2-fluoropyridinium salts and alcohols, 2-alkyloxypyridinium salts derived from the terpene alcohols nerol or geraniol were found to be unstable even at −78 °C, they are readily converted into hydrocarbon and 1-methyl-2-pyridone. For example, when nerol *(47)* is allowed to react with 1,3-dimethyl-2-fluoropyridinium tosylate *(1g)* and tri-*n*-butylamine in methylene chloride at −40 °C for 7 h, limonene *(48)* and terpinolene *(49)* are produced in 82% and 15% yield, respectively[39]. In the case of the reaction of geraniol *(50)*, uncyclized monoterpene hydrocarbons, myrcene *(51)* and ocimene *(52)*, were formed in smaller amounts. The *cis* configuration of the 2,3-double bond in the nerol moiety of the 2-neryloxypyridinium salt causes C-1 and the 6,7-double bond to be in close proximity and this leads to both the high reactivity and the high product selectivity. Thus no uncyclized product was detected when the reaction was carried out at low temperature. However, when the same reaction was undertaken at room temperature, myrcene and ocimene were also formed in *ca.* 10—15% yield along with the cyclized products.



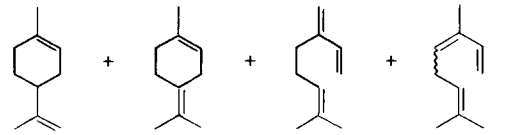
(47)



(48), 82% *(49)*, 15%

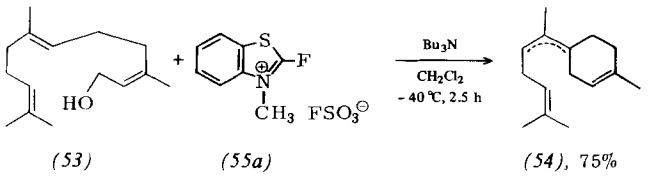


(50)



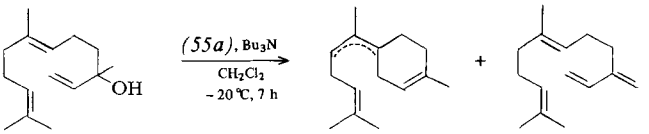
(48), 40% *(49)*, 4% *(51)*, 9% *(52)*, 9%

Application of this method to sesquiterpene alcohols was then examined[40]. In the first place the reaction of *trans,cis*-farnesol *(53)* with *(1g)* was tried, but the yield of cyclized product, bisabolene *(54)*, was low and many undetermined by-products were formed. Cyclization of *trans,cis*-farnesol using the onium salts such as 2-fluoro-3-methylbenzothiazolium fluorosulfate *(55a)* gave the best results (max. yield 75%). On the other hand, *trans,trans*-farnesol gave only a low yield of bisabolene (35%); a similar result is obtained in the reaction of geraniol.



(53) *(55a)* *(54)*, 75%

Using this method, nerolidol *(56)* was cyclized to bisabolene *(54)* in 79% yield, together with a small amount (less than 10%) of farnesene *(57)*.



(56) *(54)*, 79% *(57)*, < 10%

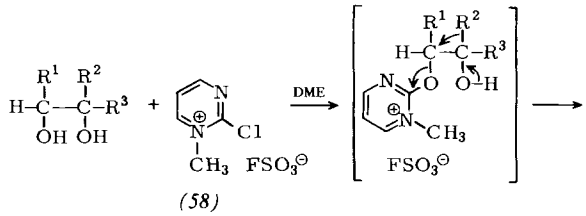
The allylic cation is more easily generated from nerolidol *(56)* than from farnesol *(53)*, so the competitive deprotonation would lead to farnesene. Naturally occurring terpenes are derived directly, or by way of stereospecific cyclizations and rearrangements, from the acyclic precursors such as geraniol or farnesol.

Non-enzymatic biogenetic-like conversion of such a precursor into the other terpenes has been of much interest and widely investigated[41]. However, most conversions of this kind involve the activation of hydroxyl group with protic acids or Lewis acids. Moreover, no method in a weakly basic medium has previously been reported, so the onium salt method provides a new entry among the biogenetic-like cyclization methods.

3.2. The Beckmann and Pinacol Rearrangements

The results of the cyclization studies on terpene alcohols suggest that the onium salts of 2-haloaza-arenes are useful reagents both for intramolecular dehydrations or rearrangements and for intermolecular reactions. Since such dehydrations or rearrangements are usually carried out in acidic media the utilization of the onium salt in weakly basic media could cause reactions to take a different course. These considerations prompted us to examine the pinacol and the Beckmann rearrangements as reactions usually carried out under strongly acidic conditions.

When a mixture of a pinacol and 2-chloro-1-methylpyrimidinium fluorosulfate *(58)* in dimethoxyethane is stirred at 0 °C for half an hour, and then refluxed for an additional half an hour, rearranged products (ketone or aldehyde) are obtained in good yield[42]. This is illustrated for phenylethanediol derivatives in Table 12.



(58)

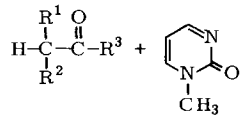


Table 12. Pinacol rearrangement with the 2-chloropyrimidinium salt *(58)* in 1,2-dimethoxyethane (DME).

R^1	R^2	R^3	Yield [%]
C_6H_5	C_6H_5	H	54
C_6H_5	C_6H_5	CH_3	88
C_6H_5	C_6H_5	C_2H_5	73
C_6H_5	C_6H_5	C_6H_5	82
C_6H_5	$C_6H_5CH_2$	$C_6H_5CH_2$	60

Further, the pinacol rearrangement of trisubstituted ethanediol derivatives by the onium salt method involves elimination of the secondary hydroxyl group; the tertiary hydroxyl group is usually lost under acidic conditions. The peculiarity of this reaction may be explained by assuming that the 2-chloropyrimidinium salt *(58)* reacts mainly with the less hindered hydroxyl group of diols to form 2-(2-hydroxyethoxy)pyrimidinium salts, which in turn are immediately converted into the corresponding ketones with concomitant elimination of 1-methyl-2-pyrimidinone.

When oximes are treated at low temperature with 1-ethyl-2-fluoro-3-methylpyridinium tetrafluoroborate *(1k)* and triethylamine or with the 2-chloropyrimidinium salt *(58)* alone, they rearrange smoothly to the amides in high yields. The facility of rearrangement may be explained by assuming initial formation of *O*-(2-pyridinio)oximes or *O*-(2-pyrimidinio)oximes, which in turn rearrange to the amides on treatment with water (Table 13)[43]. Rearrangement proceeds particularly smoothly when the pyrimidinium salt *(58)* is used; oximes are simply mixed with *(58)* (even in the absence of tertiary amine).

Furthermore, the present method gives *N-tert*-butylbenzamide in high yield from pivalophenone oxime. This oxime rearranges to pivalanilide under the acidic conditions generally employed and to *N-tert*-butylbenzamide on heating with *p*-toluenesulfonyl chloride in alkaline solution[44].

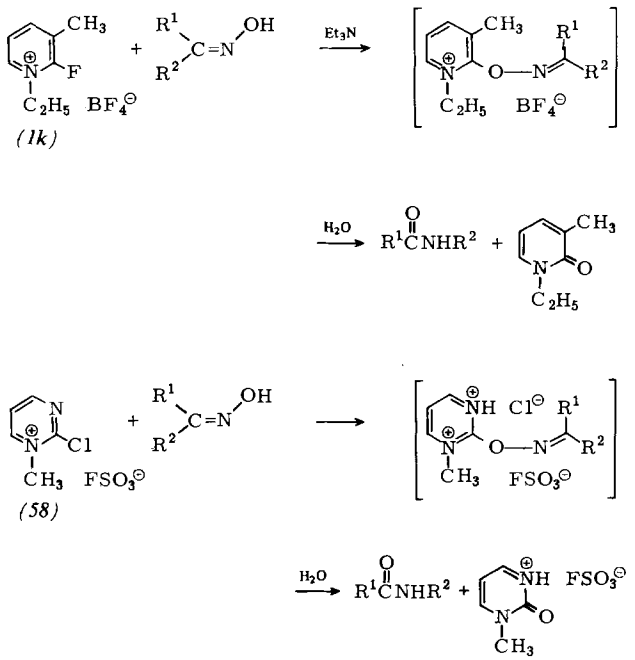


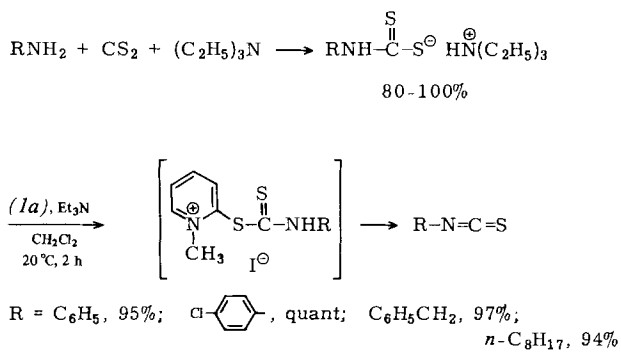
Table 13. Beckmann rearrangement of oximes with the onium salts *(1k)* (+Et_3N) and *(58)*.

Onium salt	R^1	R^2	Yield [%]
(1k)	C_2H_5	C_6H_5	94
(58)	C_2H_5	C_6H_5	92
(1k)	$C_6H_5CH_2$	C_6H_5	93
(58)	$C_2H_5CH_2$	C_6H_5	95
(58)	CH_3	C_6H_5	94
(58)	CH_3	2-$C_{10}H_7$	92
(58)	C_6H_5	*t*-C_4H_9	91
(58)	C_6H_5	C_6H_5	quant.
(58)	$(CH_2)_5$		94

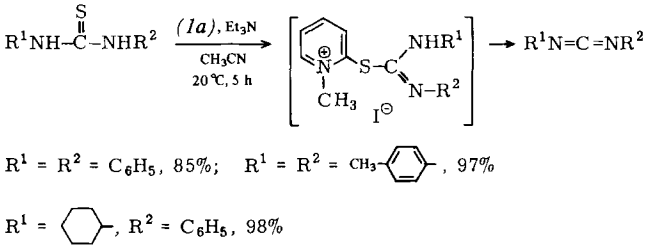
3.3. Preparation of Isothiocyanates and Carbodiimides

The ability of the sulfidopyridinium function to act as an effective leaving group was further demonstrated in the following preparation of isothiocyanate and carbodiimide.

When triethylammonium dithiocarbamate, easily prepared from amine, carbon disulfide, and triethylamine, is treated with the 2-chloropyridinium salt *(1a)* at room temperature, isothiocyanate is produced in high yield[45].



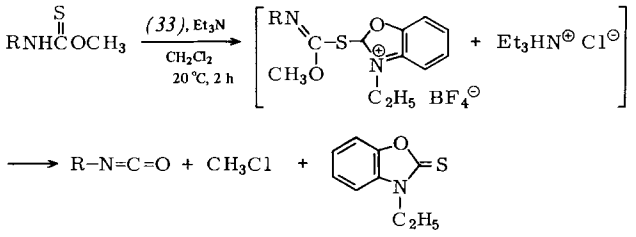
On treatment of *N,N'*-disubstituted thioureas with *(1a)* at room temperature in the presence of triethylamine, a similar β-elimination occurs smoothly to afford the corresponding carbodiimides in good yields[46].

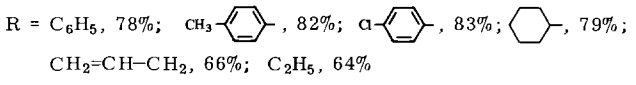


Carbodiimides are particularly important coupling reagents in the synthesis of peptides and nucleotides, and numerous publications have appeared which describe their preparation[47]. These involve, *e.g.*, catalytic conversion of isocyanates, dehydration of *N,N'*-disubstituted ureas, and desulfurization of thioureas with metal oxides and other metallic compounds, and also with alkaline hypochlorite. The new method is of quite general utility; aromatic and aliphatic carbodiimides are obtained by a simple procedure.

3.4. Preparation of Isocyanates

Methyl thiocarbamates are easily converted to the corresponding isocyanates in good yields on treatment with the more active onium salt, 2-chloro-1-ethylbenzoxazolium tetrafluoroborate *(33)*, in the presence of an equimolar amount of triethylamine[48]. The reaction proceeds *via* the initial attack of sulfur on the benzoxazolium salt to produce a 2-(iminomethylthio)benzoxazolium salt, which suffers nucleophilic attack by chloride ion at the methyl group. The method can be used for synthesis of both aliphatic and aromatic isocyanates at room temperature under neutral conditions. It also permits the preparation of allyl isocyanates which are accessible only in low yield by conventional methods[49].

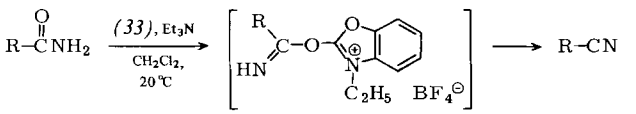


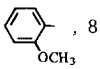


R = C_6H_5, 78%; , 82%; , 83%; , 79%;
CH_2=CH–CH_2, 66%; C_2H_5, 64%

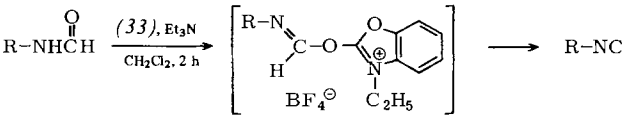
3.5. Preparation of Nitriles and Isocyanides

The 2-chlorobenzoxazolium salt *(33)* is very reactive; in the presence of triethylamine at room temperature it transforms carboxamides into nitriles[50].



R = C_6H_5, 88%;  , 81%;  , 78%; $C_6H_5CH_2$, 83%
n-C_6H_{13}, 73%

β-Elimination reactions of *N*-substituted formamides leading to isocyanide formation are also possible utilizing *(33)*. The reaction proceeds at room temperature under neutralization conditions. This isocyanide synthesis can be applied to



R = C_6H_5, 81%; 2,6-$Cl_2C_6H_3$, 69%; m-NO_2-C_6H_4, 86%;
$C_6H_5CH_2$, 82%; n-$C_{12}H_{25}$, 71%; n-C_6H_{13}–CH(CH_3), 78%

both aliphatic and aromatic formamides[51]. It is also applicable to the preparation of secondary alkyl isocyanides such as 1-methylheptyl isocyanide, which are not accessible by other methods[52].

3.6. Preparation of 1,2-Dichloroalkanes

The pronounced reactivity of 2-chlorobenzoxazolium salts such as *(33)* also enabled the following reactions to be carried out: Treatment of epoxides with *(33)* in the presence of tetraethylammonium chloride and triethylamine gives 1,2-dichloroalkanes in good yields (Table 14)[53]. The reaction probably proceeds *via* a chlorohydrin intermediate which is immediately converted into a 2-alkyloxybenzoxazolium salt. The salt is in turn attacked by chloride ion to give the 1,2-dichloroalkane.

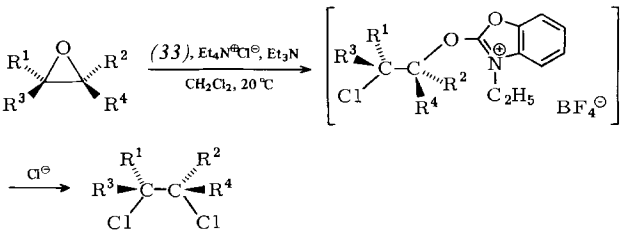


Table 14. Synthesis of 1,2-dichloroalkanes from epoxides.

R^1	R^2	R^3	R^4	t [h]	Yield [%]
C_6H_5	H	H	H	48	81
C_6H_5	H	H	C_6H_5	48	77 [a]
n-C_7H_{15}	H	H	H	48	75
p-$CH_3C_6H_4OCH_2$	H	H	H	12	95
n-$C_8H_{17}OCH_2$	H	H	H	12	84
$(CH_2)_4$		H	H	48	58 [b]

[a] DL:*meso* = 77:23. [b] *cis*:*trans* = 98:2.

Conventional preparations of 1,2-dichloroalkanes from 1,2-epoxides require prolonged heating in a solvent such as pyridine or chloroform for the completion of the reaction[54]. The transformation of cyclohexene oxide demonstrates the high stereospecificity of this reaction. *trans*-1,2-Dichloroalkane can generally be obtained directly from olefins and chlorine; the new method provides complementary effective and stereospecific route to the *cis* isomers.

3.7. Preparation of Ketones from α-Hydroxy Acids

Another example of the high reactivity of 2-chlorobenzoxazolium salts such as *(33)* is seen in the elimination of carbon monoxide and water from α-hydroxy carboxylic acids. When a mixture of α-hydroxy carboxylic acid and 2-chlorobenzoxazolium salt is added to a methylene chloride solution of triethylamine at room temperature, carbon monoxide is evolved rapidly, and the ketone is obtained in high yield (Table 15)[55].

The direct preparation of ketones from α-hydroxy carboxylic acids without using any oxidizing reagent was formerly unknown. Use of the onium salt *(33)* affords ketones in good yields under mild conditions.

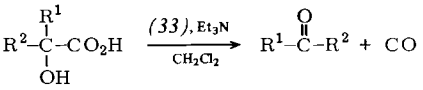
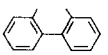


Table 15. Synthesis of ketones from α-hydroxy carboxylic acids.

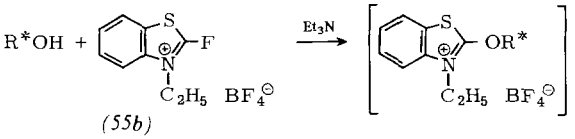
R^1	R^2	Yield [%]
C_6H_5	C_6H_5	83
C_6H_5	C_2H_5	84
$C_6H_5CH_2$	C_6H_5	85
p-$CH_3OC_6H_4CH_2$	p-$CH_3OC_6H_4$	90
CH_3	CH_3	71
		85
		66

4. Preparation of Optically Active Substances

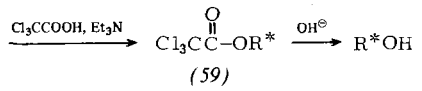
Structure-bioactivity relationships show that often only one enantiomer exhibits activity. Consequently, interest in the synthetic approach to a specific enantiomer of natural products has created a need for efficient and practical syntheses of optically active compounds. The fact that stereospecific reactions with inversion occur on use of the onium salts prompted us to examine the optical interconversion of chiral alcohols and the transformation of the alcohols into other derivatives.

4.1. Optical Interconversion of Enantiomeric Alcohols

Optically active 2-alkyloxybenzothiazolium salts, formed *in situ* from an optically active (secondary) alcohol and 2-fluorobenzothiazolium salt *(55b)*, react in the presence of triethylamine with a strong acid such as trichloroacetic acid to yield the ester *(59)*. This undergoes facile base-catalyzed hydrolysis to afford the enantiomer of the starting alcohol. Thus this sequence makes possible the interconversion of the



(55b)



(59)

Table 16. Interconversion of enantiomeric alcohols using the onium salt *(55b)*.

Starting material	$[\alpha]_D$ [°]	Product	$[\alpha]_D$ [°]
(*S*)-(+)-2-Butanol	+ 9.4	(*R*)-(−)-2-Butanol	− 7.8
(*R*)-(−)-2-Butanol	− 9.7	(*S*)-(+)-2-Butanol	+ 8.6
(*S*)-(+)-2-Octanol	+12.3	(*R*)-(−)-2-Octanol	−11.2
(*R*)-(−)-2-Octanol	−12.0	(*S*)-(+)-2-Octanol	+10.2
(*S*)-(+)-3-Nonanol	+ 9.6	(*R*)-(−)-3-Nonanol	− 7.4

enantiomeric secondary alcohols by a simple procedure (Table 16)[56]. For instance, (*S*)-(+)-2-octanol was converted into (*R*)-(−)-2-octanol in 70% overall yield.

4.2. Preparation of Alkyl Halides

The intermediate 2-alkyloxybenzothiazolium salt (see Section 4.1) also reacts with alkali metal halides to afford the alkyl halide in good yields (Table 17)[57].

Table 17. Synthesis of alkyl halides from alcohols. Isolated yields are given.

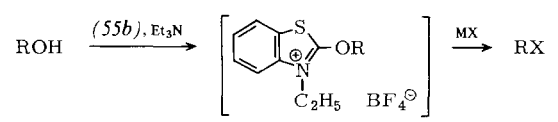
MX	RX	Yield [%]
NaI	$C_6H_5CH_2CH_2CH_2I$	92
LiBr	$C_6H_5CH_2CH_2CH_2Br$	90
LiCl	$C_6H_5CH_2CH_2CH_2Cl$	90
NaI	$C_6H_5CH_2CH_2I$	82
LiBr	$C_6H_5CH_2CH_2Br$	87
NaI	DL-$C_6H_5CH_2CH(CH_3)I$ [a]	75
LiBr	DL-$C_6H_5CH_2CH(CH_3)Br$ [a]	72
NaI	(*R*)-(−)-$C_6H_{13}CH(CH_3)I$ [b]	87
LiBr	(*S*)-(+)-$C_6H_{13}CH(CH_3)Br$ [c]	64
LiCl	(*R*)-(−)-$C_6H_{13}CH(CH_3)Cl$ [b]	56

[a] Starting material: DL-alcohol. [b] Starting material: (*S*)-(+)-alcohol. [c] Starting material: (*R*)-(−)-alcohol.

Table 18. Optical rotation of 2-halooctanes.

Alcohol [a]	2-Halooctane	$[\alpha]_D^{23}$ [b]	*c* [g/100 ml]
(*S*)-(+)-2-Octanol	(*R*)-(−)-2-Iodooctane	−53.1°	4.07
(*R*)-(−)-2-Octanol	(*S*)-(+)-2-Bromooctane	+39.9°	4.16
(*S*)-(+)-2-Octanol	(*R*)-(−)-2-Chlorooctane	−33.7°	17.0

[a] Our samples of (*S*)-(+)- and (*R*)-(−)-2-octanol had $[\alpha]_D^{20}$ (0.1 dm, neat) +9.9 and −9.7°, respectively. Literature values: +9.9 and −9.9°. [b] Optical rotation measurements recorded in a 0.1 dm tube in ether with an automatic polarimeter. Reported maximum rotations of (*R*)-(−)-2-halooctanes $[\alpha]_D^{20}$ (neat) are: −64.6 (I), −44.9 (Br), and −36.2° (Cl).

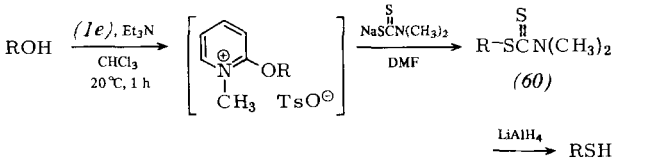


The stereochemical course of the reaction was exemplified by (*S*)-(+)- and (*R*)-(−)-2-octanol. The results shown in Table 18 clearly indicate that the benzothiazolium moiety of the salt is displaced by a halide ion with inversion of configuration to give 2-halooctane of high optical purity. Among the many examples of the preparation of optically active alkyl halides from alcohols, only a few (*e.g.* the reaction of tosylate carried out under strictly controlled experimental conditions)[58] have been found satisfactory in practice. Under the usual reaction conditions alkyl iodides in particular are generally attacked by iodide, thus resulting in racemization. The present halogenation method has several advantages over others with respect to the generality, yields, and the mildness of the reaction condition (low temperature, almost neutral medium, and equimolar amounts of the reagents, *etc.*). Side reactions and a halide ion exchange are minimized.

4.3. Preparation of Thiols

Thiols are widely used as versatile synthetic intermediates and many syntheses have been reported[59], most of them consisting of three steps: (i) conversion of alcohols into halides or tosylates; (ii) bimolecular substitution with sulfur-containing nucleophiles; and (iii) conversion of the intermediates into thiols. Although Walden inversion occurs in most of the methods, some stereochemical ambiguities remain to be resolved[60]. The utilization of the onium salts of azaarenes for the preparation of thiols appears promising, provided that a suitable combination of sulfur-containing nucleophiles and onium salts can be found.

After screening several possible combinations, it was found that 1-fluoro-2-methylpyridinium tosylate *(1e)*/sodium *N,N*-dimethyldithiocarbamate is effective for this purpose. Thus various alcohols including steroids and carbohydrates have been successfully converted into the corresponding thiols in high yields with high stereospecificity[61]. The procedure consists of: (i) reaction of alcohols with *(1e)* to give 2-alkyloxypyridinium salts; (ii) S_N2 type reaction of these salts with sodium *N,N*-dimethyldithiocarbamate to give alkyl dithiocarbamates *(60)*; and (iii) reductive cleavage to thiols.

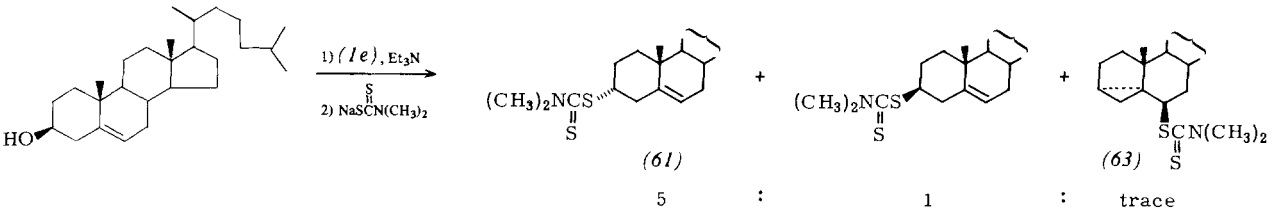


(60), R = *n*-$C_{12}H_{25}$, 97%; $C_6H_5CH_2$, 98%; $C_6H_5CH{=}CHCH_2$, 98%; DL-$C_6H_{13}CH(CH_3)$, 94%; product from (−)-menthol, 66%

(*R*)-(−)-2-Octanethiol was obtained with complete inversion of configuration from an optically active alcohol, *e.g.* (*S*)-(+)-2-octanol ($[\alpha]_D^{20}$ +9.9° (neat)), by treatment with *(1e)* and dithiocarbamate and subsequent reduction. The rotatory power of the thiol was $[\alpha]_D^{23} = -32.7°$ (1.74, C_2H_5OH).

A clean inversion of configuration also occurred in the case of alicyclic alcohols. For instance, 3β-cholestanol could be converted into 3α-cholestanethiol in 97% overall yield.

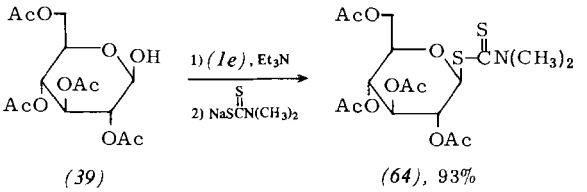
Similar treatment of 3β-cholesterol afforded a 5:1 mixture of isomeric dithiocarbamates (together 76%), where the major component was the α-isomer *(61)* (inversion) and a minor component was the β-isomer *(62)* (retention), both of which were converted into the corresponding thiols and their acetyl derivatives.



Since preparative methods for cholestenethiol using 3β-cholesteryl chloride and potassium thiocyanate[62], or 3β-cholesteryl tosylate and thiourea[63], give only the β-isomer, the formation of α-isomer with inversion according to this method seems of particular synthetic importance.

In allylic systems, *e.g.* cinnamyl alcohol, substitution takes place exclusively at the OH-substituted carbon atom; and no isomeric dithiocarbamate (S_N2') was detected.

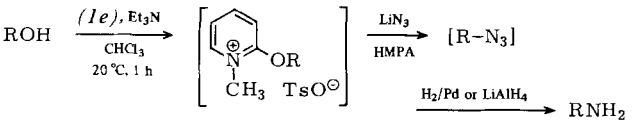
Treatment of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose *(39)* with *(1e)* and sodium dithiocarbamate produces a single dithiocarbamate, the β-isomer *(64)*, formed with retention of configuration. The result can be explained by invoking participation of the neighboring acetoxy group *trans* to the leaving group.



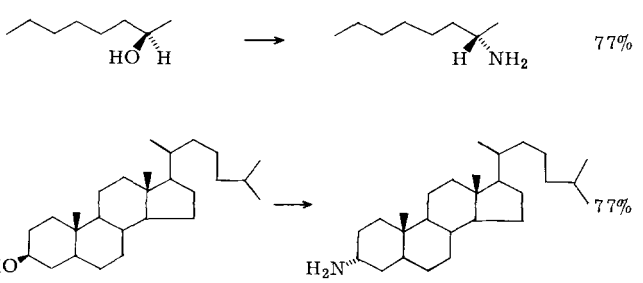
(39) *(64)*, 93%

4.4. Preparation of Primary Amines

The last example utilizing the onium salt of azaarenes is the stereospecific synthesis of primary amines from alcohols.



R = n-$C_{12}H_{25}$, 94%; $C_6H_5CH_2$, 77%; $C_6H_5CH{=}CHCH_2$, 78%; DL-$C_6H_5CH(CH_3)$, 75%

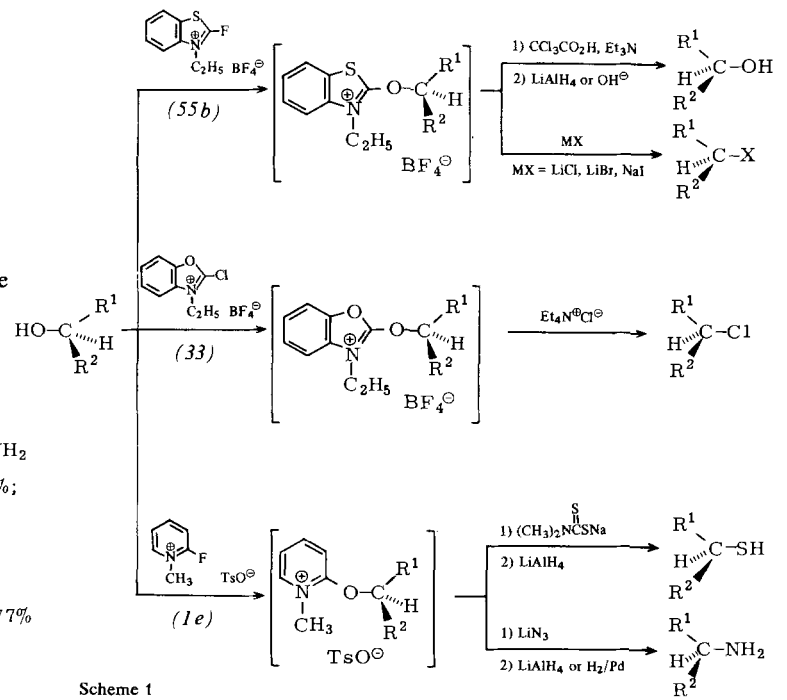


Sterically controlled introduction of amino groups is of special synthetic importance, and extensive investigations have been conducted in recent years[64].

Among the various combinations of nitrogen-containing nucleophiles and onium salts examined, lithium azide/2-fluoro-1-methylpyridinium tosylate *(1e)* gave favorable results. Treatment of the intermediate 2-alkyloxypyridinium salt with potassium phthalimide, ammonia, and lithium diarylsulfenamide[64c] proved unsuccessful. The use of the 2-fluorobenzothiazolium salt *(55a)* instead of *(1e)* gave poor yields of alkyl azides. This method seems to have general applicability, since the conversion of alkyl azides into primary amines is known to be effected under a variety of mild reductive conditions, with most of the functional groups present in a molecule remaining intact[65].

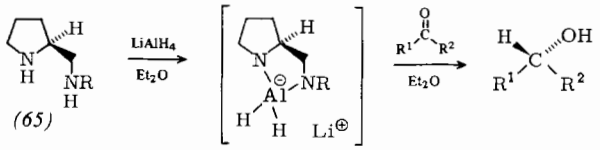
4.5. Preparation of Secondary Alcohols by Asymmetric Reduction and Alkylation

We have described an effective and convenient method for the preparation of chiral halides, thiols, and amines from chiral secondary alcohols by utilizing the onium salts of aza-arenes. Thus various types of optically active compounds are accessible when an effective route to chiral secondary alcohols could be found. Hence, we have recently investigated the asymmetric reduction and alkylation of carbonyl compounds to chiral alcohols.



Scheme 1

For the asymmetric reduction of prochiral ketones, chiral hydride reagents *(66)*, prepared *in situ* from (*S*)-2-(anilinomethyl)pyrrolidine *(65a)* or (*S*)-2-(2,6-xylidinomethyl)pyrrolidine *(65b)* and $LiAlH_4$, were found to be efficient[66]. For example, acetophenone was reduced to 1-phenylethanol in 95% optical yield (enantiomeric excess). As shown in Table 19, these chiral hydride reagents afford higher optical yields than previously reported reagents of this kind[67-70].



(65)

(a), R = Ph;

(b), R = 

(66)

Although the precise mechanism of this asymmetric reduction is not clear, we assume that the high enantioselectivity (all the alcohols produced have mainly *S*-configuration except when THF was used as solvent) to be due to the following factors: (i) The diamines *(65)*, simple compounds having only one asymmetric carbon, produce the effective chiral environment on treatment with $LiAlH_4$. This may be due to the formation of

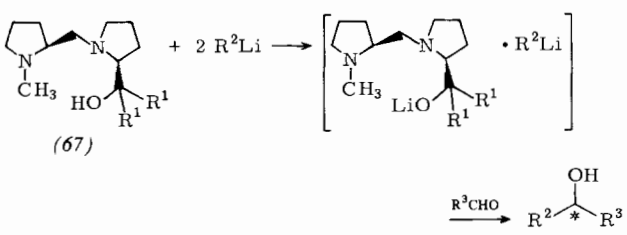
Table 19. Asymmetric reduction of ketones. Comparison of chiral reagents produced from $LiAlH_4$ and chiral ligands. (Values in parentheses: at −100 °C.) The enantiomeric excess is given.

Ketone	*(65a)*	*(65b)* [a]	Ligand Sugar derivative (see [67])	Darbon (see [68])	Chiral oxazoline (see [69])	Chiral amine (see [70])
PhCOMe	84 (92)	(95)	71	75	65	43
PhCOEt	85	(96)	46	—	62	52
$PhCOCHMe_2$	57	(89)	—	48	43	—
α-Tetralone	50	(85)	—	—	4	—
$PhCH_2COMe$	31 (42)	(11)	—	—	1	—
n-$C_6H_{13}COMe$	13	(26)	25	—	4 (6)	—

[a] *M. Asami, T. Mukaiyama*, unpublished results.

sterically restricted *cis*-fused bicyclic hydride reagents, creating the additional chiral center on the nitrogen atom in the pyrrolidine ring. (ii) The reactivity of the two hydrogen atoms present in this chiral reagent is remarkably different; only one of them reacts with ketones, the other being subject to steric hindrance. (iii) The lithium ion, which presumably coordinates to the nitrogen atom of the pyrrolidine ring and/or the side chain in *(66)*, restricts the direction of approach of the ketones.

In contrast to the asymmetric reduction of carbonyl compounds where relatively high enantiomeric excess were realized, the enantiomeric excesses in the asymmetric alkylation of



(67)

Table 20. Asymmetric addition of alkyllithium to aldehydes in the presence of the dipyrrolidine derivative *(67)*. e.e. = enantiomeric excess.

R^1	R^2	R^3	Yield [%]	e.e. [%]
H	CH_3	C_6H_5	81	40
n-C_3H_7	CH_3	C_6H_5	82	86
H	C_2H_5	C_6H_5	59	54
H	n-C_3H_7	C_6H_5	64	60
H	n-C_4H_9	C_6H_5	77	95
H	n-C_4H_9	i-C_3H_7	57	80

organometallic reagents, such as Grignard reagents[71], alkyllithium[71b,72], organocopper[73] or alkylcadmium[74], with carbonyl compounds by using chiral ligand are very low (0–40%). However, the concept of the *cis*-fused five-membered ring system formed from the aminomethylpyrrolidine moiety was also found to be effective for the asymmetric alkylation of carbonyl compounds. Thus various optically active alcohols were obtained by the asymmetric reaction of alkyllithium with aldehydes using the dipyrrolidine derivative *(67)* as the chiral ligand (Table 20)[75].

Received: September 7, 1978 [A 290 IE]
German version: Angew. Chem. *91*, 798 (1979)

[1] *T. Mukaiyama*, Angew. Chem. *89*, 858 (1977); Angew. Chem. Int. Ed. Engl. *16*, 817 (1977).
[2] *T. Mukaiyama*, Angew. Chem. *88*, 111 (1976); Angew. Chem. Int. Ed. Engl. *15*, 94 (1976).
[3] *T. Endo, S. Ikenaga, T. Mukaiyama*, Bull. Chem. Soc. Jpn. **43**, 2632 (1970).
[4] *T. Mukaiyama, M. Usui, E. Shimada, K. Saigo*, Chem. Lett. *1975*, 1045; *K. Saigo, M. Usui, K. Kikuchi, E. Shimada, T. Mukaiyama*, Bull. Chem. Soc. Jpn. *50*, 1863 (1977).
[5] *E. Bald, K. Saigo, T. Mukaiyama*, Chem. Lett. *1975*, 1163.
[6] *J. K. Sutherland, D. A. Widdowson*, J. Chem. Soc. *1964*, 4650.
[7] *T. Izawa, T. Mukaiyama*, Chem. Lett. *1977*, 1443.
[8] *R. Adams, I. J. Pachter*, J. Am. Chem. Soc. *74*, 5491 (1952).
[9] *T. Mukaiyama, H. Toda, S. Kobayashi*, Chem. Lett. *1976*, 13; *T. Mukaiyama, Y. Aikawa, S. Kobayashi, ibid. 1976*, 57; *E. Bald, S. Kobayashi, T. Mukaiyama*, Heterocycles *1976*, 1707.
[10] *Y. Watanabe, S. Shoda, T. Mukaiyama*, Chem. Lett. *1976*, 741.
[11] *S. Yamada, Y. Yokoyama, T. Shioiri*, J. Org. Chem. *39*, 3302 (1974).
[12] *K. C. Nicolaou*, Tetrahedron *33*, 683 (1977); *S. Masamune, G. S. Bates, J. W. Corcoran*, Angew. Chem. *89*, 602 (1977); Angew. Chem. Int. Ed. Engl. *16*, 585 (1977).
[13] a) *E. J. Corey, K. C. Nicolaou*, J. Am. Chem. Soc. *96*, 5614 (1974); b) *E. J. Corey, K. C. Nicolaou, L. S. Melvin, Jr., ibid. 97*, 653, 654 (1975); c) *E. J. Corey, D. J. Brunelle*, Tetrahedron Lett. *1976*, 3409.
[14] *H. Gerlach, A. Thalmann*, Helv. Chim. Acta *57*, 2661 (1974).
[15] *T. Mukaiyama, M. Usui, K. Saigo*, Chem. Lett. *1976*, 49.
[16] *T. Mukaiyama, K. Narasaka, K. Kikuchi*, Chem. Lett. *1977*, 441.
[17] *K. Narasaka, M. Yamaguchi, T. Mukaiyama*, Chem. Lett. *1977*, 959.
[18] *M. Shiono, T. Shibanuma, T. Mukaiyama*, Chem. Lett. *1976*, 1041.
[19] *K. Narasaka, K. Maruyama, T. Mukaiyama*, Chem. Lett. *1978*, 885.
[20] *A. Ishida, T. Bando, T. Mukaiyama*, Chem. Lett. *1976*, 711.
[21] *B. Stoll, W. Griehl*, Helv. Chim. Acta *48*, 1805 (1965); *H. R. Kricheldorf, E. Leppert*, Synthesis *1975*, 592; *M. Sakakibara, M. Matsui*, Agric. Biol. Chem. *37*, 1139 (1973).
[22] *A. Ishida, T. Mukaiyama*, Chem. Lett. *1977*, 467.
[23] *T. Mukaiyama, T. Tanaka*, Chem. Lett. *1976*, 303.
[24] *T. Mukaiyama, S. Ikeda, S. Kobayashi*, Chem. Lett. *1975*, 1189.
[25] *S. Kobayashi, M. Tsutsui, T. Mukaiyama*, Chem. Lett. *1976*, 373.
[26] *T. Mukaiyama, M. Imaoka, T. Izawa*, Chem. Lett. *1977*, 1257; 2-Allyloxypyridine derivatives undergo S_N2' reaction with Grignard compounds to give olefinic products [27].
[27] *T. Mukaiyama, M. Yamaguchi, K. Narasaka*, Chem. Lett. *1978*, 689.
[28] *T. Mukaiyama, K. Kawata*, Chem. Lett. *1978*, 785.
[29] *T. Mukaiyama, M. Imaoka*, Chem. Lett. *1978*, 413.
[30] *I. Kuwajima, S. Sato, Y. Kurata*, Tetrahedron Lett. *1972*, 737; *I. Kuwajima, M. Uchida, ibid. 1972*, 649; *R. L. Sowerby, R. M. Coates*, J. Am. Chem. Soc. *94*, 4758 (1972).
[31] *Y. Watanabe, M. Shiono, T. Mukaiyama*, Chem. Lett. *1975*, 871.
[32] *T. Mukaiyama, S. Shoda, Y. Watanabe*, Chem. Lett. *1977*, 383.
[33] *T. Mukaiyama, S. Shoda, T. Nakatsuka, K. Narasaka*, Chem. Lett. *1978*, 605.

[34] *H. Paulsen*, Adv. Carbohydr. Chem. Biochem. *26*, 127 (1971).
[35] *J. Davoll, B. A. Lowy*, J. Am. Chem. Soc. *73*, 1650 (1951).
[36] *T. Sato, T. Shimadate, Y. Ishido*, Nippon Kagaku Zasshi *81*, 1440 (1961).
[37] *Y. Watanabe, T. Mukaiyama*, Chem. Lett. *1978*, 349.
[38] a) *F. Cramer, K. Pawelzik, F. W. Lichtenthaler*, Chem. Ber. *91*, 1555 (1958); b) *O. Mitsunobu, K. Kato, J. Kimura*, J. Am. Chem. Soc. *91*, 6510 (1969); *O. Mitsunobu, M. Eguchi*, Bull. Chem. Soc. Jpn. *44*, 3427 (1971).
[39] *S. Kobayashi, M. Tsutsui, T. Mukaiyama*, Chem. Lett. *1976*, 1137.
[40] *S. Kobayashi, M. Tsutsui, T. Mukaiyama*, Chem. Lett. *1977*, 1169.
[41] *W. S. Johnson*, Acc. Chem. Res. *1*, 1 (1968); *E. E. van Tamelen, ibid. 1*, 111 (1968).
[42] *T. Mukaiyama, Y. Echigo, M. Shiono*, Chem. Lett. *1977*, 179.
[43] *M. Shiono, Y. Echigo, T. Mukaiyama*, Chem. Lett. *1976*, 1397.
[44] *R. F. Brown, N. M. van Gulick, G. H. Schmid*, J. Am. Chem. Soc. *77*, 1094 (1955).
[45] *T. Shibanuma, M. Shiono, T. Mukaiyama*, Chem. Lett. *1977*, 573.
[46] *T. Shibanuma, M. Shiono, T. Mukaiyama*, Chem. Lett. *1977*, 575.
[47] *H. G. Khorana*, Chem. Rev. *53*, 145 (1953); *F. Kurzer, K. Douraghi-Zadeh, ibid. 67*, 107 (1967).
[48] *Y. Echigo, Y. Watanabe, T. Mukaiyama*, Chem. Lett. *1977*, 1345.
[49] *M. Fieser, L. F. Fieser:* Reagents for Organic Synthesis. Vol. 1. Wiley, New York 1967, p. 1172; *S. R. Sandler, W. Karo:* Organic Functional Group Preparations. Vol. 1. Academic Press, New York 1968, p. 307.
[50] *T. Mukaiyama, Y. Echigo*, unpublished.
[51] *Y. Echigo, Y. Watanabe, T. Mukaiyama*, Chem. Lett. *1977*, 697.
[52] *I. Ugi:* Isonitrile Chemistry. Academic Press, New York 1971, p. 29.
[53] *Y. Echigo, Y. Watanabe, T. Mukaiyama*, Chem. Lett. *1977*, 1013.
[54] *W. Ziegenbein, K.-H. Hornung*, Chem. Ber. *95*, 2976 (1962); *J. R. Campbell, J. K. N. Jones, S. Wolfe*, Can. J. Chem. *44*, 2339 (1966); *N. S. Isaacs, D. Kirkpatrick*, Tetrahedron Lett. *1972*, 3869.
[55] *T. Mukaiyama, Y. Echigo*, Chem. Lett. *1978*, 49.
[56] *T. Mukaiyama, K. Hojo*, Chem. Lett. *1976*, 893.
[57] *K. Hojo, T. Mukaiyama*, Chem. Lett. *1976*, 619.
[58] *J. S. Filippo, Jr., L. J. Romano*, J. Org. Chem. *40*, 1514 (1975).
[59] *J. L. Wardwell* in *S. Patai:* The Chemistry of the Thiol Group, Wiley, New York 1974, p. 519.
[60] *C. K. Ingold:* Structure and Mechanism in Organic Chemistry. Cornell University Press, Ithaca 1969, p. 517; *H. M. R. Hoffmann, E. D. Hughes*, J. Chem. Soc. *1964*, 1252; *E. Beretta, M. Cinquini, S. Colonna, R. Fornasier*, Synthesis *1974*, 425.
[61] *K. Hojo, H. Yoshino, T. Mukaiyama*, Chem. Lett. *1977*, 437.
[62] *G. L. O'Connor, H. R. Nace*, J. Am. Chem. Soc. *75*, 2118 (1953).
[63] *L. C. King, R. M. Dodson, L. A. Subluskey*, J. Am. Chem. Soc. *70*, 1176 (1948); *D. A. Swann, J. H. Turnbull*, Tetrahedron *20*, 1265 (1964).
[64] a) *O. Mitsunobu, M. Wada, T. Sano*, J. Am. Chem. Soc. *94*, 679 (1972); b) *D. Landini, F. Rolla*, Synthesis *1976*, 389; c) *T. Mukaiyama, T. Taguchi, M. Nishi*, Bull. Chem. Soc. Jpn. *44*, 2797 (1971).
[65] *K. Hojo, S. Kobayashi, K. Soai, S. Ikeda, T. Mukaiyama*, Chem. Lett. *1977*, 635.
[66] *T. Mukaiyama, M. Asami, J. Hanna, S. Kobayashi*, Chem. Lett. *1977*, 783; *M. Asami, H. Ohno, S. Kobayashi, T. Mukaiyama*, Bull. Chem. Soc. Jpn. *51*, 1869 (1978).
[67] *S. R. Landor, B. J. Miller, A. R. Tachell*, J. Chem. Soc. *C 1966*, 2280; *C 1967*, 197.
[68] *S. Yamaguchi, H. S. Mosher*, J. Org. Chem. *38*, 1870 (1973).
[69] *A. I. Meyers, P. M. Kendall*, Tetrahedron Lett. *1974*, 1337.
[70] *S. Yamaguchi, F. Yasuhara, K. Kabuto*, J. Org. Chem. *42*, 1578 (1977).
[71] a) *W. French, G. F. Wright*, Can. J. Chem. *42*, 2474 (1964); b) *H. Nozaki, H. Takaya, S. Moriuchi, R. Noyori*, Tetrahedron *24*, 3655 (1968); c) *A. I. Meyers, M. E. Ford*, Tetrahedron Lett. *1974*, 1341; d) *N. Allentoff, G. F. Wright*, J. Org. Chem. *22*, 1 (1957); e) *T. D. Inch, G. J. Lewis, G. L. Sainsbury, D. J. Sellers*, Tetrahedron Lett. *1969*, 3657.
[72] *D. Seebach, H. O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Döerr, N. P. DuPreez, V. Ehrig, W. Langer, C. Nüssler, H. Oei, M. Schmidt*, Helv. Chim. Acta *60*, 301 (1977).
[73] *J. S. Zweig, J. L. Luche, E. Barreiro, P. Crabbe*, Tetrahedron Lett. *1975*, 2355.
[74] *H. J. Brauer, R. Haller*, Tetrahedron Lett. *1972*, 5227.
[75] *T. Mukaiyama, K. Soai, S. Kobayashi*, Chem. Lett. *1978*, 219; *K. Soai, T. Mukaiyama, ibid. 1978*, 491. Asymmetric addition of dialkylmagnesium to aldehydes was also successfully carried out using the same chiral ligands *(67)*; *T. Sato, K. Soai, K. Suzuki, T. Mukaiyama, ibid. 1978*, 601.

1,3-Dipolar Cycloreversions

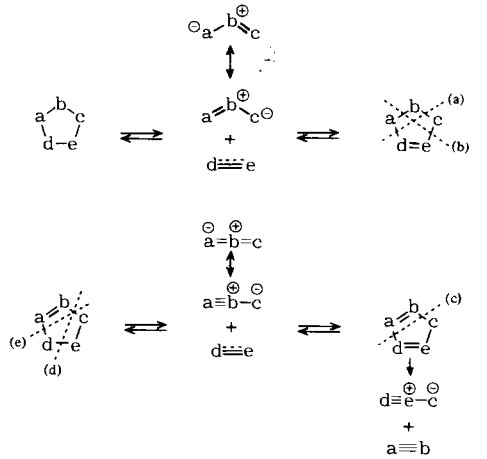
By Giorgio Bianchi, Carlo De Micheli, and Remo Gandolfi[*]

The 1,3-dipolar cycloreversion reaction represents a general scheme of fragmentation of pentaatomic heterocycles to produce 1,3-dipolar systems and dipolarophiles. This review summarizes cycloreversions which give rise to octet-stabilized 1,3-dipoles. The reaction can be either thermal or photochemical or electron impact induced. The aim of the article is to survey the published results, to emphasize the synthetic potential of this reaction, and to stimulate the study of its several not yet unambiguously defined mechanistic aspects.

1. General

The general concept of the 1,3-dipolar cycloadditions was recognized by *Huisgen* in the early 1960's[1]. Since then, an increasing number of researchers has produced an enormous amount of data on this branch of chemistry[2–11] and numerous examples have been found of the reverse reaction of 1,3-dipolar cycloaddition, *i.e.* [5→3+2][12] 1,3-dipolar cycloreversion. Scheme 1 exemplifies the cycloadditions of dipolarophiles with octet-stabilized[11] 1,3-dipoles of the allyl and propargyl-allenyl type and the corresponding cycloreversions[13].

Very often a [3+2]-cycloaddition/[3+2]-cycloreversion sequence generates a 1,3-dipole/dipolarophile couple differ-



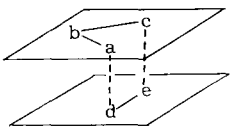
Scheme 1. 1,3-Dipolar cycloadditions and cycloreversions. Above: reactions with 1,3-dipoles of allyl type. Below: Reactions with 1,3-dipoles of propargyl-allenyl type. In the reactant shown at top left of scheme, all [5→3+2]-fragmentations are *a priori* possible. (a)—(e), see text.

[*] Dr. G. Bianchi, Dr. R. Gandolfi
Istituto di Chimica Organica, Università di Pavia
Via Taramelli 10, I-27100 Pavia (Italy)
Dr. C. De Micheli
Istituto di Chimica Farmaceutica e Tossicologica, Università di Milano
Viale Abruzzi 42, 20100 Milano (Italy)

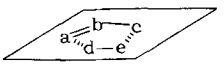
ent from the original reactants. This is the case when the cyclic adducts of Scheme 1 break down according to modes (a)—(e) ("1,3-dipole metathesis")[14]. This review will consider only the cycloreversions in which two σ bonds of the heterocycle are broken to give octet-stabilized 1,3-dipoles and double and triple bond dipolarophiles. Cycloreversions yielding vinylcarbenes, vinylazenes, ketocarbenes, ketoazenes, *etc.* as well as those giving equilibria such as azido-azomethines ⇌ tetrazoles, diazo-azomethines ⇌ triazoles, *etc.*[15-19] will not be treated.

Cycloreversions are induced thermally, photochemically, or by electron impact.

From the standpoint of orbital symmetry, thermal cycloreversions (from the ground state) are allowed[20] as suprafacial processes with regard to both fragments, and proceed *via* an aromatic (*Hückel*)[21] transition state. This $[_{\sigma}2_s + _{\sigma}2_s + _{\omega}2_s]$-concerted reaction takes place with some degree of nonsynchroneity in the σ bond cleavage. Experimental evidence for this type of mechanism has been found for anionic cycloreversions and for azides and nitrile imines (see Sections 2, 4, and 6); however, in some other instances a two-step mechanism involving a zwitterion (diazoalkanes, see Section 7) or a diradical (carbonyl oxides, see Section 12) has been advanced. As for [3+2]-cycloaddition[13,22], we consider the concerted mechanism the most plausible for the 1,3-dipolar cycloreversions too, especially for those processes in which addends are in equilibrium with adducts. The transition state geometry may vary according to the nature of the 1,3-dipole moiety. While for the reactions involving an allyl type 1,3-dipole *Huisgen*'s parallel-planes transition state *(1)* has received theoretical support from *ab initio* MO calculations[23], the same type of calculations have shown a one-plane transition state *(2)* to be most likely for 1,3-dipoles of propargyl-allenyl type[24].

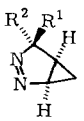


(1)

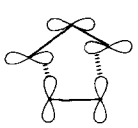


(2)

The great majority of photochemical cycloreversions takes place with the reactant in an excited singlet state[25-29]. Some of these reactions are known to be stereospecific[27,30-32]. A lack of stereospecificity may be explained in terms of photoinduced rearrangements of the final products[29,31]. No excited fragments have been detected and there is experimental evidence that the subsequent reactions of the photogenerated 1,3-dipoles take place in a thermally equilibrated ground state[25,33,34]. The efficiency of these liquid phase reactions varies, even though in some cases fairly high quantum yields (φ) have been measured (0.75 and 0.53, respectively) for extrusion of N_2 from *(3)* and *(4)* (313 nm, pentane)[30].



(3), R^1 = H, R^2 = CH_3
(4), R^1 = CH_3, R^2 = H



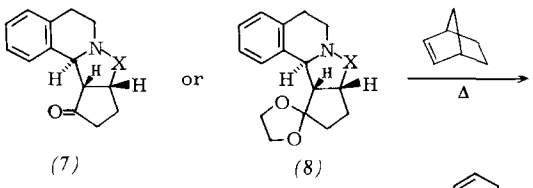
(5)



(6)

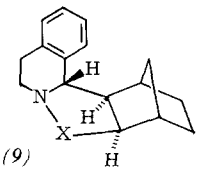
As far as the transition state geometry of the process is concerned, simple Woodward-Hoffmann orbital symmetry predictions require that, in a singlet excited state concerted fragmentation, one component has to react antarafacially as shown in *(5)*. This orientation is sterically unfavorable. However, no compelling experimental evidence exists for such a transition state structure. Some authors have proposed an alternative mechanism with a diradical such *(6)* as intermediate[35,36]. This latter hypothesis corresponds to a G_R type reaction (according to the Dougherty classification) with the system going from an excited surface (S_1) to the ground state surface (S_0). The diradical, where the two surfaces touch each other, provides a Born-Oppenheimer hole for direct passage from excited state to ground state[37]. For stereospecific cycloreversions some account should be taken of reactions of (vibrationally excited) hot ground state molecules. These originate from the excited state *via* a radiationless transition. This type of reaction is generally considered unimportant in dense media as a consequence of a very fast loss of excess vibrational energy. Yet, this reaction may become operative if a selective concentration of energy on the bonds to be broken occurs, and if the nuclei are moving toward fragmentation when the S_0 surface is reached[38,39]. Examples of possible hot ground state reactions are known[39,40].

The most commonly encountered examples of thermal and photochemical cycloreversions are those with extrusion of small thermodynamically stable molecules such as CO_2 and N_2. Conjugation gain and steric strain relief on going from adducts to fragments are the most common and important factors favoring the cycloreversion process. The former reaction driving force finds clear support in the data reported in Scheme 2[41].



(7) *(8)*

(a), X = O; *(b)*, X = NC_6H_5

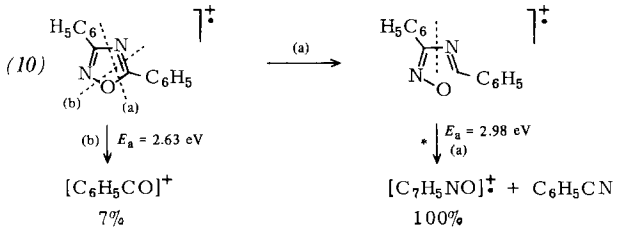


(9)

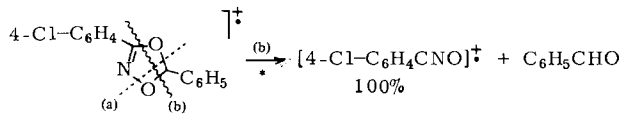
Scheme 2. Gain in conjugation energy as driving force for cycloreversion of *(7)* and *(8)*.

(7a) → *(9a)*, 9 h/ 80 °C/benzene 92% yield
(8a) → *(9a)*, 100 h/110 °C/toluene 10% yield
(7b) → *(9b)*, 100 h/140 °C/xylene 52% yield
(8b) 100 h/140 °C/xylene no reaction.

Numerous examples of electron impact induced 1,3-dipolar cycloreversion are known. Most of the five-membered heterocycles undergo this type of reaction. A very thorough mechanistic study of this type of reaction has been carried out by *Selva et al.* on 3,5-diaryl-1,2,4-oxadiazoles[42]. The radical ion $[C_7H_5NO]^+$ generated from *(10)* was shown to fragment further, to a slight extent as benzonitrile oxide and mainly as phenyl isocyanate, the rearrangement product of the 1,3-dipole[42a,b,43]. The process leading to the most abundant ion $[C_7H_5NO]^+$ [path (a)] is characterized by a higher activation energy [E_a = appearance potential − ionization potential] than that giving $[C_6H_5CO]^+$ [path (b)].



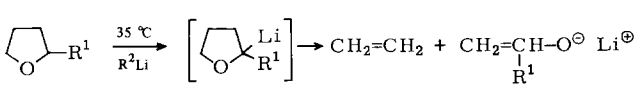
These results have been considered by the authors as good evidence for a stepwise cycloreversion in which there is a prior facile cleavage of the C–O bond [path (a)] requiring a smaller amount of energy than process (b)[42c,f]. Further investigations by the same authors, however, have shown that the ring cleavage can change from a stepwise to a concerted mechanism depending upon the substituents[42d]. In some instances, a completely different behavior of heterocycles towards thermal and electron impact induced cycloreversion has been observed. The 1,4,2-dioxazoline *(11)* fragments thermally exclusively by path (a) whereas cleavage (b) predominates on electron impact[44].



(11)

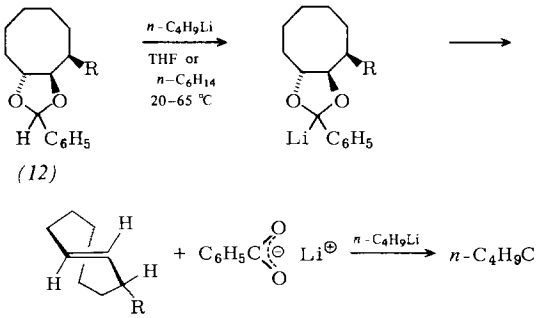
2. 1,3-Anionic Cycloreversions

The 1,3-anionic cycloreversion is particularly favored when the allyl or propargyl-allenyl anion fragment has a central carbon atom flanked by one or two electronegative atoms such as oxygen and sulfur[5,45]. This is because the negative charge is better stabilized on the triatomic anionic fragment, where it is localized at the two end atoms, than on the pentaatomic cycloanion, in which it is confined to the central C atom.

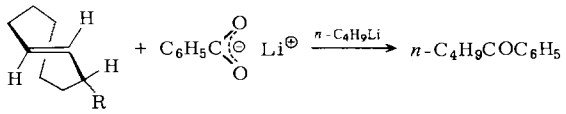


R^1 = H, R^2 = n-C_4H_9
R^1 = C_6H_5, R^2 = n-C_3H_7

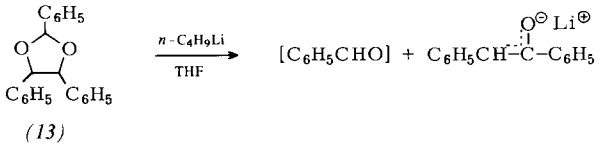
A cycloreversion reaction is often observed during slow metalation reactions with n-C_4H_9Li in tetrahydrofuran. The reaction is general for substituted tetrahydrofurans and is useful for the synthesis of enolates[46–48]. This reaction and all base-promoted fragmentations go through prior formation of an intermediate anion, which has been trapped or detected kinetically[47,49,50]. Cycloreversion proper follows. This type of mechanism applies to the transformation of cyclooctane-annelated 2-phenyl-1,3-dioxolanes *(12)* into *trans*-cyclooctenes derivatives in good yields[50,51]. However, the reaction is not generally applicable as shown by the fragmentation of *(13)*[50]. The undesired reactions encountered in the case of 1,3-dioxolanes can be avoided by using the 1,3-oxathiolanes. This is exemplified by the easy preparation of the highly strained *cis,trans*-1,5-cyclooctadiene and of *cis*-stilbene from the related precursors[52]. These compounds, however, were contaminated by traces of *cis,cis*-1,5-cyclooctadiene and *trans*-stilbene, respectively.



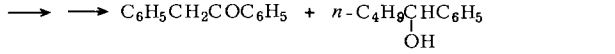
(12)

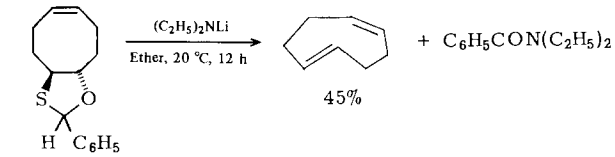


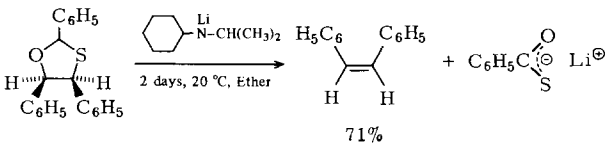
R = H, 73%
R = OH, 30%
R = OCH_3, 60%



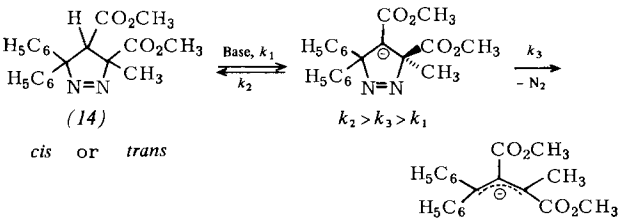
(13)







The authors do not explain whether these isomers are formed during the cycloreversion or afterwards. If the latter hypothesis were correct, the remarkable stereospecificity of the foregoing reactions suggests a concerted mechanism. The same mechanism was proposed by *Huisgen* for base-promoted extrusion of nitrogen from *cis*- and *trans*-*(14)* (sodium hydride in dimethylformamide at room temperature or sodium triphenylmethanide in tetrahydrofuran at $\geq -40\,^{\circ}C$). The rate of this reaction is $>10^{12}$ times greater than the thermal conversion of *(14)* ($>100\,^{\circ}C$) to cyclopropanes *via* the trimethylene species[49].

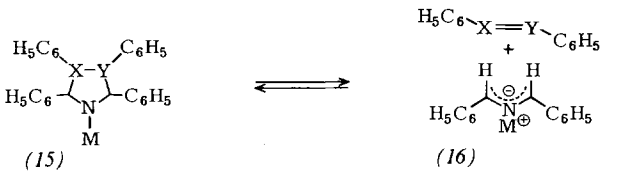


(14)

cis or *trans*

Examples of dynamic adduct ⇌ addends equilibria are those of 1,3-diphenyl-2-azaallyl anion *(16)* with various dipolarophiles. For instance, compound *(16a)* reacts with azobenzene at 20 °C to give high yields of the adduct *(15c)* which, however, at *ca.* 60 °C is in equilibrium with the addends[5]. The nature of the metals also plays a significant role, as evidenced by the fact that cycloreversion of *(15b)* is

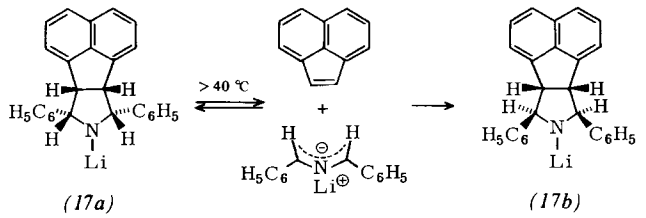
favored relative to *(15a)*[5]. This was rationalized on the basis of a hard-hard interaction between lithium cation and anion in *(15a)* and a soft-soft interaction between the potassium cation and the delocalized anion in *(16)*[45]. Quantitative transformation of the *"endo"* adduct *(17a)* into the stable *"exo"* isomer *(17b)*[5] is explained in terms of cycloreversion and subsequent cycloaddition[5]. Strain relief is probably the driving force of this reaction.



(15) *(16)*

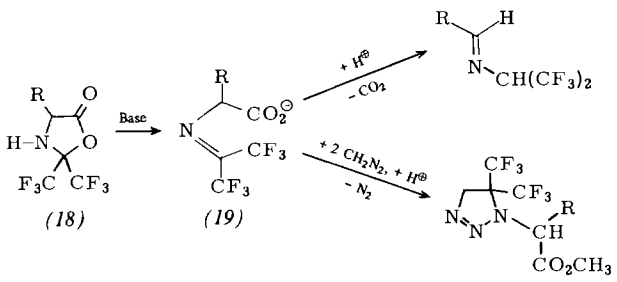
(a), X–Y = CH–CH, M = Li
(b), X–Y = CH–CH, M = K
(c), X–Y = N–N, M = Li

(a), M = Li
(b), M = K



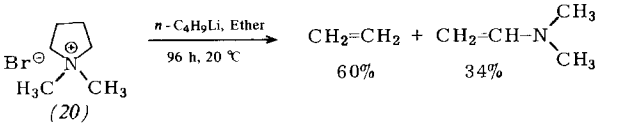
(17a) *(17b)*

The base-catalyzed fragmentations of 5-acyl-2-isoxazolines[53], 3-acyl- and 5-acyl-isoxazolidines[54,55], and 5-oxazolidones *(18)*[56] can be considered as examples of two-step cycloreversion. The intermediate *(19)* could be trapped by diazomethane.

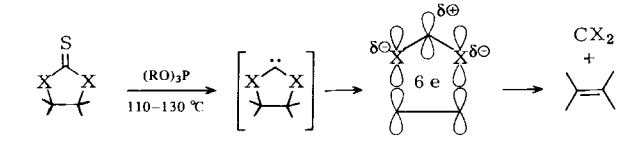


(18) *(19)*

The base-promoted fragmentations of cyclic amonium *(20)*[57] and sulfonium ions[58] and the stereospecific extrusion of CO_2 and CS_2 on reaction of 1,3-dioxolane- and 1,3-dithiolane-2-thiones with trialkyl phosphites to give alkenes[59] may be considered as further examples of anionic cycloreversions. In these cases, however, the 4π fragment extruded is electrically neutral.

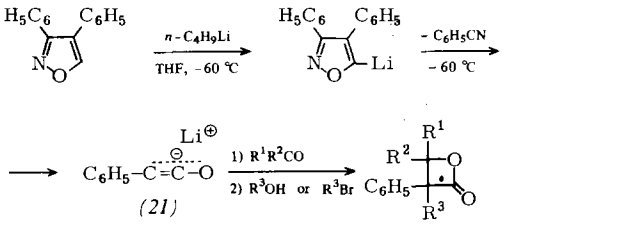


(20)



X = O, S

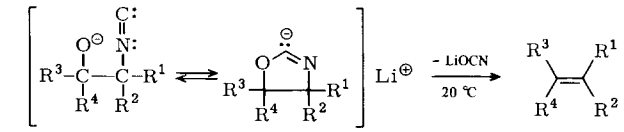
Cycloreversions leading to heteropropargyl-allenyl anions are less common[60-63]. The reaction of 3,4-diphenylisoxazole with strong bases permitted the first synthesis of the ynolate ion *(21)* which was converted into highly substituted β-lactones[62].



(21)

$R^1 = R^2 = CH_3$, $R^3 = C_6H_5CH_2$, 56%
$R^1 = R^2 = CH_3$, $R^3 = H$, 59%
$R^1 = H$, $R^2 = C_6H_5$, $R^3 = C_6H_5CH_2$, 69%

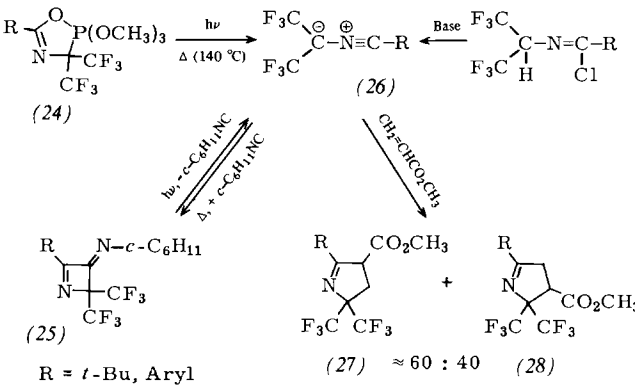
Oxazolinyl anions *(23)* exist in equilibrium with the 2-isocyano alkoxides *(22)* and are readily obtained by interaction of lithiated alkyl isocyanides with aldehydes or ketones at −70 °C. If one of the substituents is a vinyl or phenyl group the equilibrium is moved towards stereospecific fragmentation to give olefins[61].



(22) *(23)*

3. Nitrile Ylides

The nonisolable nitrile ylides *(26)* can be conveniently generated by thermolysis or photolysis of 1,4,2λ⁵-oxazaphospholines *(24)* with elimination of trimethyl phosphite and from 1-azetines *(25)* on extrusion of isocyanides[33]. The latter reaction represents a rare example of a [4→3+1] process. The ratio of regioisomers *(27)* and *(28)* found for trapping reactions of *(26)* with methyl acrylate was independent of the 1,3-dipolar precursors[33], suggesting that the photogenerated nitrile ylides *(26)* are electronically and vibrationally relaxed.



(24) *(26)*

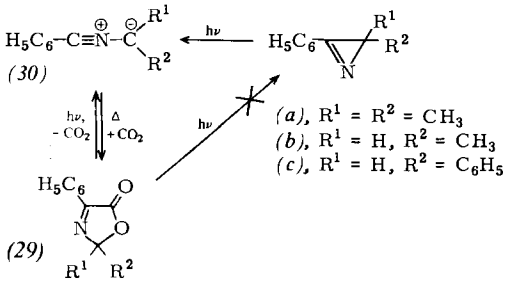
(25)

R = *t*-Bu, Aryl

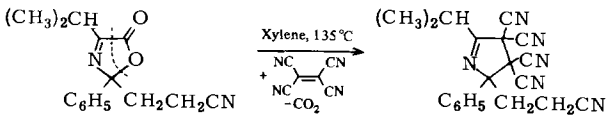
(27) ≈ 60 : 40 *(28)*

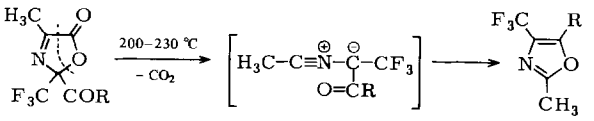
Photoextrusion of CO_2 from 3-oxazolin-5-ones *(29)*[25,64,65] was shown by *Padwa et al.* to occur from the excited singlet manifold since the reaction was not quenched by piperylene (triplet quencher) but was suppressed by xanthone (triplet sensitizer); xanthone absorbed more than 98% of the incident light[25]. The nitrile ylides *(30)* were trapped by electron poor CC double and triple bonds to give fairly good yields of 1-pyrrolines[25] and pyrroles[65]. At infinite dipolarophile (acry-

lonitrile) concentration the quantum yield for cycloaddition was 0.30 for reaction of compound *(29a)* at 253.7 nm. Although cycloaddition experiments with nitrile ylides *(30)* formed from 2*H*-azirines gave the same isomer distribution as that obtained from *(29)*, azirines are not intermediates in the transformation *(29)*→*(30)*[25].



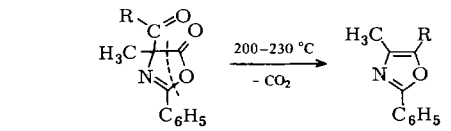
Several trisubstituted 3-oxazolin-5-ones undergo extrusion of CO_2 when heated at the appropriate temperatures[66-69].



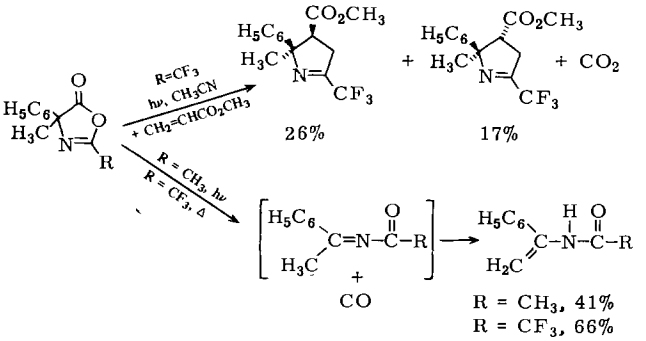


R = C_6H_5, 94%
R = 4-NO_2-C_6H_4, 61%
R = CH_3, 26%

Photochemical[36] and thermal[66,67] extrusion of CO_2 is known also for trisubstituted 2-oxazolin-5-ones. The 1,3-dipolar cycloreversion is not the sole reaction reported for these latter compounds: in some instances [5→4+1]-cycloreversion with extrusion of CO was observed[36,68].



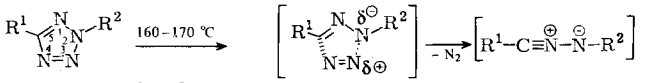
R = CH_3, C_6H_5, OCH_3, $CO_2C_2H_5$ 71–95%



Cycloreversion to a nitrile ylide radical ion and a C=S fragment was detected in the mass spectra of 2,4-dimethyl-2-thiazoline[70].

4. Nitrile Imines

Thermolysis[34,71-73] and photolysis[34,73,74] of 2,5-diaryltetrazoles *(31)* represents a ready route to nitrile imines *(33)*[1,2]. The thermal decomposition of 2,5-diphenyltetrazole follows first order kinetics little influenced by the solvent polarities[72]: $E_a = 32.4$ kcal mol^{-1} and $\Delta S^{\neq} = -2.6$ cal K^{-1} mol^{-1}[71]. A transition state such as *(32)* in which N^2–N^3 bond has suffered more extensive heterolytic cleavage than N^4–C^5 was proposed by *Baldwin et al.* on the basis of Hammett ρ values of +1.16 and −0.23 for 2-aryl-5-phenyl- and 5-aryl-2-phenyltetrazoles, respectively[71].

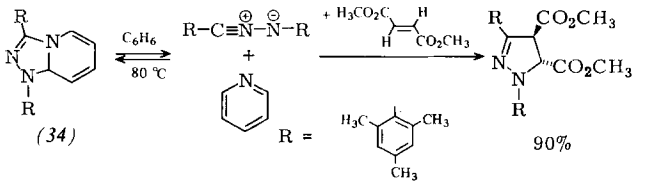


(31) R¹, R² = Aryl *(32)* *(33)*

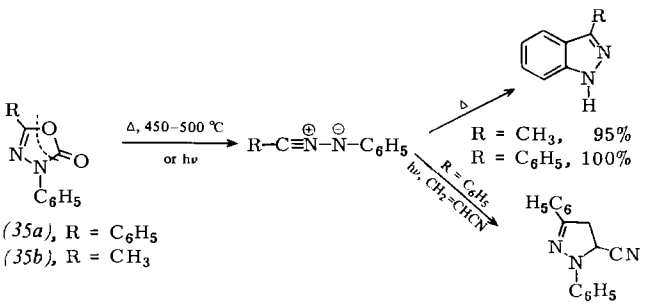
The same behavior has been observed for several other tetrazoles[75-80]. 5-Phenyl-2-(trimethylsilyl)tetrazole yields the nitrile imine above 190 °C[75], 5-phenyl-2-phthalimidotetrazole at *ca.* 80 °C[76], and 5-aryltetrazoles above 165 °C[77]. 2,5-Diphenyltetrazole was calculated to react 38 times faster than 5-phenyltetrazole in benzonitrile at 175 °C[77]. In the fragmentation of 2-methyl-5-phenyltetrazole higher temperatures are required (≥220 °C) and it has been reported that the extrusion of nitrogen competes with a second less important 1,3-dipolar cycloreversion to methyl azide and benzonitrile[78].

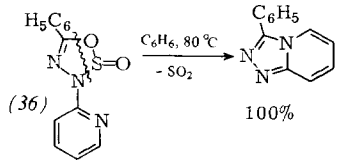
Photolytic studies on 5-phenyltetrazole[74] and 2-methyl-5-phenyltetrazole[80] gave results best explained by a 1,3-dipolar ring cleavage, although a different mechanism was proposed for the latter compound.

Dimesitylnitrile imine yields stable 1:1 adducts of type *(34)* with aromatic heterocycles such as pyridine, quinoline, and isoquinoline[81]. These adducts readily dissociate into reactants when heated and the newly formed nitrile imine can be trapped with dipolarophiles.



The extrusion of carbon dioxide and sulfur dioxide from 1,3,4-oxadiazol-2-ones *(35)*[82,83] and 1,2,3,4-oxathiadiazole *S*-oxides *(36)*[85], respectively, is of interest. 2,4-Diphenyl-1,3,4-oxadiazol-2-one *(35a)* is fairly stable up to about 300 °C[84]; however, it can be transformed by flash vacuum pyrolysis at 500 °C into 3-phenylindazole in nearly quantita-

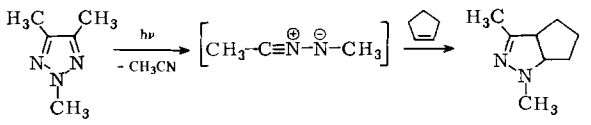




(36) 100%

tive yield[82]. In contrast to its thermal stability, compound *(35a)* gives good yields of diphenylnitrile imine adducts when irradiated in absolute ethyl acetate in the presence of various dipolarophiles[83].

Analogously, 2,4,5-trimethyl-2*H*-1,2,3-triazole gave acetonitrile and the adduct *(37)* on irradiation in ether (Vycor filter) in the presence of an excess of cyclopentene[28]. The 2,4,5-triphenyl derivative, on the other hand, failed to react under the same conditions[28].

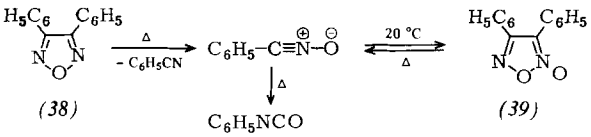


(37) 25%

Several heterocycles embodying the nitrile imine system in their rings undergo [3 + 2]-cycloreversion on electron impact. They include the previously cited 2,5-disubstituted tetrazoles[86] and 5-aryltetrazoles[87], the 1,3,4-Δ^2-oxadiazolines[88,89], the 1,3,4-Δ^2-thiadiazolines[88,89], and Δ^2-pyrazolines[89,90]. The charge is preferentially retained by the 1,3-dipole.

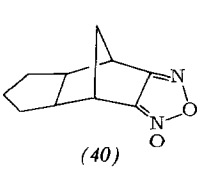
5. Nitrile Oxides, Nitrile Sulfides, and Nitrile Selenides

The thermal cleavage of 3,4-diphenylfurazan *(38)* and 3,4-diphenylfurazan *N*-oxide *(39)*, discovered at the end of the last century[91 93], are probably the first examples of 1,3-dipolar cycloreversions.

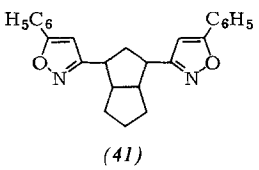


(38) (39)

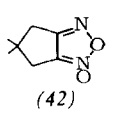
The cycloreversion of furazan *N*-oxides was recently used by *Boulton*[94], *Chapman*[95], and *Paton*[96b] to generate nitrile oxides as an alternative to more common methods[96a]. The reaction is favored by steric strain relief. For example, while *(40)* gives the adduct *(41)* on heating with excess phenylacetylene at 55 °C, compound *(42)* is recovered unchanged under the same reactions conditions[94]. Moreover,



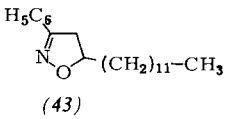
(40)



(41)



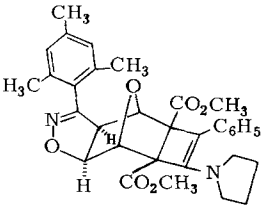
(42)



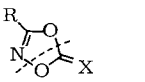
(43)

while sterically encumbered 3,4-bis(1-adamantyl)furazan *N*-oxide was found to undergo cycloreversion at *ca.* 77 °C[97], compound *(39)* requires much more drastic conditions and reacts with 1-tetradecene (as dipolarophile and solvent) only at 245 °C to give *(43)* in 82% yield[95]. It remains an open question whether the cycloreversion is concerted or proceeds as a two-step process *via* an intermediate dinitrosoalkene[96c].

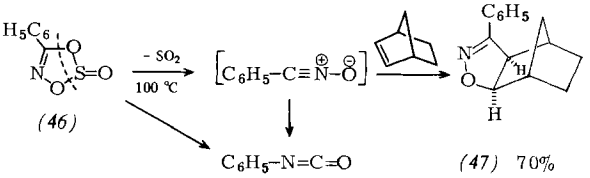
2-Isoxazolines and isoxazoles, which are readily prepared by reaction of nitrile oxides with alkenes and alkynes, are quite thermostable compounds. However, under the conditions of flash-vacuum pyrolysis at 600—650 °C, the 2-isoxazoline *(44)* gives a quantitative yield of 2,4,6-trimethylbenzonitrile oxide[98].



(44)

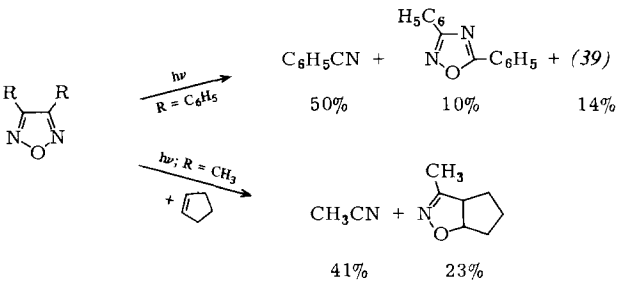


(45) X = O, S



(46) (47) 70%

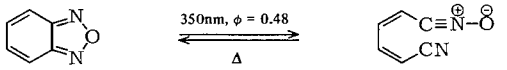
Hydroxamic acids react with acid chlorides such as phosgene to give heterocycles *(45)* and *(46)* in high yields[99]. While in the case of *(45)* the thermal and photochemical elimination of CO_2 and COS gives the corresponding acylnitrene, which has been trapped with suitable scavengers[99], compound *(46)* undergoes thermal cycloreversion to benzonitrile oxide as a major fragmentation path. In fact when compound *(46)* was heated with an excess of norbornene, adduct *(47)* was obtained with some phenyl isocyanate[100].



Light irradiation of 3,4-diphenylfurazan alone in benzene (Pyrex filter)[101] and of 3,4-dimethylfurazan in ether (Vycor filter) in the presence of cyclopentene[28] yielded products in agreement with 1,3-dipolar cycloreversion processes. Under conditions such that added xanthone absorbed 99% of the incident light the 3,4-diphenylfurazan yielded benzonitrile at a rate of *ca.* 12% of that on direct irradiation[28]. The foregoing results suggest that the cleavage of the furazans occurs predominantly in a singlet excited state.

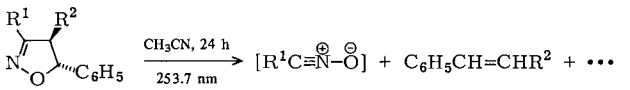
The benzofurazans behave similarly. Irradiation of benzofurazan *(48)* at room temperature in strongly polar solvents (*e.g.* H_2O) yielded exclusively *(49)*, detected and characterized by UV and IR spectroscopy[102] and trapped with dime-

thyl acetylenedicarboxylate[103]. Compound *(49)* undergoes thermal reconversion into *(48)*[102], k (20 °C) = 2×10^{-5} s^{-1}.



(48) *(49)*

Also, 2-isoxazolines *(50)* and particularly the 4,5-disubstituted derivatives are reported to undergo light-induced cycloreversion to nitrile oxides and alkenes in admixture with other compounds (see Scheme 3). Detailed mechanistic investigation showed that the reaction possibly takes place in a singlet excited state of the ketoxime group[29].



(50) *(51)* *(52)*

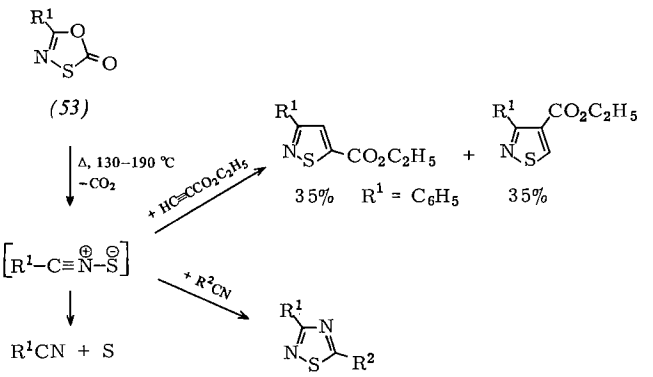
Scheme 3. Cycloreversion of substituted 2-isoxazolines *(50)*. Yields based on reacted starting material.

(50) →	*(51)* +	*(52)* +	*(50)* [a]
$R^1 = CH_3$, $R^2 = C_6H_5$	29% [b]	66% [c]	59%
$R^1 = R^2 = C_6H_5$	—	39% [d]	31%
$R^1 = C_6H_5$, $R^2 = H$	—	1.6%	24%

[a] Recovered. [b] Trapped with cyclopentene. [c] *cis:trans-(52)* = 1:1. [d] *cis:trans-(52)* = 2:1.

No examples of electron impact induced 1,3-dipolar cycloreversion have been reported for isoxazoles[104]. Conversely, this process is important for 2-isoxazolines[43,105] and several heterocycles containing the nitrile oxide moiety such as 1,2,4-oxadiazoles[42,108b], Δ^2-1,2,4-oxadiazolin-5-ones[106a], 1,4,2-oxathiazole 4-oxides[106b], 1,4,2-dioxazoles[44], furazan *N*-oxides[97,107], and furazans[101,108] with the positive charge retained preferentially in the 1.3-dipole fragment.

So far, the sole synthetically practical route to nitrile sulfides is the cycloelimination of CO_2 from 1,3,4-oxathiazol-2-ones *(53)*[109]. The 1,3-dipole was trapped by CC and CN triple bonds to give good yields of isothiazoles and 1,2,4-thiadiazoles, respectively[109].



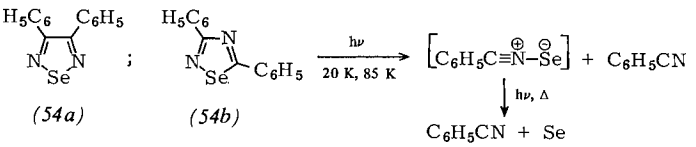
(53)

$R^1 = C_6H_5$, $R^2 = CO_2C_2H_5$, 88%
$R^1 = CO_2C_2H_5$, $R^2 = C_6H_5$, 33%

A yield of 22% of dimethyl 3-phenyl-4,5-isothiazoledicarboxylate was obtained on irradiation of 5-phenyl-1,3,4-oxathiazol-2-one (Pyrex filter) in neat dimethyl acetylenedicarboxylate as reagent and solvent[110]. Moreover, irradiation of 3,4-dimethyl (Vycor filter) and of 3,4-diphenyl-1,2,5-thiadiazole (Corex filter) in ether gave fair yields of the corresponding nitrile and sulfur[28].

The nitrile sulfide radical ion was found to be the most abundant peak in the mass spectra of several 1,2,5- and 1,2,4-thiadiazole derivatives[108a,111]. In contrast to isoxazoles, the isothiazoles show extensive electron impact induced 1,3-dipolar cycloreversion[112].

A recent study on low temperatures photolysis of diphenylselenadiazoles such as *(54a)* and *(54b)* has shown (IR and UV spectroscopic detection) that a new type of 1,3-dipole, *viz.* benzonitrile selenide, occurs as intermediate. Attempts to trap the 1,3-dipole with dimethyl acetylenedicarboxylate were unsuccessful[113].

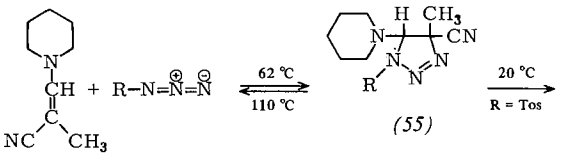


(54a) *(54b)*

The benzonitrile selenide radical ion has been also detected in the mass spectra of 1,2,5-selenadiazole derivatives[108a,114].

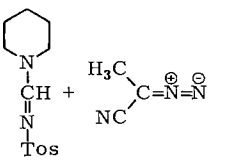
6. Azides

The reaction of Δ^1-1,2,3-triazolines to give azomethines or aziridines on extrusion of nitrogen has been widely studied[115]. However, triazolines undergo two other important fragmentation processes: 1,3-dipolar cycloreversions to azides and alkenes and to diazoalkanes and azomethines, respectively. For example, phenyl azide and β-piperidinomethacrylonitrile are in mobile equilibrium with adduct *(55a)*[116,117]. Below 62 °C, triazoline *(55a)* is favored over the addends, and after 10 days the reaction yield is quantitative, while at 110 °C the only ≤5% of same heterocycle is present[116].



(55)

(a), R = C_6H_5
(b), R = Tos

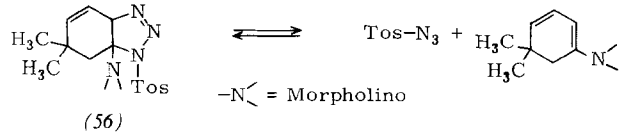


In the case of *(55b)* (not isolated) even at room temperature the equilibrium lies completely to the right with complete dissociation to diazoalkane and azomethine[116].

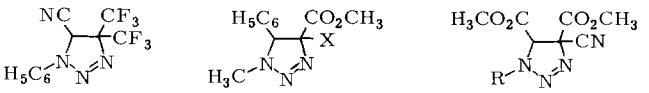
Adduct *(56)*, which can be isolated as a fairly stable solid at −20 °C, is in equilibrium with the products of [3+2]-cycloreversion in solution[118].

Cycloreversion was found to compete with aziridine formation in the case of compounds of type *(57)* at the temperatures indicated[119].

The foregoing examples show that both electron-rich and electron-poor conjugated double bonds are easily extruded from 1,2,3-triazolines.



(56)

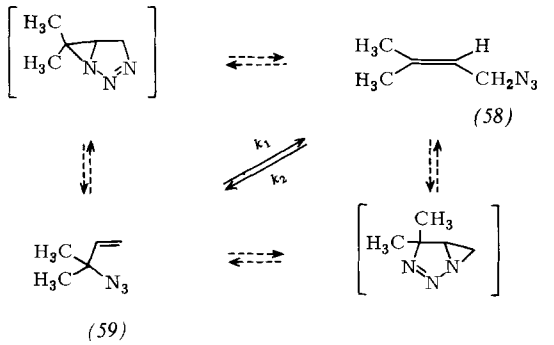


(57a), 110 °C (in $C_6H_5CH_3$)

(57b), X = CN, 80 °C (in C_6H_6); X = CO_2CH_3, 140 °C (in $(CH_3)_2C_6H_4$)

(57c), R = CH_3, 61 °C (in $CHCl_3$); R = $CH_2C_6H_5$, 80 °C (in C_6H_6)

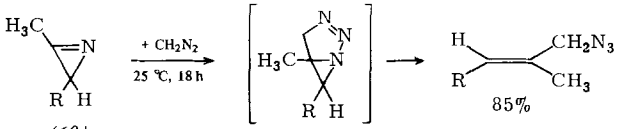
Of interest is the equilibrium between the azides *(58)* and *(59)* [*(58)*:*(59)* ≈ 3:1 at 25 °C] which requires both 1,3- and 1,1-intramolecular dipolar cycloadditions and cyclorever-



(59)

Scheme 4

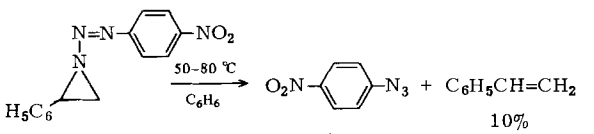
sions. As the rates constants k_1 and k_2 are only slightly sensitive to solvent polarity and no solvolysis processes were detected in 70% aqueous acetone, it was concluded that no ion pair is formed during the rearrangement[120]. The mechanism formulated in Scheme 4 finds further support in the results of the reactions of diazoalkanes with 2*H*-azirines such as *(60)*[121] and of the fragmentation of *N*-(4-nitrophenylazo)-2-phenylaziridine *(61)*[122].



(60)

85%

R = 2,4-$(NO_2)_2C_6H_3$

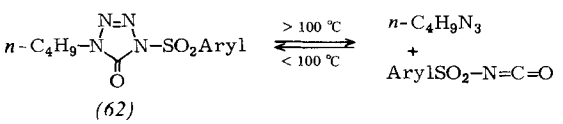


(61)

79%

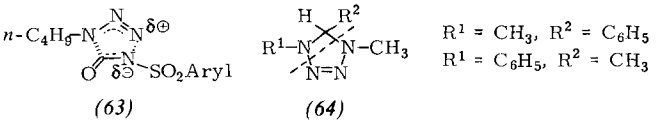
10%

The 1,3-dipolar cycloreversion has also been observed in 2-tetrazolin-5-ones and found to be dependent on the substituents[123,124]. For the tetrazolinones *(62)* the activation energy was in the range 29—34 kcal mol^{-1} with activation entropy values of 0—7 cal K^{-1} mol^{-1}. The reaction rates were little influenced by solvent polarity but were increased by



(62)

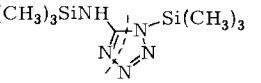
the electronegativity of the isocyanate group ($\rho = +1.4$). These findings led *L'abbé et al.* to propose a concerted mechanism involving charge imbalance in the transition state of type *(63)*[123].



(63)

(64)

R^1 = CH_3, R^2 = C_6H_5
R^1 = C_6H_5, R^2 = CH_3



(65)

The thermal fragmentation of 2-tetrazolines *(64)* (at *ca.* 120 °C)[125] and of tetrazole *(65)* (at 150—160 °C)[75] are noteworthy examples of cycloreversions leading to azomethines and cyano compounds.

Tetrazolinones *(66)*[126], tetrazolinethiones, and tetrazolinimines *(67)*[127] undergo [3+2]-cycloreversion on electron impact. Pathway (a) is always dominant over pathway (b), and the positive charge has been found to be retained preferentially by the dipolarophilic group. This is often the base peak of the spectrum. In dialkyl-substituted tetrazolinones the pathways (a) and (b) can be neglected.



(66)

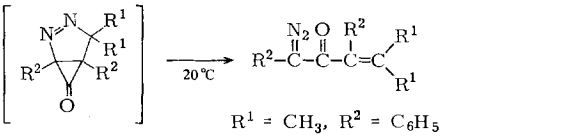
(67)

R^1 = C_6H_5, R^2 = H, CH_2=CH, CH_3, 4-Cl-$C_6H_4SO_2$;
R^1 = CH_2=CH, R^2 = H, *n*-C_4H_9, CH_3SO_2
R^1 = $CH_2CH(C_6H_5)$, CH_2=$C(C_6H_5)$, R^2 = $ArylSO_2$, H

X = S, R = H
X = NH, NCH_3, R = CH_3

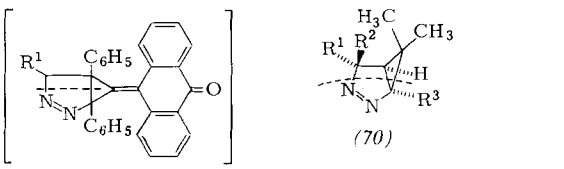
7. Diazoalkanes

The driving force for most of the known thermal and photochemical cycloreversions of 1-pyrazolines condensed with three- and four-membered carbocycles to give diazoalkanes and C=C dipolarophile systems is the relief of strain. It is not surprising, therefore, that the adducts of diazoalkanes with cyclopropenones *(68)*[128,129], with triafulvenes *(69)*[130], and with diphenylthiirene dioxide[131] are labile compounds which readily undergo intramolecular [5→3+2]cyclorever-



(68)

R^1 = CH_3, R^2 = C_6H_5
R^1 = C_6H_5, R^2 = H

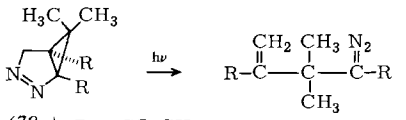


(69), R^1 = H, C_2H_5, CH_3

(70)

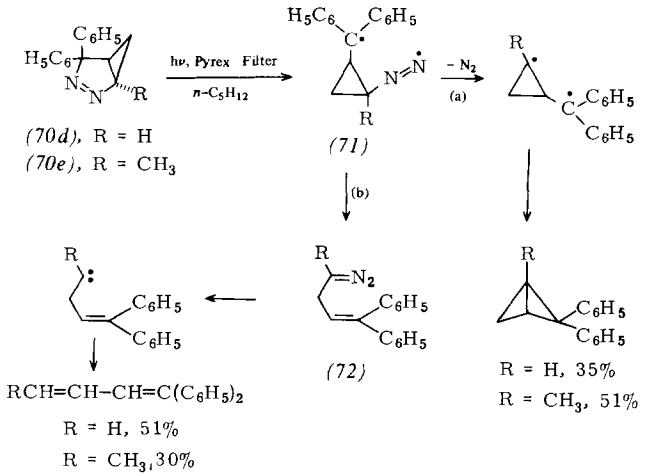
(a), R^1 = R^2 = C_6H_5, R^3 = $P(OCH_3)_2$
(b), R^1 = R^3 = H, R^2 = $CO_2C_2H_5$

sion. However, the diazoalkane/cyclopropene adducts *(70)* are relatively stable and their cycloreversion properties depend largely on the substituents[26, 35, 128, 132, 133]. For instance, while compound *(70a)* cycloreverts smoothly at 80 °C[132c], *(70b)* undergoes cycloreversion at 0 °C and could not be isolated[132a]. In general, electron-withdrawing substituents attached to the incipient olefin moiety accelerate cycloreversion[132d].



(70c), R = CO_2CH_3

A clean photoinduced reaction of 2,3-diazabicyclo[3.1.0]hex-2-enes such as *(70c)* is exemplified by direct photolysis to give the diazoalkane indicated in the equation[128]. A more complex behavior has been found in the photolysis of compounds *(70d)—(70h)* and of 2,3-diazabicyclo[3.2.0]hept-2-enes *(73)* and *(74)*. The formation of the reaction products from *(70d)* and *(70e)* was rationalized as due to the two competitive processes (a) and (b)[35]. The 1,5-diradical *(71)* was considered the common intermediate for both processes. Diazoalkane *(72)* was detected by NMR.



(70d), R = H
(70e), R = CH_3

(71)

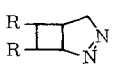
(72)

$RCH{=}CH{-}CH{=}C(C_6H_5)_2$
R = H, 51%
R = CH_3, 30%

R = H, 35%
R = CH_3, 51%

Scheme 5

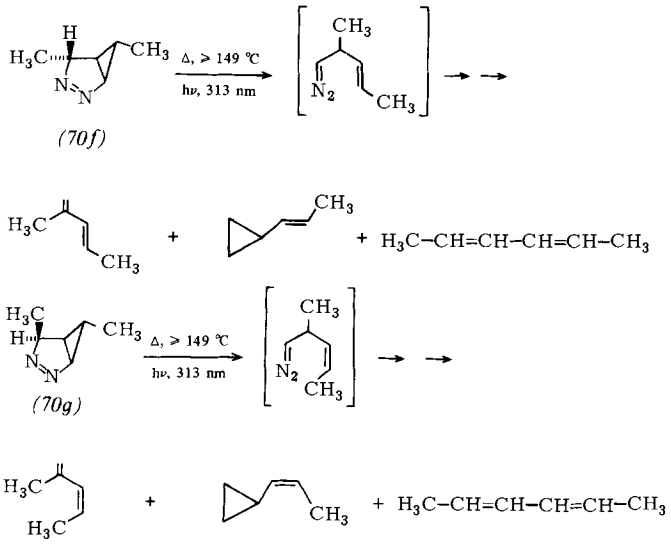
A similar reaction pattern was proposed for the direct ($\lambda > 300$ nm) and sensitized (acetophenone) photolysis of compound *(73)* where, however, cycloreversion [path (b), Scheme 5] is a minor process[26, 134]. By contrast, in the thermolytic fragmentation of *(73)* and *(74)* path (b) again prevails over path (a)[26, 135].



(73), R = H
(74), R = CH_3

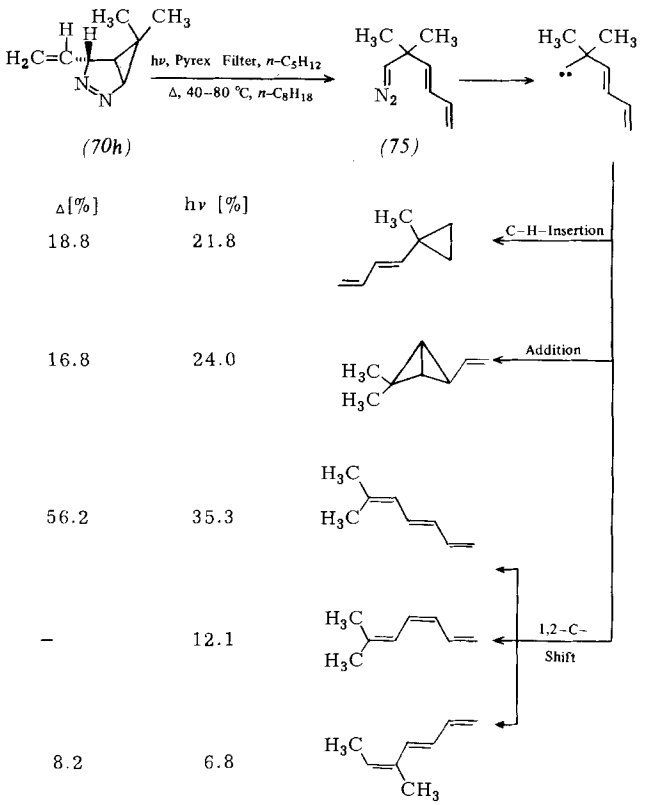
Thermolysis and photolysis of *(70f)* and *(70g)* are stereospecific reactions initiated by a cycloreversion mechanism[30].

Schneider et al. recently showed that the cycloreversion mechanism may be the sole photochemical and thermal fragmentation route for 2,3-diazabicyclo[3.1.0]hex-2-enes *(70)*[133]. The authors were able to demonstrate that diazoalkane *(75)* is the sole primary product of *(70h)* on photochemical (and most probably also on thermal) treatment by trapping reactions and on the basis of spectroscopic detection. Thermodynamic data were also determined: the thermal cycloreversion of *(70h)* is characterized by $\Delta H^{\neq} = 24.8 \pm 1$ kcal mol^{-1} and $\Delta S^{\neq} = -1 \pm 2$ cal K^{-1} mol^{-1}.



(70f)

(70g)

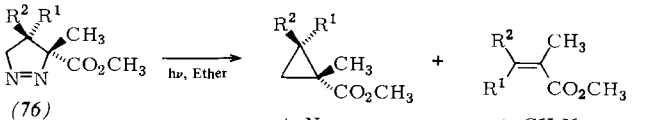


(70h) *(75)*

Δ [%]	hν [%]
18.8	21.8
16.8	24.0
56.2	35.3
–	12.1
8.2	6.8

C-H-Insertion
Addition
1,2-C-Shift

To our knowledge, no examples of cycloreversion have been reported for cyclopentane-condensed 1-pyrazolines[136]. Monocyclic 1-pyrazolines such as *(76)* are found to undergo 1,3-dipolar cycloreversion with difficulty[27, 31, 32, 137, 138].

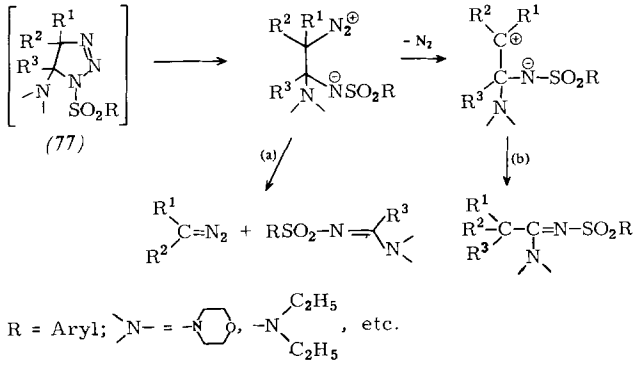


(76)

	+ N_2	+ CH_2N_2
R^1 = H, R^2 = C_2H_5	84%	16%
R^1 = C_2H_5, R^2 = H	94%	6%

The photochemical process is a singlet state stereospecific reaction favored by short wavelengths and low pressures[27]. A vibrationally excited S_1 state was postulated as initiating the cycloreversion.

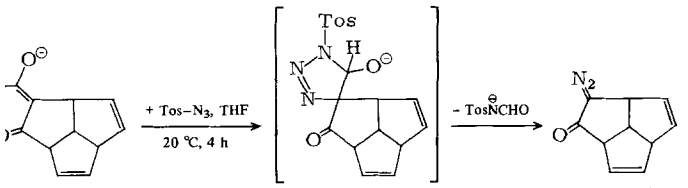
The pericyclic ring opening of 1,2,3-triazolines to give C=N dipolarophiles and diazoalkanes is also well documented[16, 128, 132a, 139–143]. For instance, sulfonyl azides react readily with enamines at room temperature to give the non-isolable 1,2,3-triazolines *(77)* whose decomposition by pathway (a) or (b) is determined by the substituents. 1,3-Dipolar cycloreversion [path (a)] was the only fragmentation path detected (except for R^3 = cyclopropyl) when $R^1 = R^2 = H$, $R^1 = H$ or alkyl and R^2 = formyl, acyl, vinyl and phenyl. This process is therefore a convenient route to α-diazo aldehydes[16, 140, 141].



(77)

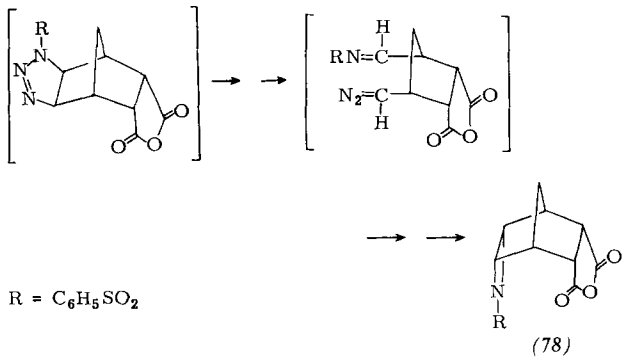
R = Aryl; $\rangle N-$ = , , etc.

Of great synthetic value is also the reaction of tosyl azide with the salts of β-carbonyl vinyl alcohols to give α-diazocarbonyl compounds[16] as exemplified by the synthesis of 3-diaza-2,3-dihydrotriquinacen-2-one[142].



100%

Specific fragmentation to diazoalkanes and C=N fragments was observed in the course of the reactions of the adducts of phosphono or phosphinyl azides with enol ethers[143a], tosyl azide with tetrakis(dimethylamino)allene[143b], tosyl azide with tetramethoxyethane[143c], and picryl azide with a vinylporphyrin[143d]. Such a fragmentation has also

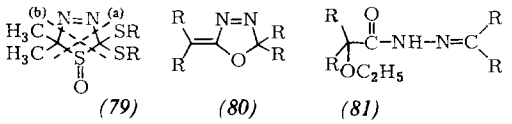


R = $C_6H_5SO_2$

(78)

been postulated to explain the frequently predominant formation of the *endo*-aziridines such as *(78)* in the reaction of benzenesulfonyl azide with norbornene derivatives[144].

Less common are cycloreversions leading to diazoalkanes and C=O[145–148], C=Se[150], C=S[149, 150], and N=P[151] double bonds. Only a few examples of these reactions can be mentioned. Sulfene-diazoalkane adducts dissociate at room temperature into their components. In some cases, both of the two possible decomposition pathways have been observed, as for the adduct *(79)*[149].

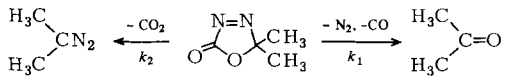


(79) *(80)* *(81)*

(a), 60%; *(b)*, 30% R = C_6H_5

Another example is the [3 + 2]-cycloadduct of diphenyldiazomethane and diphenylketene *(80)*, which undergoes cycloreversion when heated to 150 °C[147]. Photochemical cycloreversion of compounds *(80)* is a two-step process, as evidenced by the isolation of *(81)* when operating in absolute ethanol[147].

Finally, the thermal behavior of 5,5-dimethyl-5*H*-1,3,4-oxadiazol-2-one in methanol and carbon tetrachloride is of interest[148]. The compound decomposes by two potential routes. The great rate enhancement of cycloreversion induced by solvent polarity causes decomposition to 2-diazopropane and carbon dioxide to predominate in methanol.

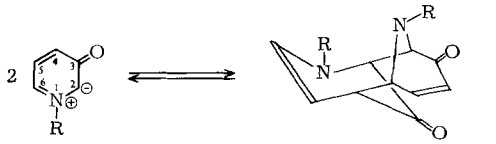


84 °C, CCl_4 : $k_1 = 10^{-4}s^{-1}$, $k_2 = 0.25\times10^{-4}s^{-1}$

84 °C, CH_3OH : $k_1 = 0.9\times10^{-4}s^{-1}$, $k_2 = 4\times10^{-4}s^{-1}$

8. Azomethine Ylides

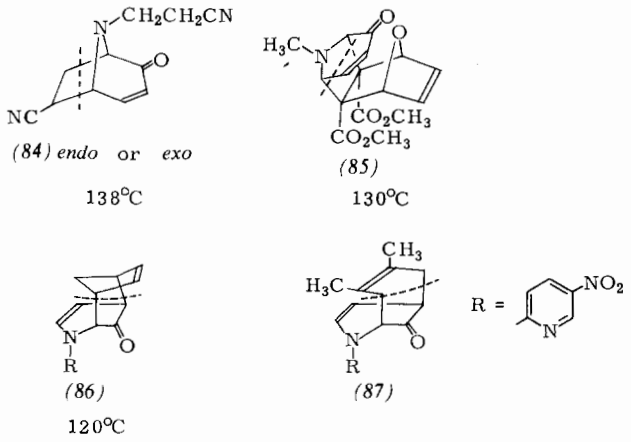
The 1,3-dipolar cycloadditions of a variety of pyridinium betaines with 2π, 4π, and 6π dipolarophiles have been extensively studied by *Katritzky et al.*[7]. A characteristic of almost all the azomethine ylides of type *(82)* is a dynamic equilibrium with the dimer *(83)* (the latter often as a mixture of two regioisomers)[7]. Dimers *(83)* also cyclorevert on electron impact, although in several cases the thermal process precedes the electron impact in the mass spectrometer[152].



(82) *(83)* + Regioisomer

Compounds *(82)* react as 1,5-dipole at the 2,4-position and as 1,3-dipole at the 2,6-position with dipolarophiles. Some of these adducts undergo cycloreversion: *(84)*[153], *(85)*[154], and *(86)* on heating[155] (at the temperature indicated), whereas compound *(87)* cycloreverts only on electron impact[155].

The conditions for the cycloreversion process are not always so drastic. The azomethine ylide 2-(2,4-dinitrophenyl)isoquinolinium-4-olate forms cycloadducts with *cis*-stilbene and with various heterodipolarophiles which could not



(84) endo or exo — 138°C

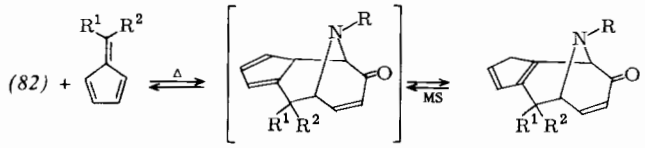
(85) — 130°C

(86) — 120°C

(87)

be isolated because they rapidly suffered 1,3-dipolar cycloreversion[156].

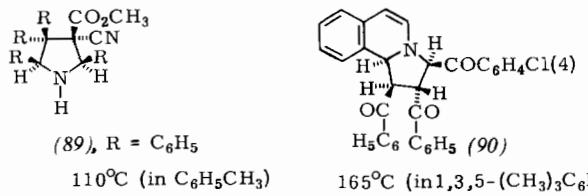
The cycloadducts *(88)* of fulvenes with the betaines *(82)* decompose in the mass spectrometer (MS) thus indicating a rare 1,3-dipolar cycloreversion following a 1,5-hydrogen shift[155].



(82) + (88)

$R^1 = R^2 = CH_3$
$R^1 = H,\ R^2 = 4\text{-}CH_3OC_6H_4$
$R^1 = H,\ R^2 = C_6H_5$

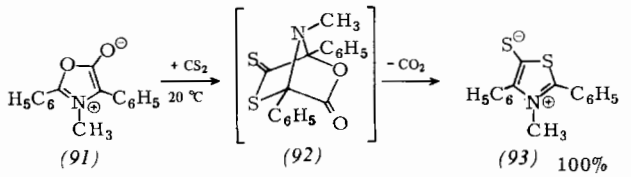
Compounds *(89)*[157] and *(90)*[158] are two examples of adducts of azomethine ylides whose 1,3-dipolar skeleton is not an integral part of an aromatic systems, for which thermal cycloreversion has been reported.



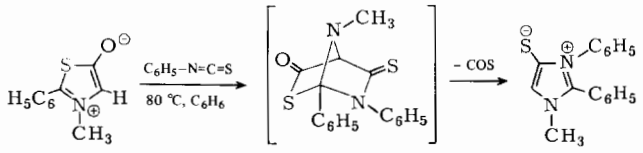
(89), R = C_6H_5 — 110°C (in $C_6H_5CH_3$)

(90) — 165°C (in 1,3,5-$(CH_3)_3C_6H_3$)

Particularly interesting is the easy synthesis of compounds *(93)*[159] and *(96)*[160] from the mesoionic oxazolone *(91)* and thiazolone *(94)*, respectively, *via* the nonisolable intermediates *(92)* and *(95)*. The intermediacy of compounds of type *(92)* (not yet isolated) has also been formulated for the reaction of *(91)* with C=C double bonds to give, on extrusion of CO_2, a new azomethine ylide system[1,2]. However, *(94)* reacts at room temperature with alkenes to give isolable adducts of type *(95)*. A great proclivity for COS extrusion on heating and on electron impact has expectedly been observed for these adducts[160].

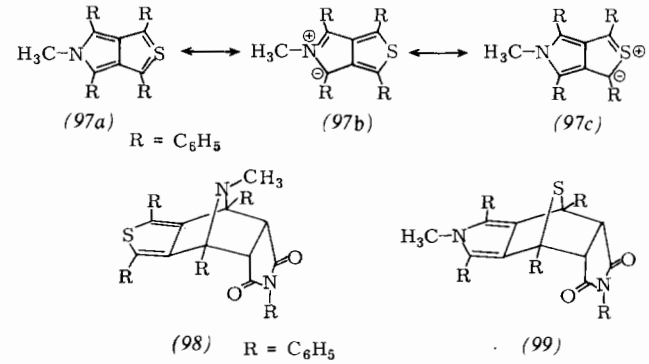


(91) (92) (93) 100%



(94) (95) (96), 64%

Using a semiempirical MO approach (CNDO/2) in which d orbital participation was included, *Cava et al.* have found that the contribution of *(97b)* to the structure of thieno[3,4-*c*]pyrrole *(97)* is of greater importance than that of *(97c)*[161]. It does not come as a surprise, therefore, that *Cava*[161] and *Potts*[162] have found thieno[3,4-*c*]pyrrole to add alkenes at the azomethine ylide system to give compounds such as *(98)*. However, on heating, these adducts revert to the addends which finally give the thermodynamically more stable thiocarbonyl ylide adducts of type *(99)*.



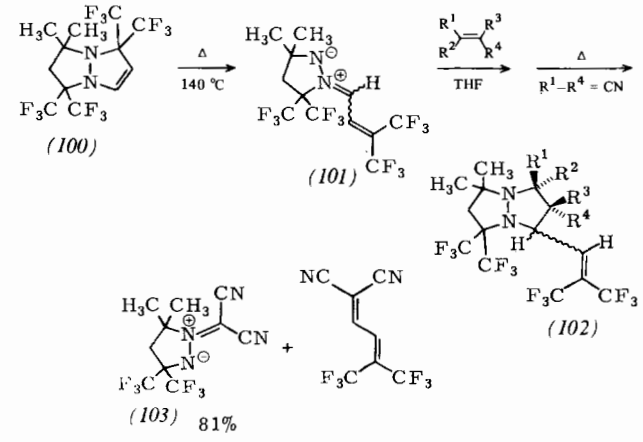
(97a) R = C_6H_5 (97b) (97c)

(98) R = C_6H_5 (99)

9. Azomethine Imines

The reaction of sydnones with alkenes represents a general synthesis of 2-pyrazolines[1,2]. The [3+2]-cycloadduct formed in the rate determining step spontaneously eliminates carbon dioxide by [3+2]-cycloreversion.

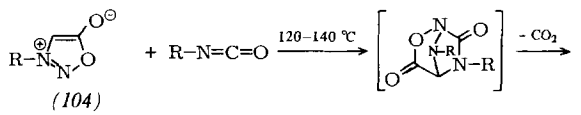
A case of 1,3-dipole metathesis has recently been described by *Burger et al.*[14]. The stable azomethine imine system *(101)* generated almost quantitatively from *(100)* gives [3+2]-cycloadducts *(102)* with numerous dipolarophiles. Those formed from *(101)* and dimethyl fumarate, dimethyl maleate, fumaronitrile, and ethenetetracarbonitrile in THF under reflux decompose particularly readily. *(102)*, R^1—R^4 = CN, transforms at ≈60 °C into a new stable azomethine imine *(103)* and 5,5,5-trifluoro-4-(trifluoromethyl)-1,3-pentadiene-1,1-dicarbonitrile.



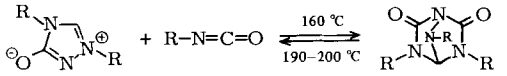
(100) (101) (102)

(103) 81%

Examples are known of equilibria between [3 + 2]-cycloadduct and 1,3-dipole + dipolarophile in which the dipolarophile is an heteromultiple bond. For instance, the 1,3-dipole *(104)* reacts with phenyl isocyanate to give the mesoionic triazolone *(105)*[163] which in the presence of an excess of phenyl isocyanate equilibrates with the cycloadduct *(106)*[164].

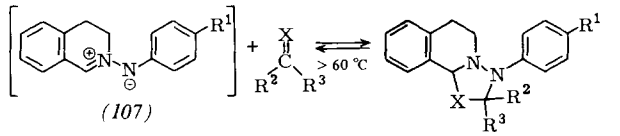


(104)

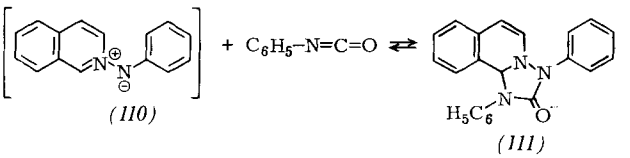


(105) R = C_6H_5 *(106)*

The thermolability of 1,3,4-oxadiazolidines *(108)*, particularly for $R^1 = NO_2$[165], and of 1,2,4-triazolidines *(109)*[166] and *(111)*[167] is easily detectable by reversible thermochromism on heating the substances in inert solvent.



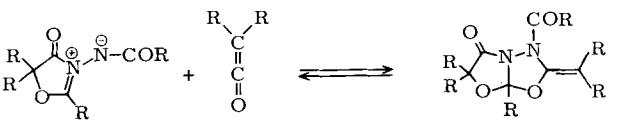
(107) *(108)*, X = O; *(109)*, X = N–CH_3



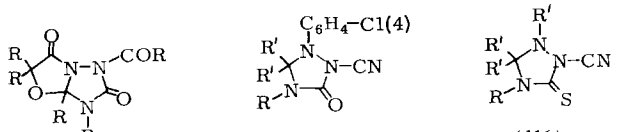
(110) *(111)*

In contrast to the isoquinolinio-*N*-anilide *(110)*, the 1,3-dipole *(107)* was trapped with phenyl isocyanate and isothiocyanate to give thermostable [3 + 2]-adducts[167].

The azomethine imine *(112)*, formed from dibenzoyldiazene and diphenylketene, reacts further with a second equivalent of the same diphenylketene to give the bicyclic compound *(113)* which is in equilibrium with the reactants at elevated temperature[168]. While compounds *(112)* reacts with phenyl isocyanate to give the stable [3 + 2]-adduct *(114)*[168] the 1,2,4-triazolidine-3-ones *(115)* and -3-thiones *(116)* are relatively unstable products, reverting to the reactants even in cold solution[169].

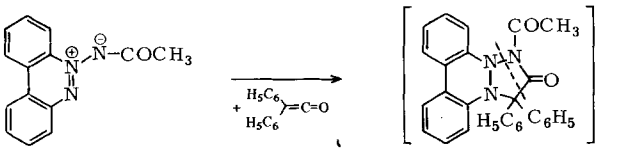


(112) *(113)*

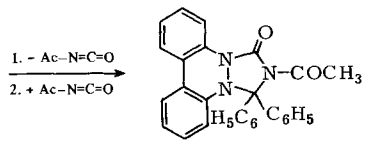


(114) R = C_6H_5, R' = Aryl *(115)* *(116)*

A cycloreversion is probably involved in the reaction of the azimines such as benzo[*c*]cinnolinio-*N*-acetylimide *(117)* with diphenylketene to give a complex mixture of compounds in which the 1:1 adduct *(119)* is formed in 12% yield[170]. According to the authors, adduct *(118)* is unstable by virtue of its three saturated adjacent nitrogen atoms.



(117) *(118)*



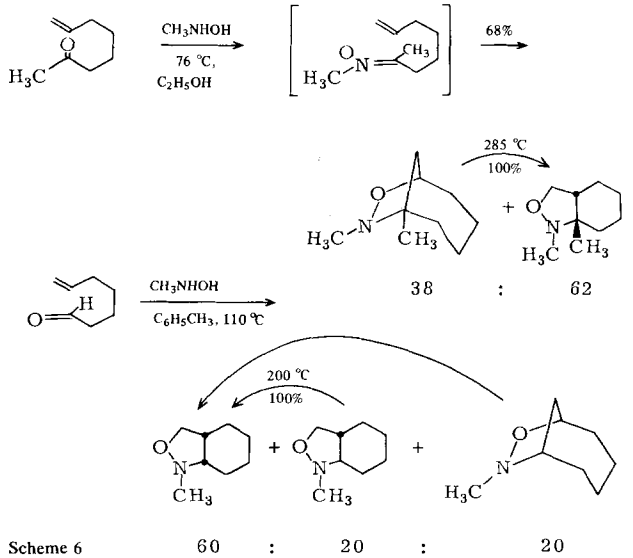
(119)

1,3-Dipolar cycloreversions have been also postulated in the reactions of some carbonyl ylides[171] or diazoalkanes[172] with azo derivatives.

An electron impact induced [4→3 + 1]-cycloreversion has been reported by *Deyrup* for 3-iminodiazetidines obtained from *(107)*, $R^1 = NO_2$, and *tert*-butyl isocyanide[173].

10. Nitrones (Azomethine Oxides)

Many isoxazolidines have been reported to undergo [3 + 2]-cycloreversion under mild reaction conditions. The reactions depicted in Scheme 6[174] represent typical examples of the occurrence of the dynamic equilibrium between polycyclic isoxazolidines and nitrone + alkene. Presumably, the easy [3 + 2]-cycloreversion found for these and similar systems is a consequence of the remarkable stability of nitrones.

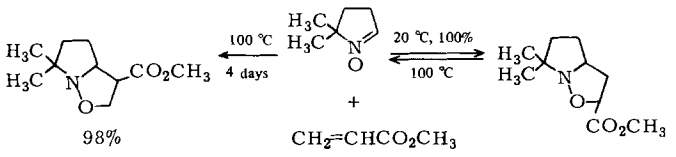


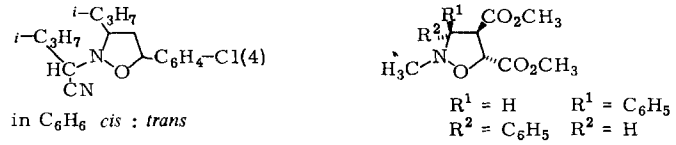
Scheme 6

As shown in Scheme 6, the correct choice of reaction conditions permits formation of a sole adduct. These reactions

are interesting examples of 1,3-dipolar reactions in which the stereochemical and regiochemical course can be controlled. The synthetic importance of these reactions has already been widely discussed elsewhere[8, 175].

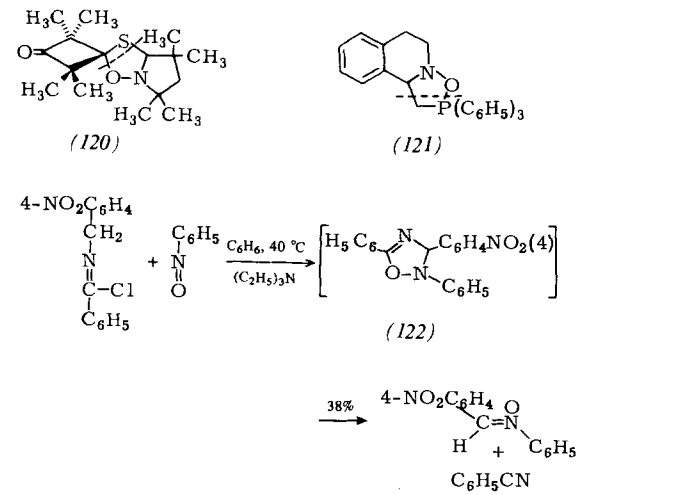
Even milder reaction conditions are required for [3+2]-cycloreversion of monocyclic isoxazolidines derived from nitrones and conjugated CC double bond systems[176–183] as exemplified in Scheme 7[176, 178, 180a].



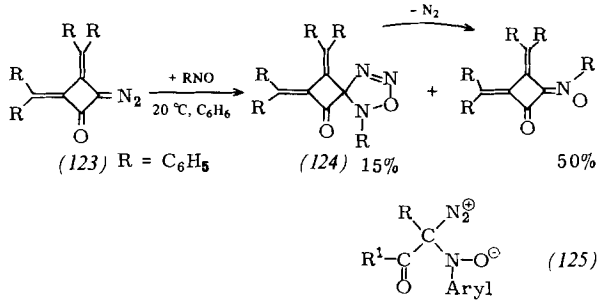


Scheme 7

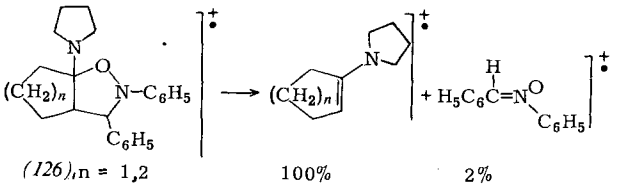
The rate-enhancing effect of carbonyl groups is evidenced by the adducts of 3,4-dihydroisoquinoline *N*-oxide with tricarbonyl(tropone)iron[41] and of *C*-benzoyl-*N*-phenylnitrone with α,β-unsaturated esters[55, 183] which both cyclorevert at room temperature. Of relevence in connection with the foregoing results is the fact that triphenylnitrone reacts with dimethyl maleate to give the corresponding isoxazolidine, whereas no adduct is obtainable with the more reactive dipolarophile dimethyl fumarate. In order to rationalize this observation, it has been suggested that, although the addends ⇌ adduct equilibrium is reached more easily with fumarate than in the addition with maleate, the equilibrium is nevertheless shifted mainly towards the reactants because of the greater thermodynamic stability of dimethyl fumarate[180a]. Cycloadducts of nitrones to heterodouble bonds also exhibit a great propensity to cycloreversion. Thus adduct *(120)* cycloreverts to the addends in solution at room temperature[184] and compound *(121)* requires a temperature of 100 °C to undergo cycloreversion[185], while the adduct *(122)* of a nitrile ylide and nitrosobenzene could not been even isolated[186].



Finally, the isolation of adduct *(124)* in the reaction of diazoketone *(123)* with nitrosobenzene is of interest[187]. This contradicts previously accepted mechanistic concepts invoking the zwitterionic intermediate *(125)*[188].

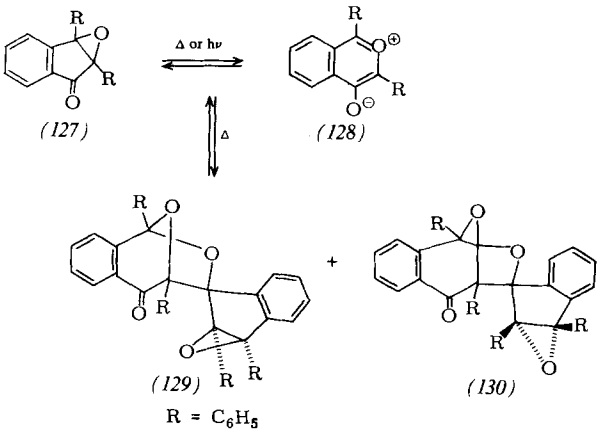


Electron bombardment also induces [3+2]-cycloreversion in isoxazolidines[189, 190]. The possibility of a prior thermal cycloreversion in the mass spectrometer has been ruled out by comparing the mass spectrum of the adducts *(126)* with those recorded for the related addends[189].



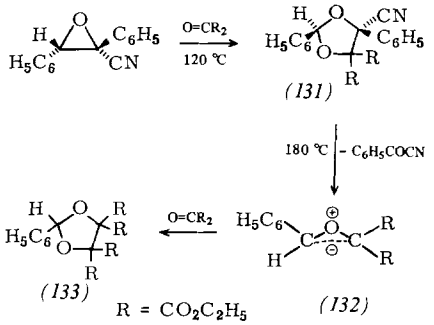
11. Carbonyl Ylides and Thiocarbonyl Ylides

2,3-Diphenylindenone oxide *(127)*, which is in thermal (symmetry-forbidden disrotatory process) and photochemical equilibrium with the red benzopyrylium olate *(128)*, is converted by heat into *(129)* and *(130)* in benzene or diethyl

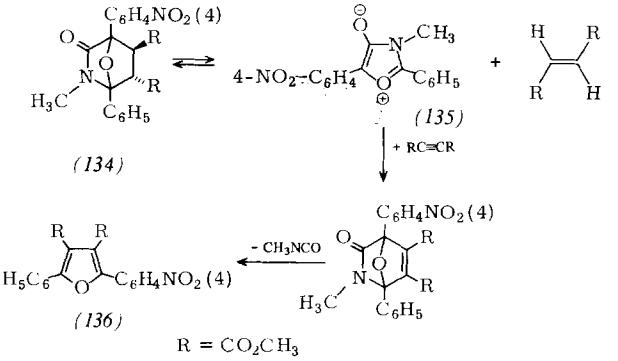


succinate as solvents. The two dimers undergo 1,3-dipolar cycloreversion, as proved by their thermochromism and by trapping *(128)* with dimethyl acetylenedicarboxylate[191]. The cycloadduct *(131)* obtained by heating a *trans*-stilbene oxide derivative with diethyl mesoxalate undergoes 1,3-dipolar cycloreversion to the carbonyl ylide *(132)* which adds afresh to diethyl mesoxalate to give *(133)*[192].

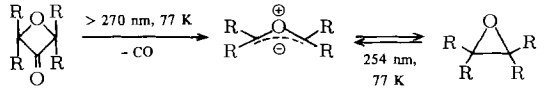
Hamaguchi and *Ibata* described trapping reactions of the thermally generated carbonyl ylide *(135)*; on heating to 200 °C in *o*-dichlorobenzene with a fivefold excess of dimethyl acetylenedicarboxylate the bicyclic compound *(134)*,



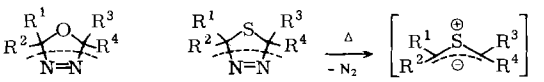
used as carbonyl ylide source, furnished the furan derivative *(136)* in quantitative yield together with large amounts of dimethyl fumarate[193].



Do-Minh et al. reported an interesting [4→3+1]-photofragmentation of the tetraphenyl oxetanone *(137)* into carbonyl ylide *(138)* and carbon monoxide[194].



While photolysis of Δ^3-1,3,4-oxadiazolines *(139)* gives rise to a complex fragmentation pattern[195], thermolysis of the same class of heterocycles represents a convenient source of carbonyl ylides[2, 10, 196].

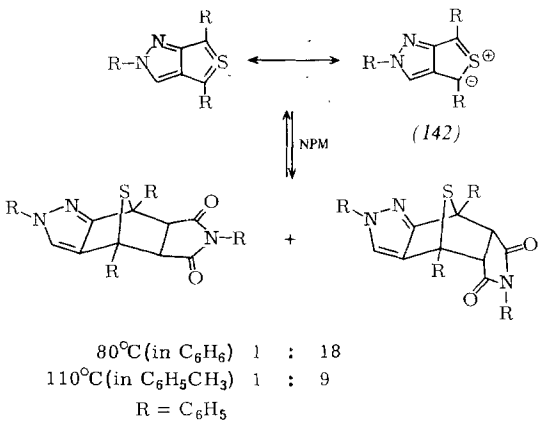


The thermal behavior of compounds *(140)* parallels that of compounds *(139)*. Temperatures in the range 40—100 °C suffice to generate the thiocarbonyl ylide *(141)* from *(140)*[2, 10]. Kinetic measurements of cycloreversion of few Δ^3-1,3,4-thiadiazolines permitted determination of the Arrhenius parameters; the enthalpy and entropy values were in the range 26.0—31.4 kcal mol^{-1} and 1.1—11.6 cal K^{-1} mol^{-1} respectively[197].

On irradiation, compounds *(140)* lose sulfur to give azines[198].

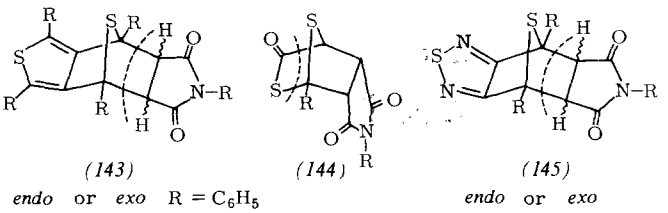
A dynamic equilibrium between adduct and addends is present in the reaction of the nonclassical thiophene system *(142)* with *N*-phenylmaleimide (NPM) (Scheme 8)[199].

Additional examples of systems undergoing [3+2]-cycloreversions to give thiocarbonyl ylides are *(143)*, *(144)*, and *(145)*; heating the polycyclic compound *(143)* to its melting



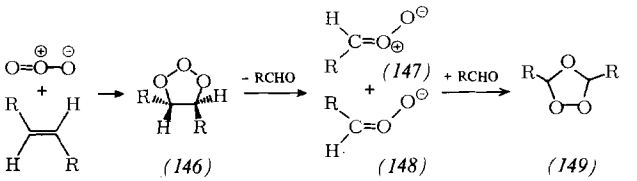
Scheme 8

point produces the addends[200], while the thermostable compounds *(144)*[201] and *(145)*[202] cyclorevert on electron bombardment.



12. Carbonyl Oxides and Ozone

The present consensus of opinion[203-209] is that liquid phase ozonolysis of olefins occurs exclusively according to the modified Criegee mechanism (Scheme 9).



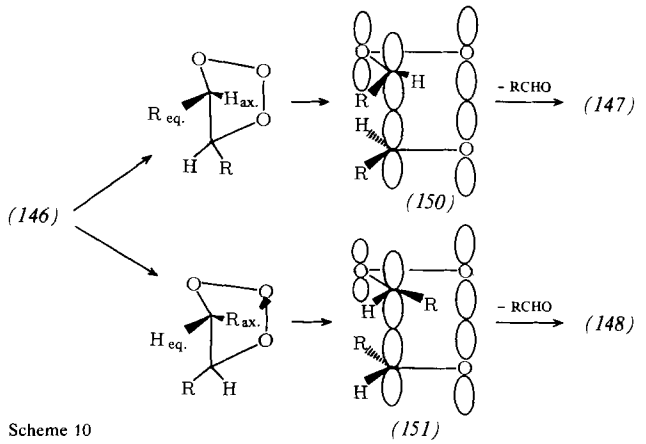
Scheme 9

Thus the final ozonides *(149)* are formed in a two-step exothermic process[210] with prior 1,3-dipolar cycloreversion of primary ozonides *(146)* to give a mixture of *anti*- *(147)* and *syn*-carbonyl oxides *(148)* and a carbonyl compound. In general, these spontaneous 1,3-dipolar cycloreversions take place at very low temperatures; for example, in the case of *trans*-3-hexene the 1,2,3-trioxolane *(146)* (R = CH_3) cycloreverts at −100 °C with $k = 5.4 \times 10^{-4}$ s^{-1}[211].

In addition, the kinetically formed carbonyl oxides *(147)* and *(148)* tend to equilibrate[204, 207]. This process is favored by temperature and solvent polarity but disfavored by π-complexing substances which stabilize carbonyl oxides and by high concentrations of added aldehydes which trap the kinetically formed *syn* and *anti* carbonyl oxides.

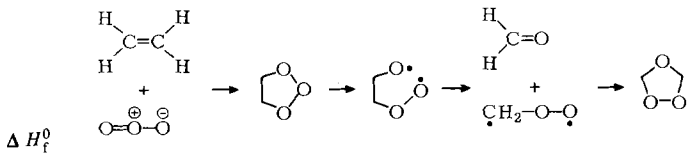
According to *Kuczkowski et al.*, the concerted cleavage of the 1,2,3-trioxolanes *(146)* should proceed *via* an envelope conformation of the molecule (Scheme 10)[212]. The substituent at the carbon atom destined to become part of the zwitterion can assume either an equatorial or an axial orienta-

tion, so as to give rise to final *anti- (147)* or *syn*-carbonyl oxide *(148)*, respectively. The energies involved in the two transition states *(150)* and *(151)* will be determined by the sum of interactions between substituents and lone pairs. This mechanism is supported by *ab initio* SCF MO calculations[213] from which $E_a = 11$ kcal mol^{-1} was estimated. This is in good agreement with the experimental values found for the cycloreversion of the primary ozonides of 1-hexene ($E_a = 7$ kcal mol^{-1})[214] and *trans*-3-hexene ($E_a = 8$ kcal mol^{-1})[211].



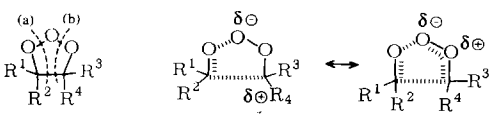
Scheme 10

By contrast, a nonconcerted cycloreversion has been proposed by *Goddard et al.*[215]. Calculated heats of formation (ΔH_f^0) are shown below the respective formulas[215].

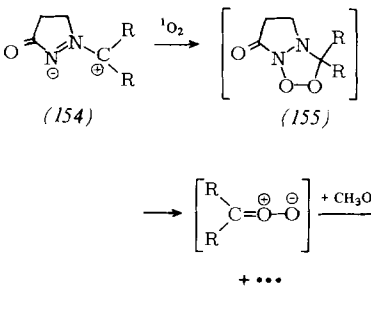


As suggested by the authors, the intermediate carbonyl oxide should possess a singlet diradical structure lying, according to generalized valence bond and configuration interaction calculations, at an energy level lower by 27 kcal mol^{-1} than that of the zwitterionic structure of the same carbonyl oxide. *Criegee*, however, contended that singlet diradical carbonyl oxide should attack methanol at a C–H bond instead of the experimentally found O–H bond[203]. A nonconcerted diradical pathway was also proposed for the cycloreversion of 1,2,3-trioxolanes in the gas phase[216].

Unsymmetrically substituted 1,2,3-trioxolanes *(152)* cyclorevert in solution according to pathways (a) and (b)[217]. The direction of cleavage was found to be unaffected by temperature and solvent polarity but greatly influenced by substituents; the dominant carbonyl oxide obtained is that whose substituents are most capable of stabilizing a partial positive charge [see transition state *(153)* for path (a)].

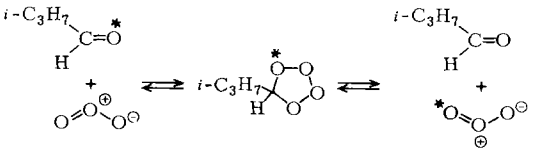


The short-lived 1,2,3,4-dioxadiazolidines *(155)*, the probable intermediates of cycloaddition of azomethine imines *(154)* and excited singlet oxygen, undergo spontaneous cycloreversion[218]. The carbonyl oxides are trapped by methanol as methoxyhydroperoxides or by acetaldehyde as [3+2]-cycloadducts.



Two [3+2]-cycloreversion pathways, *viz.* fragmentation to carbonyl compounds and carbonyl oxides and to oxygen and carbonyl ylides, are to be seen in the mass spectra of 1,3,4-trioxolanes, albeit with low intensity[219].

Klopman and *Joiner* found that ^{18}O-labeled isobutyraldehyde in contact with ozone loses its label readily even at −78 °C. In order to rationalize the result the authors proposed a reversible type of [3+2]-cycloaddition of ozone with a carbonyl compound[220].



13. Conclusion

The examples selected here should illustrate the generality of the reaction in confirming, at least in part, a 1972 statement anticipating "a future growth in the scope of the retro 1,3-dipolar reaction comparable with that which has taken place for the forward reaction ..."[58].

Recent techniques will serve to increase the scope of this field; we consider flash thermolysis to be particularly promising. In the future it is to be hoped that more attention will be paid to exploring the synthetic possibilities of [3+2]-cycloreversion, and that a better understanding of the remaining mechanistic questions will soon be reached.

We are indebted to all who have provided us with examples of 1,3-dipolar cycloreversions; we wish to thank especially Nicholas Dennis, Alan R. Katritzky, Rolf Huisgen, Paolo Grünanger, Robert Carrié, Richard M. Kellogg, Kevin T. Potts, and Antonio Selva. Our thanks are also due to Silvana Bellaviti for carefully typing the manuscript.

Received: March 7, 1978 [A 288 IE]
German version: Angew. Chem. *91*, 781 (1979)

[1] *R. Huisgen*, Angew. Chem. *75*, 604, 742 (1963); Angew. Chem. Int. Ed. Engl. *2*, 565, 633 (1963).
[2] *G. Bianchi, C. De Micheli, R. Gandolfi* in *S. Patai*: The Chemistry of Functional Groups. Suppl. A. Interscience, New York 1977, pp. 369ff.
[3] *J. Bastide, J. Hamelin, F. Texier, Y. V. Quang*, Bull. Soc. Chim. Fr. *1973*, 2555.
[4] *C. G. Stuckwisch*, Synthesis *1973*, 469.
[5] *T. Kauffmann*, Angew. Chem. *86*, 715 (1974); Angew. Chem. Int. Ed. Engl. *13*, 627 (1974).

[6] *D. St. C. Black, R. F. Crozier, V. C. Davis,* Synthesis *1975*, 205.
[7] *N. Dennis, A. R. Katritzky, Y. Takeuchi,* Angew. Chem. *88*, 41 (1976); Angew. Chem. Int. Ed. Engl. *15*, 1 (1976).
[8] *A. Padwa,* Angew. Chem. *88*, 131 (1976); Angew. Chem. Int. Ed. Engl. *15*, 123 (1976).
[9] *P. Gilgen, H. Heimgartner, H. Schmid,* Heterocycles *6*, 143 (1977).
[10] *R. M. Kellogg,* Tetrahedron *32*, 1 (1977).
[11] *Y. Takeuchi, F. Furusaki,* Adv. Heterocycl. Chem. *21*, 207 (1977).
[12] *R. Huisgen,* Angew. Chem. *80*, 329 (1968); Angew. Chem. Int. Ed. Engl. *7*, 321 (1968).
[13] *R. Huisgen,* J. Org. Chem. *41*, 403 (1976).
[14] *K. Burger, H. Schickaneder, C. Zettl,* Angew. Chem. *89*, 60 (1977); Angew. Chem. Int. Ed. Engl. *16*, 54 (1977).
[15] *S. Auricchio, G. Vidari, P. Vita Finzi,* Gazz. Chim. Ital. *106*, 1 (1976).
[16] *M. Regitz,* Angew. Chem. *79*, 786 (1967); Angew. Chem. Int. Ed. Engl. *6*, 733 (1967); Synthesis *1972*, 351.
[17] *R. N. Butler,* Adv. Heterocycl. Chem. *21*, 402 (1977).
[18] *G. W. Griffin,* Angew. Chem. *83*, 604 (1971); Angew. Chem. Int. Ed. Engl. *10*, 537 (1971); *C. Dietrich-Buchecker, M. Franck-Neumann,* Tetrahedron *33*, 745, 751 (1975).
[19] *D. J. Miller, T. E. Nemo, L. A. Hull,* J. Org. Chem. *40*, 2675 (1975).
[20] *R. B. Woodward, R. Hoffmann,* Angew. Chem. *81*, 797 (1969); Angew. Chem. Int. Ed. Engl. *8*, 781 (1969).
[21] *M. J. S. Dewar,* Angew. Chem. *83*, 859 (1971); Angew. Chem. Int. Ed. Engl. *10*, 761 (1971).
[22] *R. A. Firestone,* Tetrahedron *33*, 3009 (1977).
[23] *G. Leroy, M. Sana,* Tetrahedron *32*, 1379 (1976); *G. Leroy, M. T. Nguyen, M. Sana, ibid. 32*, 1529 (1976).
[24] *G. Leroy, M. Sana,* Tetrahedron *31*, 2091 (1975); *D. Poppinger,* J. Am. Chem. Soc. *97*, 7486 (1975); Aust. J. Chem. *29*, 465 (1976).
[25] *A. Padwa, S. I. Wetmore, Jr.,* J. Am. Chem. Soc. *96*, 2414 (1974).
[26] *D. H. White, P. B. Condit, R. G. Bergman,* J. Am. Chem. Soc. *94*, 1348 (1972); see also *M. E. Hendrick, M. Jones,* Tetrahedron Lett. *1978*, 4249.
[27] *R. Moore, A. Mishra, R. J. Crawford,* Can. J. Chem. *46*, 3305 (1968); *G. L. Loper, F. H. Dorer,* J. Am. Chem. Soc. *95*, 20 (1973).
[28] *Th. S. Cantrell, W. S. Haller,* Chem. Commun. *1968*, 977.
[29] *Y. Ito, T. Matsuura,* Tetrahedron *31*, 1373 (1975).
[30] *D. F. Eaton, R. G. Bergman, G. S. Hammond,* J. Am. Chem. Soc. *94*, 1351 (1972).
[31] *Th. V. Von Auken, K. L. Rinehart,* J. Am. Chem. Soc. *84*, 3736 (1962).
[32] *D. E. McGreer, W. S. Wu,* Can. J. Chem. *45*, 461 (1967).
[33] *K. Burger, J. Albanbauer, F. Manz,* Chem. Ber. *107*, 1823 (1974).
[34] *J. S. Clovis, A. Eckell, R. Huisgen, R. Sustmann,* Chem. Ber. *100*, 60 (1967).
[35] *P. G. Gassman, W. J. Greenlee,* J. Am. Chem. Soc. *95*, 980 (1973).
[36] *M. R. Johnson, L. R. Sousa,* J. Org. Chem. *42*, 2439 (1977).
[37] *M. J. S. Dewar, R. C. Dougherty:* The PMO Theory of Organic Chemistry. Plenum-Rosetta 1975, pp. 431 ff., 452 ff.
[38] *J. Michl* in *G. Klopman:* Chemical Reactivity and Reaction Paths. Wiley, New York 1974, pp. 301 ff.
[39] *E. F. Ullmann,* Acc. Chem. Res. *1*, 353 (1968).
[40] *G. D. Andrews, J. E. Baldwin,* J. Am. Chem. Soc. *99*, 4853 (1977).
[41] *C. De Micheli, R. Gandolfi, L. Toma,* Heterocycles *12*, 5 (1979).
[42] a) *A. Selva, L. F. Zerilli, B. Cavalleri, G. G. Gallo,* Org. Mass Spectrom. *6*, 1347 (1972); b) *A. Selva, P. Traldi, L. F. Zerilli, B. Cavalleri, G. G. Gallo,* Ann. Chim. (Roma) *64*, 229 (1974); c) *A. Selva, P. Traldi, L. F. Zerilli, G. G. Gallo,* Org. Mass Spectrom. *11*, 217 (1976); d) Ann. Chim. (Roma), *67*, 371 (1977); e) *A. Selva, L. F. Zerilli, B. Cavalleri, G. G. Gallo,* Org. Mass Spectrom. *9*, 558 (1974); f) *A. Selva, P. Traldi, E. Fantucci,* Adv. Mass Spectrom. *7B*, 1204 (1978).
[43] *G. F. Bettinetti, S. Facchetti,* Org. Mass Spectrom. *9*, 753 (1974).
[44] *A. Selva, A. Citterio, E. Pella, R. Tonani,* Org. Mass. Spectrom. *9*, 1017 (1974).
[45] *S. W. Staley* in *A. P. Marchand, R. E. Lehr:* Pericyclic Reactions. Vol. 1. Academic Press, New York 1977, pp. 254 ff.
[46] *R. L. Letsinger, D. F. Pollart,* J. Am. Chem. Soc. *78*, 6079 (1956).
[47] *R. B. Bates, L. M. Kroposki, D. E. Potter,* J. Org. Chem. *37*, 560 (1972).
[48] *P. Tomboulian, D. Amick, S. Beare, K. Dumke, D. Hart, R. Hites, A. Metzger, R. Nowak,* J. Org. Chem. *38*, 322 (1973).
[49] *P. Eberhard, R. Huisgen,* J. Am. Chem. Soc. *94*, 1345 (1972); see [13], pp. 403, 404.
[50] *J. N. Hines, M. Peagram, E. J. Thomas, G. H. Whitham,* J. Chem. Soc. Perkin Trans. I *1973*, 2332.
[51] *G. H. Whitham, M. Wright,* J. Chem. Soc. *C 1971*, 886.
[52] *M. Jones, P. Temple, E. J. Thomas, G. H. Whitham,* J. Chem. Soc. Perkin Trans. I *1974*, 433.
[53] *G. Bianchi, A. Gamba, R. Gandolfi,* J. Chem. Soc. Perkin Trans. I *1974*, 1757.
[54] *G. Bianchi, R. Gandolfi,* unpublished.
[55] *M. Joucla, J. Hamelin, R. Carrié,* Tetrahedron *30*, 1121 (1974).
[56] *K. Burger, E. Burgis,* Justus Liebigs Ann. Chem. *741*, 39 (1970).
[57] *G. Wittig, W. Tochtermann,* Chem. Ber. *94*, 1692 (1961); *F. Weygand, H. Daniel, ibid. 94*, 1688 (1961).
[58] *T. L. Gilchrist, R. C. Storr:* Organic Reactions and Orbital Symmetry. Cambridge University Press, Cambridge 1972, p. 123.
[59] *E. J. Corey, R. A. E. Winter,* J. Am. Chem. Soc. *85*, 2677 (1963); *E. J. Corey, F. A. Carey, R. A. E. Winter, ibid. 87*, 934 (1965).
[60] *A. Alemagna, T. Bacchetti, C. Rizzi,* Gazz. Chim. Ital. *102*, 311 (1972).
[61] *D. Hoppe,* Angew. Chem. *86*, 878 (1974); Angew. Chem. Int. Ed. Engl. *13*, 789 (1974).
[62] *U. Schöllkopf, I. Hoppe,* Angew. Chem. *87*, 814 (1975); Angew. Chem. Int. Ed. Engl. *14*, 765 (1975).
[63] *J. Kalvoda, H. Kaufmann,* J. Chem. Soc. Chem. Commun. *1976*, 209.
[64] *W. Sieber, P. Gilgen, S. Chaloupka, H. J. Hansen, H. Schmid,* Helv. Chim. Acta *56*, 1679 (1973).
[65] *N. Gakis, M. Marky, H. J. Hansen, H. Heimgartner, H. Schmid, W. E. Oberanski,* Helv. Chim. Acta *59*, 2149 (1976).
[66] *W. Steglich, P. Gruber, H. V. Heininger, F. Kneidl,* Chem. Ber. *104*, 3816 (1971).
[67] *G. Höfle, W. Steglich,* Chem. Ber. *104*, 1408 (1971).
[68] *P. Grüber, L. Müller, W. Steglich,* Chem. Ber. *106*, 2863 (1973).
[69] *W. Steglich, B. Kübel, P. Grüber,* Chem. Ber. *106*, 2870 (1973).
[70] *J. Llinares, E. J. Vincent, G. Salmona,* Org. Mass Spectrom. *11*, 873 (1976).
[71] *S. Y. Hong, J. E. Baldwin,* Tetrahedron *24*, 3787 (1968).
[72] *R. Huisgen, R. Grashey, M. Seidl, G. Wallbillich, H. Knupfer, R. Schmidt,* Justus Liebigs Ann. Chem. *653*, 105 (1962); see [1], pp. 608 and 570.
[73] *H. Meier, H. Heimgartner,* Helv. Chim. Acta *60*, 3035 (1977).
[74] *P. Scheiner,* J. Org. Chem. *34*, 199 (1969); *P. Scheiner, J. F. Dinda, Jr.,* Tetrahedron *26*, 2619 (1970); *C. S. Angadiyayar, M. V. George,* J. Org. Chem. *36*, 1589 (1971).
[75] *L. Birkofer, A. Ritter, P. Richter,* Chem. Ber. *96*, 2750 (1963).
[76] *T. L. Gilchrist, G. E. Gymar, C. W. Rees,* J. Chem. Soc. Perkin Trans. I *1975*, 1747.
[77] *J. H. Markgraf, S. H. Brown, M. W. Kaplinsky, R. G. Peterson,* J. Org. Chem. *29*, 2629 (1964); *R. Huisgen, J. Sauer, M. Seidel,* Justus Liebigs Ann. Chem. *654*, 146 (1962).
[78] *R. Huisgen,* Angew. Chem. *72*, 359 (1960); *M. Seidel,* Dissertation, Universität München 1960.
[79] *R. Huisgen, J. Sauer, M. Seidel,* Chem. Ber. *94*, 2503 (1961); *R. Huisgen, M. Seidel, ibid. 94*, 2509 (1961).
[80] *R. R. Fraser, Guruduta, K. E. Hague,* J. Org. Chem. *34*, 4118 (1969).
[81] *Ch. Grundmann, K. Flory,* Justus Liebigs Ann. Chem. *721*, 91 (1969).
[82] *W. Reichen,* Helv. Chim. Acta *59*, 1636 (1976); *C. Wentrup, A. Damerius, W. Reichen,* J. Org. Chem. *43*, 2037 (1978).
[83] *J. Sauer, K. K. Mayer,* Tetrahedron Lett. *1968*, 325.
[84] *M. Freund, B. B. Goldsmith,* Ber. Dtsch. Chem. Ges. *21*, 2456 (1888).
[85] *H. Reimlinger, J. J. M. Vandewalle, G. S. D. King, W. R. F. Lingier, R. Merényi,* Chem. Ber. *103*, 1918 (1970).
[86] *G. Szeimies, K. Mannhardt, W. Mickler,* Chem. Ber. *110*, 2922 (1977).
[87] *A. Könnecke, E. Lippmann,* Org. Mass Spectrom. *11*, 167 (1976).
[88] *P. Wolkoff, S. Hammerum,* Org. Mass Spectrom. *9*, 181 (1974).
[89] *S. Hammerum, P. Wolkoff,* J. Org. Chem. *37*, 3965 (1972).
[90] *J. L. Aubagnac, D. Bourgeon, R. Jacquier,* Bull. Soc. Chim. Fr. *1976*, 867.
[91] *S. Gabriel, M. Koppe,* Ber. Dtsch. Chem. Ges. *19*, 1145 (1886).
[92] *K. Auwers, V. Meyer,* Ber. Dtsch. Chem. Ges. *21*, 784 (1888); *22*, 705 (1889).
[93] *F. D. Dodge,* Justus Liebigs Ann. Chem. *264*, 178 (1890).
[94] *J. Ackrell, M. Altaf-ur-Rahman, A. J. Boulton, R. C. Brown,* J. Chem. Soc. Perkin Trans. I *1972*, 1587.
[95] *J. Chapman, J. Crosby, C. A. Cummings, R. A. C. Rennie,* J. Chem. Soc. Chem. Commun. *1976*, 240.
[96] a) *C. Grundmann, P. Grünanger:* The Nitrile Oxides. Springer, Berlin 1971; b) *W. R. Mitchell, R. M. Paton,* Tetrahedron Lett. *1979*, 2443; c) *M. Marky, H. Meier, A. Wunderli, H. Heimgartner, H. Schmid, H. J. Hansen,* Helv. Chim. Acta *61*, 1477 (1978).
[97] *A. Dondoni, G. Barbaro, A. Battaglia, P. Giorgianni,* J. Org. Chem. *37*, 3196 (1972).
[98] *D. N. Reinhoudt, C. G. Kouwenhoven,* Recl. Trav. Chim. Pays-Bas *95*, 67 (1976).
[99] *J. Sauer, K. K. Mayer,* Tetrahedron Lett. *1968*, 319; *G. Trickes, H. Meier,* Angew. Chem. *89*, 562 (1977); Angew. Chem. Int. Ed. Engl. *16*, 555 (1977).
[100] *J. E. Franz, H. K. Pearl,* J. Org. Chem. *41*, 1296 (1976).
[101] *T. Mukai, T. Oine, A. Matsubara,* Bull. Chem. Soc. Jpn. *42*, 581 (1969).
[102] *W. Heinzelmann, P. Gilgen,* Helv. Chim. Acta *59*, 2727 (1976), references cited therein.
[103] *I. Yavari, S. Esfandiari, A. J. Mostashari, P. W. W. Hunter,* J. Org. Chem. *40*, 2880 (1975).
[104] *G. L. Aldous, J. H. Bowie,* Org. Mass Spectrom. *10*, 64 (1975).
[105] *S. Facchetti, G. F. Bettinetti,* Ann. Chim. (Roma) *64*, 131 (1974), references cited therein; *C. De Micheli, R. Gandolfi, P. Grünanger,* Tetrahedron *30*, 3765 (1974).
[106] a) *A. Selva, P. Traldi,* Ann. Chim. (Roma) *66*, 57 (1976); b) *B. F. Bonini, G. Maccaguani, G. Mazzanti, L. Thijs, H. P. M. M. Ambrosius, B. Zwanenburg,* J. Chem. Soc. Perkin Trans. I *1977*, 1468.

[107] *S. Morrocchi, A. Ricca, A. Selva, A. Zanarotti,* Gazz. Chim. Ital. *99*, 165 (1969); *C. Grundmann, H. D. Frommeld, K. Flory, S. K. Dotto,* J. Org. Chem. *33*, 1464 (1968); *A. J. Boulton, P. Hadjimihalakis, A. R. Katritzky, A. Majid Hamid,* J. Chem. Soc. *C 1969*, 1900; *H. E. Ungnade, E. D. Loughran,* J. Heterocycl. Chem. *1964*, 61.

[108] a) *C. L. Pedersen, J. Møller,* Acta Chem. Scand. *29*, 483 (1975); b) *R. Kroft, P. Henklein, G. Etzold, H. J. Zöpfl,* Org. Mass Spectrom. *11*, 304 (1976); c) *F. Razmona, E. S. Waight,* Org. Mass Spectrom. *11*, 1227 (1976).

[109] *R. K. Howe, J. E. Franz,* J. Chem. Soc. Chem. Commun. *1973*, 524; J. Org. Chem. *39*, 962 (1974); *J. E. Franz, R. K. Howe, H. K. Pearl, ibid. 41*, 620 (1976); *R. K. Howe, T. A. Gruner, J. E. Franz, ibid. 42*, 1813 (1977).

[110] *A. Holm, N. Harrit, N. N. Toubro,* J. Am. Chem. Soc. *97*, 6197 (1975).

[111] *A. H. Miller, R. Pancirov,* J. Heterocycl. Chem. *1971*, 163; *Ch. P. Joshua, K. N. Rajasekharan,* Aust. J. Chem. *30*, 563 (1977).

[112] *T. Naito,* Tetrahedron *24*, 6237 (1968); *B. J. Millard,* J. Chem. Soc. *C 1969*, 1231.

[113] *C. L. Pedersen, N. Hacker,* Tetrahedron Lett. *1977*, 3981.

[114] *C. L. Pedersen,* Acta Chem. Scand. *B 30*, 675 (1976).

[115] *P. Scheiner* in *B. S. Thyagarajan:* Selective Organic Transformations. Vol. 1. Interscience, New York 1970, pp. 327 ff.

[116] *F. Texier, J. Bourgois,* J. Heterocycl. Chem. *1975*, 505.

[117] *J. Bourgois, F. Tonnard, F. Texier,* Bull. Soc. Chim. Fr. *1976*, 2025.

[118] *D. Pocar, M. C. Ripamonti, R. Stradi, P. Trimarco,* J. Heterocycl. Chem. *14*, 173 (1977).

[119] *Y. M. Saunier, R. Danion-Bougot, D. Danion, R. Carrié,* Tetrahedron *32*, 1995 (1976); *R. Carrié,* personal communication.

[120] *A. Gagneux, S. Winstein, W. G. Young,* J. Am. Chem. Soc. *82*, 5956 (1960).

[121] *A. L. Logothetis,* J. Org. Chem. *29*, 3049 (1964); *V. Nair,* J. Org. Chem. *33*, 2121 (1968); *J. H. Bowie, B. Nussey, A. D. Ward,* Aust. J. Chem. *26*, 2547 (1973); see also *P. W. Manley, R. Somanathan, D. L. R. Reeves, R. C. Storr,* J. Chem. Soc. Chem. Commun. *1978*, 396.

[122] *R. Huisgen, R. Sustmann, K. Bunge,* Chem. Ber. *105*, 1324 (1972).

[123] *J. M. Vandensavel, G. Smets, G. L'abbé,* J. Org. Chem. *38*, 675 (1973); *G. L'abbé,* Bull. Soc. Chim. Fr. *1975*, 1127.

[124] *H. Suschitzky, R. E. Walrond, R. Hull,* J. Chem. Soc. Perkin Trans. I *1977*, 47.

[125] *T. Isida, T. Akiyama, N. Mihara, S. Kozima, K. Sisido,* Bull. Chem. Soc. Jpn. *46*, 1250 (1973).

[126] *D. Denecker, G. Smets, G. L'abbé,* Tetrahedron *31*, 765 (1975).

[127] *V. A. Antonova, R. Borsdorf, R. Herzschuh, G. Fischer, H. Engelmann,* J. Prakt. Chem. *315*, 313 (1973); *N. W. Rokke, J. J. Worman, W. S. Wadsworth,* J. Heterocycl. Chem. *1975*, 1031.

[128] *M. Franck-Neumann, C. Buchecker,* Tetrahedron Lett. *1969*, 2659.

[129] *R. Breslow, M. Oda,* J. Am. Chem. Soc. *94*, 4787 (1972).

[130] *T. Eicher, E. V. Angerer,* Chem. Ber. *103*, 339 (1970); *R. Scott-Pyron, W. M. Jones,* J. Org. Chem. *32*, 4048 (1967).

[131] *L. A. Carpino, L. V. McAdams III, R. H. Rynbrandt, J. W. Spiewak,* J. Am. Chem. Soc. *93*, 476 (1971).

[132] a) *D. H. Aue, G. S. Helwig,* Tetrahedron Lett. *1974*, 721; b) *L. G. Zaitseva, I. B. Avezov, O. A. Subbotin, I. G. Bolesov,* J. Org. Chem. USSR *11*, 1400 (1975); c) *W. Welter, M. Regitz,* Tetrahedron Lett. *1976*, 1473; d) *D. H. Aue, R. B. Lorens, G. S. Helwig,* J. Org. Chem. *44*, 1202 (1979); e) *M. Regitz, W. Welter, A. Hartmann,* Chem. Ber. *112*, 2509 (1979).

[133] *M. Schneider, B. Csacsko,* Angew. Chem. *89*, 905 (1977); Angew. Chem. Int. Ed. Engl. *16*, 867 (1977).

[134] For further examples, see: *T. H. Kinstle, R. L. Welch, R. W. Exley,* J. Am. Chem. Soc. *89*, 3660 (1967); *M. Franck-Neumann,* Tetrahedron Lett. *1968*, 2979.

[135] *R. A. Keppel, R. G. Bergman,* J. Am. Chem. Soc. *94*, 1350 (1972).

[136] *M. P. Schneider, R. J. Crawford,* Can. J. Chem. *48*, 628 (1970); *P. D. Condit, R. G. Bergman,* Chem. Commun. *1971*, 4; *G. Greiner, M. Schneider, H. Rau,* Tetrahedron Lett. *49*, 4507 (1976).

[137] *R. J. Crawford, A. Mishra,* J. Am. Chem. Soc. *88*, 3963 (1966); *A. E. Brook, P. F. Jones,* Can. J. Chem. *49*, 1841 (1971).

[138] *S. L. Buchwalter, G. L. Closs,* J. Org. Chem. *17*, 2549 (1975); cf., however, *M. Schneider, A. Strohacker,* Tetrahedron *32*, 619 (1976).

[139] *W. R. Carpenter, A. Haymaker, D. W. Moore,* J. Org. Chem. *31*, 789 (1966).

[140] *D. Pocar, R. Stradi,* Ann. Chim. (Roma) *61*, 161 (1971); *D. Pocar, P. Trimarco,* J. Chem. Soc. Perkin Trans. *1976*, 622; *P. Dalla Croce, R. Stradi,* Tetrahedron *33*, 865 (1977), references cited therein.

[141] *J. Kucera, Z. Janousek, Z. Arnold,* Collect. Czech. Chem. Commun. *35*, 3618 (1970).

[142] *L. A. Paquette, H. C. Berk, C. R. Degenhardt, G. D. Ewing,* J. Am. Chem. Soc. 99, 4764 (1977).

[143] a) *K. D. Berlin, M. A. R. Khayat,* Tetrahedron *22*, (1966); b) *R. Gompper, J. Schelbe, C. S. Schneider,* Tetrahedron Lett. *1978*, 3897; c) *R. W. Hoffmann, U. Bressel, J. Gelhaus, H. Hauser, G. Mühl,* Chem. Ber. *104*, 2611 (1971); d) *A. H. Jackson, S. A. Matlin, A. H. Rees, R. Towill,* J. Chem. Soc. Chem. Commun. *1978*, 646.

[144] *A. C. Oehlschlager, L. H. Zalkow,* Can. J. Chem. *47*, 461 (1969); *R. L. Hale, L. H. Zalkow,* Tetrahedron *25*, 1393 (1969); *L. H. Zalkow, R. H. Hill, ibid. 31*, 831 (1975).

[145] *F. S. Bridson-Jones, G. D. Buckley, L. H. Cross, A. P. Driver,* J. Chem. Soc. *1951*, 2999; *F. S. Bridson-Jones, G. D. Buckley, ibid. 1951*, 3009.

[146] *H. K. Reimlinger, L. Skattebol,* Chem. Ber. *94*, 2429 (1961).

[147] *C. J. Micheida,* Tetrahedron Lett. *1968*, 2281; *R. M. Kellogg* in *O. Buchardt:* Photochemistry of Heterocyclic Compounds. Wiley, New York 1976, pp. 385, 386.

[148] *S. L. Lee, A. M. Cameron, J. Warkentin,* Can. J. Chem. *50*, 2326 (1972); *H. Meier, K. P. Zeller,* Angew. Chem. *89*, 876 (1977); Angew. Chem. Int. Ed. Engl. *16*, 835 (1977).

[149] *L. Thijs, A. Wagenaar, E. M. M. Van Rens, B. Zwanenburg,* Tetrahedron Lett. *1973*, 3589; *B. F. Bonini, G. Maccagnani, A. Wagenaar, L. Thijs, B. Zwanenburg,* J. Chem. Soc. Perkin Trans. I *1972*, 2490; *C. G. Venier, C. G. Gibbs,* Tetrahedron Lett. *1972*, 2293.

[150] *Th. G. Back, D. H. R. Barton, M. R. Britten-Kelly, F. S. Guziec, Jr.,* J. Chem. Soc. Perkin Trans. I *1976*, 2079.

[151] *P. Ykman, G. L'abbé, G. Smets,* Tetrahedron *29*, 195 (1973), references cited therein.

[152] *N. Dennis, B. Ibrahim, A. R. Katritzky,* Org. Mass. Spectrom. *11*, 814 (1976).

[153] *J. Banerji, N. Dennis, J. Franck, A. R. Katritzky, T. Matsuo,* J. Chem. Soc. Perkin Trans. I *1976*, 2334.

[154] *T. Sasaki, K. Kanematsu, K. Hayakawa, M. Uchide,* J. Chem. Soc. Perkin Trans. I *1972*, 2750.

[155] *N. Dennis, B. Ibrahim, A. R. Katritzky,* J. Chem. Soc. Perkin Trans. I *1976*, 2307.

[156] *N. Dennis, A. R. Katritzky, S. K. Parton,* Chem. Pharm. Bull. Jpn. *23*, 2899 (1975).

[157] *S. Sinbandhit, J. Hamelin,* J. Chem. Soc. Chem. Commun. *1977*, 768.

[158] *B. E. Landberg, J. W. Lown,* J. Chem. Soc. Perkin Trans. I *1975*, 1326.

[159] *E. Funke, R. Huisgen, F. C. Schaefer,* Chem. Ber. *104*, 1550 (1971).

[160] *K. T. Potts, J. Baum, E. Houghton, D. N. Roy, U. P. Singh,* J. Org. Chem. *39*, 3619 (1974).

[161] *M. P. Cava, M. A. Sprecker, W. R. Hall,* J. Am. Chem. Soc. *96*, 1817 (1974).

[162] *K. T. Potts, D. McKeough,* J. Am. Chem. Soc. *95*, 2749 (1973); *96*, 4268 (1974).

[163] *H. Kato, S. Sato, M. Ohta,* Tetrahedron Lett. *1967*, 4261.

[164] *H. Kato, T. Shiba, E. Kitajima, T. Kiyosawa, F. Yamada, T. Nishiyama,* J. Chem. Soc. Perkin Trans. I *1976*, 863.

[165] *R. Grashey, K. Adelsberger,* Angew. Chem. *74*, 292 (1962); Angew. Chem. Int. Ed. Engl. *1*, 267 (1962).

[166] *R. Grashey, H. Leitermann, R. Schmidt, K. Adelsberger,* Angew. Chem. *74*, 491 (1962); Angew. Chem. Int. Ed. Engl. *1*, 406 (1962).

[167] Cf. [1], pp. 584, 585.

[168] *J. Markert, E. Fahr,* Tetrahedron Lett. *1970*, 769.

[169] *A. Eckell, R. Huisgen,* Chem. Ber. *110*, 571 (1977).

[170] *S. H. Alsop, J. J. Barr, R. C. Storr, A. Forbes Cameron, A. A. Freer,* J. Chem. Soc. Chem. Commun. *1976*, 888.

[171] *H. Hamberger, R. Huisgen, V. Markowski, S. Sustmann,* Heterocycles *5*, 147 (1976).

[172] *G. F. Bettinetti, L. Capretti,* Gazz. Chim. Ital. *95*, 33 (1965); *R. A. Izydore, S. McLean,* J. Am. Chem. Soc. *97*, 5611 (1975); cf., however, *R. Huisgen, R. Fleischmann, A. Eckell,* Chem. Ber. *110*, 500 (1977).

[173] *J. A. Deyrup,* Tetrahedron Lett. *1971*, 2191.

[174] *N. A. Le Bel, E. G. Banucci,* J. Org. Chem. *36*, 2440 (1971).

[175] *W. Oppolzer,* Angew. Chem. *89*, 10 (1977); Angew. Chem. Int. Ed. Engl. *16*, 10 (1977).

[176] *M. Masui, K. Suda, M. Yamauchi, C. Yijima,* Chem. Pharm. Bull. *21*, 1605 (1973).

[177] *R. Huisgen, H. Hauck, R. Grashey, H. Seidl,* Chem. Ber. *101*, 2568 (1968).

[178] *G. R. Delpierre, H. Lamchen,* J. Chem. Soc. *1963*, 4693.

[179] *C. Belzécki, I. Panfil,* J. Chem. Soc. Chem. Commun. *1977*, 303.

[180] a) *R. Huisgen, H. Hauck, R. Grashey, H. Seidl,* Chem. Ber. *102*, 736 (1969); b) *J. J. Tufariello, G. B. Mullen,* J. Am. Chem. Soc. *100*, 3638 (1968).

[181] *M. Lamchen, T. W. Mittag,* J. Chem. Soc. *C 1968*, 1917.

[182] *C. W. Brown, K. Marsden, M. A. T. Rogers, C. M. B. Taylor, R. Wright,* Proc. Chem. Soc. (London) *1960*, 254.

[183] *M. Joucla, J. Hamelin, R. Carrié,* Bull. Soc. Chim. Fr. *1973*, 3116.

[184] *D. St. C. Black, K. G. Watson,* Aust. J. Chem. *26*, 2491 (1973).

[185] *R. Huisgen, J. Wulff,* Chem. Ber. *102*, 746 (1969).

[186] *K. Bunge, R. Huisgen, R. Raab, H. J. Sturm,* J. Chem. Ber. *105*, 1307 (1972).

[187] *K. Ueda, M. Igaki, F. Toda,* Bull. Chem. Soc. Jpn. *49*, 3173 (1976).

[188] *O. Tsuge, I. Shinkai, M. Koga,* Org. Prep. Proced. Int. *4*, 169 (1972).

[189] *Y. Nomura, F. Furusaki, Y. Takeuchi,* J. Org. Chem. *37*, 502 (1972).

[190] *N. Singh, K. Krishan,* Indian J. Chem. *11*, 1076 (1973).

[191] *E. F. Ullman, J. E. Milks,* J. Am. Chem. Soc. *86*, 3814 (1964).

[192] *R. Huisgen, S. Sustmann,* Heterocycles *5*, 141 (1976).

[193] *M. Hamaguchi, T. Ibata,* Chem. Lett. *1975*, 499.

[194] *T. Do-Minh, A. M. Trozzolo, G. W. Griffin,* J. Am. Chem. Soc. *92*, 1402 (1970).

[195] *R. W. Hoffmann, H. J. Luthardt,* Chem. Ber. *101*, 3861 (1968).

[196] *G. F. Bettinetti, A. Donetti,* Gazz. Chim. Ital. *97*, 730 (1967).

[197] J. Buter, S. Wassenaar, R. M. Kellogg, J. Org. Chem. 37, 4045 (1972).
[198] R. M. Kellogg, S. Wassenaar, Tetrahedron Lett. 1970, 1987; D. H. R. Barton, B. J. Willis, J. Chem. Soc. Perkin Trans. I 1972, 305.
[199] K. T. Potts, D. M. McKeough, J. Am. Chem. Soc. 96, 4276 (1974).
[200] M. P. Cava, M. V. Lakshmikantham, Acc. Chem. Res. 8, 139 (1975).
[201] K. T. Potts, D. R. Choudhury, A. J. Elliott, U. P. Singh, J. Org. Chem. 41, 1724 (1976).
[202] J. D. Bower, R. H. Schlessinger, J. Am. Chem. Soc. 91, 6891 (1969).
[203] R. Criegee, Angew. Chem. 87, 765 (1975); Angew. Chem. Int. Ed. Engl. 14, 745 (1975), references cited therein.
[204] P. S. Bailey, A. Rustaiyan, T. M. Ferrel, J. Am. Chem. Soc. 98, 638 (1976); C. W. Gillies, ibid. 99, 7239 (1977); P. S. Bailey, Th. M. Ferrel, ibid. 100, 899 (1978), references cited therein.
[205] W. G. Alcock, B. Mile, J. Chem. Soc. Chem. Commun. 1976, 5; B. Mile, G. M. Morris, ibid. 1978, 263.
[206] K. L. Gallaher, R. L. Kuczkowski, J. Org. Chem. 41, 892 (1976).
[207] D. P. Highley, R. W. Murray, J. Am. Chem. Soc. 98, 4526 (1976).
[208] D. R. Kerur, D. G. M. Diaper, Can. J. Chem. 55, 588 (1977).
[209] K. Griesbaum, P. Hofmann, J. Am. Chem. Soc. 98, 2877 (1976).
[210] R. Criegee, G. Schröder, Chem. Ber. 93, 689 (1960).
[211] F. L. Greenwood, L. J. Durham, J. Org. Chem. 34, 3363 (1969).
[212] R. P. Lattimer, R. L. Kuczkowski, C. W. Gillies, J. Am. Chem. Soc. 96, 348 (1974); cf. also R. A. Rouse, ibid. 96, 5095 (1974).
[213] P. C. Hiberty, J. Am. Chem. Soc. 98, 6088 (1976); see also P. C. Hiberty, J. P. Devidal, Tetrahedron 35, 1015 (1979).
[214] S. D. Razumovskii, L. V. Berezova, Izv. Akad. Nauk SSSR 1, 207 (1968).
[215] W. R. Wadt, W. A. Goddard III, J. Am. Chem. Soc. 97, 3004 (1975); see also L. B. Arding, W. A. Goddard III, ibid. 100, 7180 (1978).
[216] H. E. O'Neal, C. Blumstein, Int. J. Chem. Kinet. 5, 397 (1973); N. J. Pitts, B. J. Finlayson, Angew. Chem. 87, 18 (1975); Angew. Chem. Int. Ed. Engl. 14, 1 (1975).
[217] S. Fliszár, M. Granger, J. Am. Chem. Soc. 91, 3330 (1969); 92, 3361 (1970); S. Fliszár, J. Renard, Can. J. Chem. 48, 3002 (1970); S. Fliszár, J. Renard, O. Z. Simon, J. Am. Chem. Soc. 93, 6953 (1971).
[218] M. Schulz, N. Grossmann, J. Prakt. Chem. 318, 575 (1976).
[219] M. Bertrand, J. Carles, S. Fliszár, Y. Rousseau, Org. Mass Spectrom. 9, 297 (1974).
[220] G. Klopman, C. M. Joiner, J. Am. Chem. Soc. 97, 5287 (1975).

New analytical methods (16)

Applications of SEPIL to the Solid State Defect Chemistry of Fluorites and Ultra-trace Inorganic Analysis

By John C. Wright, D. R. Tallant, F. J. Gustafson, M. V. Johnston, M. P. Miller, D. S. Moore, L. C. Porter, and J. R. Akse[*]

Although it has been recognized for many years that the spectra of lanthanoid ions can provide useful information about short range phenomena in the neighborhood of these ions in a solid material, lanthanoid spectroscopy has only infrequently been used for studying complex materials because of the problem of line-sorting the complex spectra that are obtained. The advent of convenient tuneable lasers has eliminated this problem. By *s*electively *e*xciting *p*robe *i*on *l*uminescence (SEPIL), it is possible to obtain fluorescence and excitation spectra from a single kind of crystallographic environment. Two applications of this method are discussed in this paper. The first application is the study of the defect chemistry of fluorite materials (compounds with CaF_2 lattice). It is shown how this method can provide unique information about the solid state chemistry, thus clarifying many of the unexplained behaviors of this important class of material. The second application shows how ultra-trace analysis can be carried out by causing an association between an analyte ion and a fluorescent probe ion. The unique crystal field levels of a probe ion associated with a particular analyte can be selectively excited so that traces of the ion to be analyzed can be detected with very high selectivity and with very low detection limits.

1. Introduction

The optical spectroscopy of lanthanoid-doped materials has been studied for many years[1]. Early efforts were concerned with understanding the physical mechanisms for the characteristic sharp line spectra and strong fluorescence of lanthanoids (rare earth metals)[2, 3]. The discovery that many lanthanoid compounds function very well as lasers[4] brought about a sudden surge in interest in the spectroscopy of this group of elements, particularly with a view to understanding the relaxation mechanisms and dynamic processes which determine the efficiency of the quantum electronic applications[5]. This work has led to a clearer understanding of both the static and dynamic aspects of lanthanoid spectroscopy and in many cases has furnished a degree of predictive power.

It was realized in the early spectroscopic studies that because the line positions and transition probabilities depend upon the immediate environment of the lanthanoid ion, one had at ones disposal a probe for the local crystal field[1]. By measuring the polarization of the transition, the line positions and/or the Zeeman splitting tensor, the local symmetry of a lanthanoid ion could be determined in many cases[2, 3, 6-10]. Some workers have succeeded in gaining information about the static and dynamic properties of lattice phonons[11-15] and about exciton propagation[16]. The majority of the work has been carried out on simple materials, usually single crystals in which the lanthanoid ion occupies a unique crystallographic site. Fundamental investigations of more complex materials have usually been avoided because of the difficulty in characterizing the site of the lanthanoid

[*] Prof. Dr. J. C. Wright, Dr. D. R. Tallant [**], Dr. F. J. Gustafson, M. V. Johnston, Dr. M. P. Miller, D. S. Moore, L. C. Porter, Dr. J. R. Akse
Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706 (USA)
[**] Present address: Sandia Laboratories, Albuquerque, NM 87115 (USA).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1010-0738 $ 02.50/0

ion or in interpreting the spectroscopic data. If a lanthanoid ion can occupy several different kinds of crystallographic sites, the spectroscopy is much more difficult since each lanthanoid site contributes a unique set of lines to the overall spectrum observed. Each line in the spectrum has to be studied individually in order to measure the polarization and the intensity as a function of the dopant concentration, the crystal treatment, the temperature, the symmetry of the Zeeman splittings, and/or the lifetime[7-10,17]. All of the lines can then be divided into groups that have the same behavior and correspond to the lanthanoid sites that are present. This process has been successfully used by a number of groups but it is generally time-consuming, tedious, and subject to error. Even after such a procedure is carried out, the results can still be ambiguous. Two groups studying $KCl:Sm^{2+}$ came to diametrically opposed views and wrote a series of passionate articles about their different conclusions[8,9].

In order to function efficiently as probes of short range order in more general situations where one is not dealing with simple materials, it is necessary to use techniques that can simplify the spectroscopy of a complex material (*i.e.* of a material where there are several environments encountered by a lanthanoid ion). A key idea for surmounting the problems was published in 1966 by *Voron'ko et al.*[18]. They used a mercury lamp and a monochromator with a 3 Å bandpass to selectively excite a specific absorption line of a specific lattice site of the lanthanoid ion and obtained fluorescence from that site alone. By exciting other absorption lines, they could obtain the fluorescence spectrum of each of the other sites. Using this method, they were able to classify the lines in the spectrum of $CaF_2:Er^{3+}$ into three different Er^{3+} sites. The method was not used for later studies, however, because the fluorescence intensities encountered with this excitation method were low and the bandwidth could not be made sufficiently narrow. The advent of tuneable dye lasers has eliminated these problems and made the selective excitation method quite practical[19,20]. In addition to obtaining fluorescence spectra from single sites by exciting a specific absorption line, one can also obtain single site excitation spectra by monitoring a specific fluorescence line as the laser excitation wavelength is changed. A complex absorption spectrum can therefore be split into the spectra of individual sites by monitoring different fluorescence transitions and obtaining excitation spectra. The problem of line classification then becomes quite simple (Fig. 1). Figure 1a shows the absorption spectrum of CaF_2:0.05 mol-% Er. This absorption spectrum is reproduced as the upper trace in Figures 1b—d. The bottom trace in these three figures is the excitation spectrum that results when different fluorescence lines are monitored. Figures 1b—d show how the absorption lines can be assigned to three lattice sites. The excitation line from the site shown in Figure 1d is in the same position as a line in Figure 1b, yet both excitation spectra can be obtained without interference from each other because the fluorescence lines monitored do not overlap.

We believe that selective laser excitation methods (also called site selective spectroscopy by later workers[21]) will extend the application of lanthanoid ions from studies aimed at understanding the spectroscopy of the lanthanoids to studies of more general interest where the lanthanoids are used as probes of short range environments in complex materials. In this paper, we present two examples of how the methods might be used—one example is a fundamental study of the solid state chemistry which occurs in charge compensated crystals, while the second example is the development of practical techniques for the ultra-trace analysis of inorganic ions.

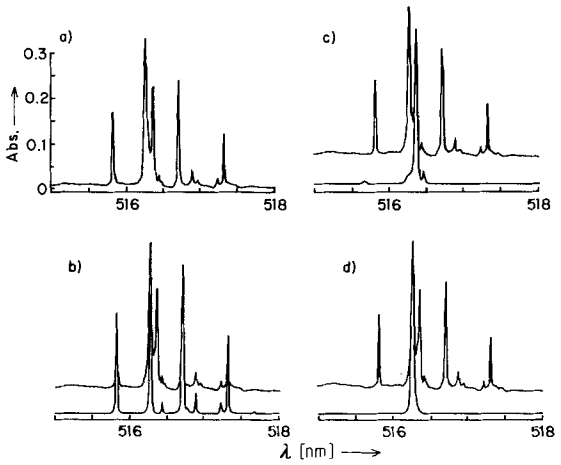


Fig. 1. a) Absorption spectrum of the $Z \rightarrow F(^4I_{15/2} \rightarrow {}^2H_{11/2})$ transition in CaF_2:0.05 mol-% Er^{3+}. This spectrum is reproduced as the top trace in Fig. 1b—d. b—d) Excitation spectrum of the Z→F transition obtained while monitoring the fluorescence line at 540.0 nm (b), 539.15 nm (c) or 537.98 nm (d).

2. Solid State Chemistry of Fluorites

One of the most important problems in materials science is the description of point defects. In most cases the defects in a material determine its overall properties[22-26]. Compounds having the fluorite structure have played an important role in understanding defects both because of their practical importance and their use as model systems. A great deal of work has been carried out with compounds having a fluorite structure, particularly as regards dielectric relaxation, ionic conductivity, thermal conductivity, diffuse and Bragg neutron scattering, diffusion, density measurements, NMR, ESR, ENDOR, UV, visible and IR spectroscopy[27-44]. In this paper, we shall restrict our discussion to the fluorites CaF_2, SrF_2, and BaF_2.

It is generally accepted that the predominant defects in CaF_2, SrF_2, and BaF_2 are fluoride interstitials (F_i')[45] and fluoride vacancies ($V_F^{\cdot}$) which exist in equal numbers because of charge neutrality requirements[23,46]. If trivalent cations like Er^{3+} are introduced into a lattice such as $CaF_2(Er_{Ca}^{\cdot})$, additional fluoride interstitial ions are required for charge compensation. There will be Coulombic interactions between $Er_{Ca}^{\cdot}$ and F_i' promoting association into single pairs $(Er_{Ca}^{\cdot} \cdot F_i')^x$ which can have different symmetries depending upon the relative positions of $Er_{Ca}^{\cdot}$ and F_i'. The two most important symmetries are tetragonal and trigonal[10]. The relative numbers of the different symmetry pairs is determined by the relative free energies of association and the temperature of the crystal[47]. In addition, the $Er_{Ca}^{\cdot}$ and F_i' can be distant from each other and occupy sites of cubic symmetry. The free F_i' that are found then force a decrease in the $V_F^{\cdot}$ concentration. The model can be described in terms of two equilibria analogous to solution equilibria.

$$\text{Perfect } CaF_2 \text{ lattice} \rightleftharpoons F_i' + V_F^{\cdot}$$
$$+$$
$$Er_{Ca}^{\cdot}$$
$$\downarrow\uparrow$$
$$(Er_{Ca}^{\cdot} \cdot F_i')$$

This simple model has been extensively employed in many studies with apparent success. Particularly convincing evidence was provided by EPR measurements, which conclusively identified the tetragonal and trigonal site symmetries expected for the lanthanoid ion in an associated pair and the cubic symmetry of the site expected for a lanthanoid in an unassociated pair[47,48]. ENDOR measurements identified the presence of the F_i' in the tetragonal and trigonal sites[49,50].

There were several observations however that did not agree even qualitatively with this model[50–52]. The ratio of associated pairs to non-associated pairs (or trigonal + tetragonal to cubic pairs) was measured by EPR spectroscopy as a function of the crystal temperature[53]. $CaF_2:Gd^{3+}$ samples were heated in an oxygen-free atmosphere until the distribution of site populations reached equilibrium and then were quenched rapidly to freeze the high temperature distribution. The simple model would predict that the ratio of associated to non-associated pairs would decrease as the effective crystal temperature was raised in order to maximize the entropy of the system. Instead, exactly the opposite behavior was observed: The number of associated pairs increased as the temperature was raised. The ratio was also measured as a function of the Gd^{3+} concentration[53–58]. According to the simple model the ratio of associated to non-associated pairs should increase as the dopant concentration is raised, but the measurements actually showed that the ratio decreases.

Problems were also encountered in the interpretation of Bragg neutron diffraction and diffuse neutron scattering data in highly doped samples of $CaF_2:Y^{3+}$. These experiments revealed two types of F_i' ions, those with distortions along the ⟨110⟩ direction and those with distortions in the ⟨111⟩ direction from the central (½, ½, ½) cubic position of a normal F_i' site[28,29]. Fluoride vacancies could also be observed. The relative concentrations of these three types of defects could be explained by postulating that the two types of F_i' ions and the $V_F^{\cdot}$ form a cluster designated as a 2:2:2 cluster since it contains two of each type of defects. There are also a number of variations in the structure and composition of this basic cluster. The $Y_{Ca}^{\cdot}$ ions in the sample could not be observed directly; though there was evidence from the diffuse neutron scattering measurements that the $Y_{Ca}^{\cdot}$ were only loosely associated with the clusters. It was further argued that the cation mobility in CaF_2 should be sufficiently small that one would not expect $Y_{Ca}^{\cdot}$ to cluster extensively[30,59]. If there is only a loose association of $Y_{Ca}^{\cdot}$ with the 2:2:2 clusters, the clusters would possess a net negative charge which would favor their dissociation. What stabilizes the formation of negatively charged clusters? Furthermore, the distance required between two F_i' with ⟨110⟩ distortions in the 2:2:2 cluster was 2.0 Å, much closer than the 2.3 Å separation expected theoretically[28–30]. In order to explain these two problems, *Catlow* proposed that an additional covalent interaction existed between F_i' which both stabilized the negatively charged 2:2:2 clusters and produced the 2.0 Å separation between F_i'[59]. We shall see later how *Catlow*'s proposal also explains the anomalous changes in the ratio of the associated to non-associated pairs.

2.1. Experiments on Selective Excitation in CaF_2

We have investigated materials having a fluorite lattice by the selective laser excitation technique. This technique is the only one that has permitted the examination of all the different sites occupied by a trivalent dopant. Most of our work has been concentrated on $CaF_2:Er^{3+}$[19,20,60–62], although we have found that SrF_2[63] and BaF_2[64] exhibit a similar behavior. The excitation spectrum that one observes for a CaF_2:0.2 mol-% Er^{3+} sample when fluorescence from all Er sites is monitored is shown in Figure 2. The lines in this excitation

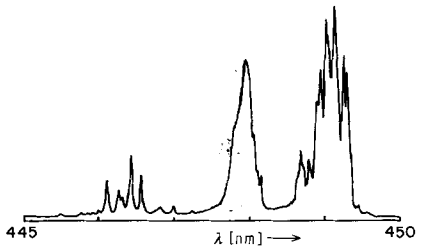


Fig. 2. Excitation spectrum of CaF_2:0.2 mol-% Er^{3+} that results on monitoring the fluorescence of all E→Z ($^4S_{3/2}\rightarrow{}^4I_{15/2}$) transitions with a broad bandwidth monochromator while a dye laser is scanned over the possible Z→H ($^4I_{15/2}\rightarrow{}^4F_{5/2}$) transitions.

spectrum can be divided into groups corresponding to the different Er sites by monitoring a single fluorescence line from an individual site. The single-site excitation spectra obtained in this way are shown in Figure 3. Each line in Figure 3 corresponds to a line of the excitation spectrum in Figure 2.

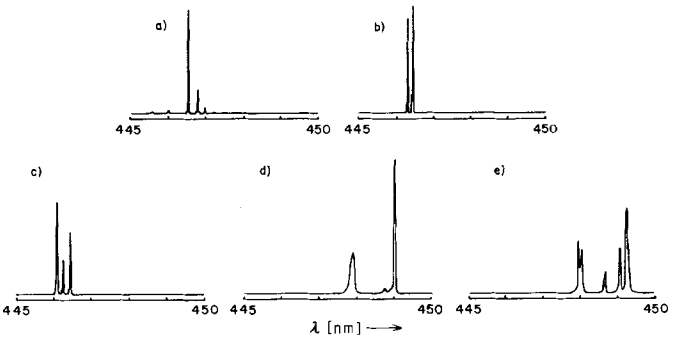


Fig. 3. Single site excitation spectra of CaF_2:0.2 mol-% Er^{3+} (see Fig. 2) [Z→H ($^4I_{15/2}\rightarrow{}^4F_{5/2}$) transitions]. The spectra are observed by monitoring the fluorescence at: a) 835.4 nm (A site), b) 835.8 nm (B site), c) 836.1 nm (C site), d) 843.1 nm (D(1a) site), e) 654.4 nm (D(2a) site).

Only two representative spectra (Fig. 3d and 3e) of the many that make up the bands shown in Figure 2 have been shown. It was possible to show that at least 15 sites contributed lines to the bands, 11 which had spectra similar to Figure 3d and four which had spectra similar to Figure 3e. The site whose spectrum is shown in Figure 3a corresponds to an Er^{3+} ion with a F_i' in the nearest possible interstitial position producing a tetragonal site symmetry. This identification could be made because *Rector et al.*[7] had previously shown that the lines from this site had a Zeeman splitting tensor that possessed tetragonal symmetry. Similarly, the spectrum in Figure 3b corresponds to an Er^{3+} ion with a F_i' that produces a

trigonal site symmetry. The spectra in Figures 3c—e were shown to correspond to different clusters of Er^{3+} ions whose symmetry remains undetermined. It is clear from Figure 2 that these clusters cause the dominant features in the overall spectrum at the 0.2 mol-% concentration level. A great deal of effort was spent in showing that clusters of Er^{3+} actually cause these spectral features, both because of their importance in the optical spectrum and because many workers did not believe that Er^{3+} clusters could be important[50-52] or in fact even be formed because of low Er^{3+} mobilities[59]. A prime reason for this disbelief was the inability of EPR measurements to identify any features that would correspond to Er^{3+} ion clusters[50]. It should, however, be pointed out that many optical spectroscopists have observed the lines and correctly assigned them to Er^{3+} clusters because of their rapid increase with dopant concentration[10,17-20,31-33,65]. In 1966, *Voron'ko et al.* were particularly successful in unraveling the optical spectrum into four sites which are essentially those represented in Figure 3[10] and in attributing two of the sites to clusters of Er^{3+} ions.

2.2. Proof of Clustering in Fluorites

Two experiments show quite conclusively that clusters of Er^{3+} ions are responsible for the features shown in Figures 3c—e. If a particular electronic multiplet within the $4f^n$ electron configuration of a particular lanthanoid ion is excited, resonant or non-resonant energy transfer can occur with another lanthanoid ion[60,66]. Non-resonant energy transfer is generally quite weak if the initial and final energy states differ by more than a few hundred cm^{-1}. However, if the two ions involved in the energy transfer are quite close to each other, as is the case for the clusters, the non-resonant energy transfer rate can become efficient. In fact, non-resonant energy transfer is generally the dominant non-radiative relaxation mechanism for the clusters. A series of measurements were performed on CaF_2 in order to determine how the transfer rate depends upon the energy mismatch between the initial and final energy states. The results are shown in Figure 4 as the isolated points. It can be seen that there is a strong dependence upon the energy mismatch. The multiphonon relaxation rate was also measured for CaF_2 as a function of the amount of energy lost by the non-radiative relaxation (line (a) in Figure 4). In this process, an excited electronic level can relax non-radiatively to a lower electronic level by dissipating the energy difference as lattice phonons. Although multiphonon relaxation is more rapid than non-resonant energy transfer for a particular value of energy dissipation, there are generally enough different electronic levels for two arbitrary lanthanoid ions that a combination of lower levels will lie closer in energy to an excited level than the gap appropriate for multiphonon relaxation. Non-resonant energy transfer is therefore very important in clusters. No energy transfer has been observed for the tetragonal and trigonal Er sites which are isolated from other Er ions.

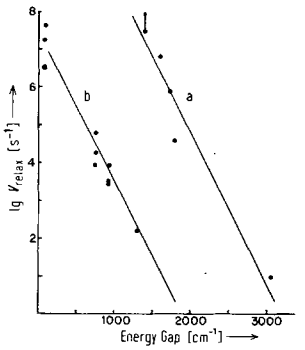


Fig. 4. The points of curve a represent the non-radiative rate for multiphonon relaxation as a function of the energy gap between the emitting level and the next lowest level. The points of curve b represent the non-radiative rate due to non-resonant energy transfer between two ions in a cluster. All of the data is for CaF_2 with Er^{3+} as dopant.

The energy transfer causes some interesting phenomena. Up-conversion of excitation energy can be particularly efficient if two ions in the clusters are excited[20,60]. One ion transfers its excitation energy to the neighboring excited ion and causes a fluorescence from a level much higher in energy than that originally pumped. Thus, one can visually observe green fluorescence from a $CaF_2:Er^{3+}$ crystal when the Er clusters are being excited in the red. If one monitors the green fluorescence, the red excitation spectrum obtained will only contain lines from the Er clusters. The single pairs (*i.e.* the tetragonal and trigonal sites) cannot undergo the energy transfer and consequently cannot produce the up-converted fluorescence. This method provides a convenient way in which to discriminate between the single ($Er_{Ca} \cdot F_i$) pairs and Er^{3+} clusters.

The second experiment which shows the presence of clusters involves the double doping of CaF_2 samples[61]. In a sample of CaF_2:0.2 mol-% Yb^{3+}, 0.01 mol-% Er^{3+}, the site distribution is determined by the Yb^{3+} concentration, which is large enough that the optical spectrum is dominated by the clusters. The Er^{3+} will also be distributed among the various possible sites, and some Er^{3+} ions will form mixed clusters with Yb^{3+}. The Er^{3+} concentration is sufficiently low that pure Er clusters are improbable. However, if one monitors the Er transitions, mixed Er—Yb clusters can be seen. The lines are shifted slightly from those observed in $CaF_2:Er^{3+}$ samples because Yb^{3+} has a different ionic radius from that of Er^{3+}. An example of the differences observed is shown in Figure 5. Since it is clear that Yb^{3+} is sufficiently close to Er^{3+} to affect the Er spectrum, it follows that these transitions must arise from clustering of the cation dopants.

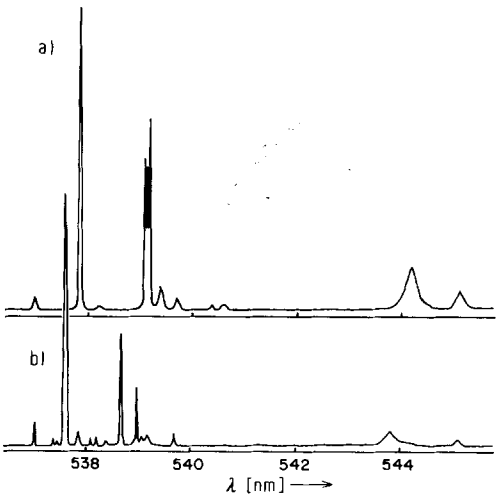


Fig. 5. Single site fluorescence spectrum for the $E \rightarrow Z(^4S_{3/2} \rightarrow {}^4I_{15/2})$ transition of the C site in a) $CaF_2:Er^{3+}$ and b) $CaF_2:Er^{3+}$, Yb^{3+}. Note the shift of the lines due to the influence of the Yb^{3+} on the clusters.

2.3. Concentration of Clusters

Secemski and *Low* pointed out that the observation of clustered ions in the optical spectrum does not necessarily mean that clusters are important[50]. The ions in the clusters may simply have much more favorable radiative transition probabilities and quantum efficiencies than single pairs and therefore may look brighter in the fluorescence spectra. Their actual concentration could still be quite low and thus might prevent EPR spectroscopic detection. The authors point out that transition probabilities for EPR are much simpler than for optical transitions. The measurement of the cluster concentrations therefore constitutes an important experimental step in solving the solid state chemistry of the fluorites.

The only technique that permits observation of the cluster species is optical spectroscopy. However, the relationship between the fluorescence intensity or absorption coefficient and concentration is complex. One can follow how any given site will change in samples of different concentrations but the transition probabilities must be known in order to determine an absolute concentration. The transition probability for an absorption transition can be obtained if that same transition can be observed in fluorescence where a fluorescence lifetime can be determined[6]. The fluorescence lifetime determines the total relaxation rate for the level. The radiative quantum efficiency must be measured in order to obtain the total radiative relaxation rate for the level. Finally, the radiative relaxation rate for a particular transition of interest can be derived by measuring what fraction that transition represents of the total fluorescence from the level[60]. The actual procedure for obtaining all the concentrations is more involved than described here (for further details see reference[61]). The results thus obtained are shown in Figure 6, where the site concentrations are plotted as a function of total dopant concentration in the system $CaF_2:Er^{3+}$. The C

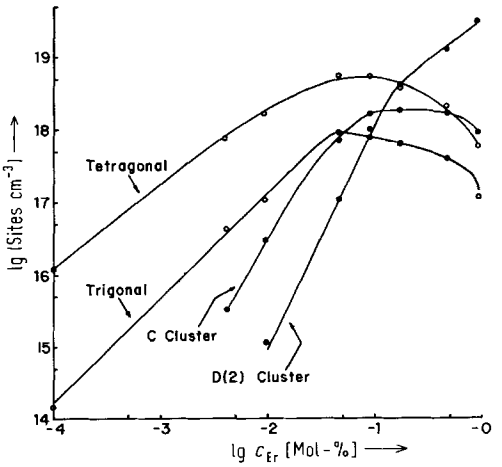


Fig. 6. Absolute concentrations of the Er sites in $CaF_2:Er^{3+}$ as a function of Er^{3+} dopant concentration.

and D(2) designations refer to Er clusters that have the spectra shown in Figures 3c and e. The concentration of the unassociated or cubic Er site does not appear in Figure 6 because it cannot be observed: electric dipole transitions are forbidden in a cubic crystal field[2]. It should be clear from this data that the clusters are a dominant feature of the site distribution at almost all commonly used dopant concentrations and must be included in any description of the solid state equilibria.

2.4. Discussion

As shown in Figure 6, at very low concentrations the single pair sites (the tetragonal and trigonal sites) change linearly with concentration. As soon as the clusters appear, the number of single pair sites changes more slowly until their absolute concentration actually begins to decrease. A decrease in the absolute concentration of any site is unexpected, since a simple equilibrium of defects will allow only changes in the rate of increase of a site population with dopant concentration, but never a decrease[61].

Our explanation for this behavior requires an extension of the simple model presented earlier[45,61].

$$\begin{array}{l}\text{Perfect } CaF_2 \text{ lattice} \rightleftharpoons F_i' + V_F^{\cdot} \\ \qquad\qquad\qquad\qquad + \\ \qquad\qquad\qquad\qquad Er_{Ca}^{\cdot} \\ \qquad\qquad\qquad\qquad \downarrow\uparrow \\ (Er_{Ca}\cdot F_i)^x + (Er_{Ca}\cdot F_i)^x \rightleftharpoons (2\,Er_{Ca}\cdot 2\,F_i)^x + \cdots \\ \qquad\qquad\qquad\qquad\qquad\qquad + \\ \qquad\qquad\qquad\qquad\qquad\qquad F_i' \\ \qquad\qquad\qquad\qquad\qquad\qquad \downarrow\uparrow \\ \qquad\qquad\qquad\qquad\qquad\qquad (2\,Er_{Ca}\cdot 3\,F_i)'\end{array}$$

The clustering has been shown explicitly as an additional equilibrium. The additional covalent interaction between F_i' ions that was proposed by *Catlow*[59] has been represented by an equilibrium in which $(2\,Er_{Ca}\cdot 3\,F_i)'$, a charged cluster, is formed. This last type of equilibrium is the key to the explanation of the anomalous behavior of CaF_2 and may well be the equilibrium that controls the solid state equilibria in the fluorites. At high temperatures, the $Er_{Ca}^{\cdot}$ and F_i' are both free to move about in the lattice. As the temperature is lowered, the $Er_{Ca}^{\cdot}$ lose mobility and the distribution becomes frozen. This event fixes the total number of $Er_{Ca}^{\cdot}$ that exist as single ions, dimers, trimers, *etc.* However, the F_i' are still mobile and can be distributed among the different $Er_{Ca}^{\cdot}$ sites to form different species. In particular, if the bonding of a F_i' to make a charged species like $(2\,Er_{Ca}\cdot 3\,F_i)'$ is very favorable, the concentration of free F_i' would be forced lower. However, the equilibrium between unassociated $Er_{Ca}^{\cdot}$ and the single associated pairs $(Er_{Ca}\cdot F_i)^x$ must follow a simple mass action relation

$$K = [F_i'][Er_{Ca}^{\cdot}]/[(Er_{Ca}\cdot F_i)^x]$$

which determines the ratio of unassociated to associated $Er_{Ca}^{\cdot}$. If $[F_i']$ is small because of the formation of $(2\,Er_{Ca}\cdot 3\,F_i)'$, the ratio $[Er_{Ca}^{\cdot}]/[(Er_{Ca}\cdot F_i)^x]$ will become large as the associated single pairs are forced to dissociate. Higher dopant concentrations produce more clusters which form the $(2\,Er_{Ca}\cdot 3\,F_i)'$ type of species that removes F_i' from the equilibria. Thus, the absolute concentrations of the tetragonal and trigonal sites will decrease, as is observed experimentally (Fig. 6). The same argument provides an explanation of the anomalous behavior observed in EPR measurements: the cubic site concentration increases relative to the associated single pair sites as the total dopant concentration is increased.

This model also provides an understanding of the temperature dependence observed by *Franklin* and *Marzullo*[53], who found that the concentration of cubic sites decreases relative to the concentration of tetragonal sites as the temperature of the sample is raised. At high temperatures, species such as $(2\,Er_{Ca}\cdot 3\,F_i)'$ will dissociate and raise the concentration of free F_i'. The free F_i' ions can then recombine with Er^{3+} ions in cubic sites to form the associated single pairs.

The results from Bragg neutron diffraction and the diffuse scattering experiments relate very directly to this model. The selective laser excitation studies showed clearly that contrary to some expectations, there is extensive clustering of Er^{3+} ions. The presence of several Er^{3+} ions in a cluster would help to stabilize it against the dissociation discussed for the (2:2:2) cluster model presented by *Cheetham et al.*[28,29], *Steele et al.*[30] and *Catlow*[59]. The cluster of Er^{3+} ions would be further stabilized by the additional covalent bonding of F_i' proposed by *Catlow*[59]. This interaction also produces the charged species which determines the defect equilibrium discussed.

This model is supported by density measurements carried out by *Franklin* as a function of dopant concentration[27]. *Franklin* observed that the density of $CaF_2:Gd^{3+}$ increased too rapidly with concentration to be explained by having a single Gd^{3+} charge compensated by a single F_i'. He suggested that HF from the atmosphere around the crystal during its growth had entered the lattice and formed associations with $(Gd_{Ca}\cdot F_i)^x$ pairs. No evidence could be found for the F H F groups that would be formed. However, the additional HF could be brought into the lattice in association with the cluster species and result in the anomalously high values for the density.

Although this model provides a self-consistent explanation for the behavior of CaF_2, it remains a speculative model that must be proven. We are presently engaged in experiments that will monitor the populations of all the sites as the temperature of the crystal is changed. We expect to see the population of species like $(2\,Er_{Ca}\cdot 3\,F_i)'$ decrease as the temperature is raised while the $(2\,Er_{Ca}\cdot 2\,F_i)^x$ and $(Er_{Ca}\cdot F_i)^x$ concentrations increase correspondingly. These experiments are not complete but it is clear that temperature changes cause large redistributions in site population.

3. Ultra-trace Chemical Analysis

When we began our experiments in selective laser excitation, we were struck by both the excellent signal/noise ratio and ability to selectively excite a specific site without interference from other sites. These two features are also of great importance for a good trace analysis method. One would like to have analytical methods that can measure very low concentrations with a high degree of selectivity for the analyte of interest. Could the trace analysis of lanthanoids be carried out using the laser methods? Our systems at that time were single crystals, not particularly interesting samples for an analytical determination. In order to use our selective laser excitation methods, we had to find a convenient way of incorporating lanthanoid analytes from a material of analytical interest into a material suitable for our methods.

3.1. Analysis of Lanthanoids

We found that coprecipitation from aqueous solution was a suitable way to incorporate analytes[67]. Treatment of a solution containing unknown amounts of different lanthanoid ions with $Ca(NO_3)_2$ and then with NH_4F leads to coprecipitation of the lanthanoids in the resulting CaF_2 microcrystals. We have measured the amount of coprecipitation that occurs as a function of the total amount of CaF_2 precipitated and have found that the distribution law for lanthanoid coprecipitation is very favorable. The precipitation therefore performs several functions:

1) it incorporates the analyte into a suitable matrix,
2) it serves as a preconcentration step,
3) it serves as a separation step, especially since other ions with much different ionic radii are not likely to coprecipitate.

Although it might be expected that the quality of the micro-crystals would be too poor to show sharp line structure, the lanthanoid transitions are reasonably sharp. An example of the excitation spectrum of a $CaF_2:Er^{3+}$ precipitate is shown in Figure 7a. There are lines from both the tetragonal

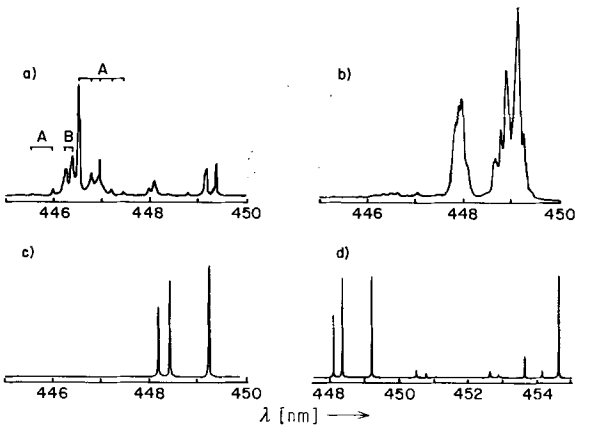


Fig. 7. Excitation spectra of the $Z\rightarrow H(^4I_{15/2}\rightarrow{}^4F_{5/2})$ transition for a $CaF_2:Er^{3+}$ precipitate dried at different temperatures. A monochromator with a very wide bandpass was used to monitor the fluorescence in order to include fluorescence from all the sites present. a) Room temperature (A, B see text), b) 350 °C, c) 500 °C, d) 1000 °C.

and trigonal Er sites present which are labeled A and B respectively. If the precipitate is dried at 350 °C, dramatic changes occur in the spectrum as shown in Figure 7b. Lines that have the same appearance as the cluster site lines shown in Figure 3e become prominent while the lines from single pair sites almost disappear. This behavior is quite unexpected and cannot be explained with any degree of certainty. It would appear to indicate that the Er^{3+} ions initially coprecipitate in isolated positions in the lattice and do not have sufficient mobility at room temperature to reach the equilibrium distribution. As the temperature is increased, they finally achieve sufficient mobility (in precipitates at least) to move and form clusters with each other. At higher temperatures (Fig. 7c), the spectrum changes once more. All the previously observed lines and bands disappear and are replaced by lines from a single site—labeled G1. The fluorescence intensity from this site is several orders of magnitude higher than those of the previously discussed sites. Other workers have studied CaF_2 under very similar conditions to ours and have discovered the reason for the appearance of the new

site[68-72]. The fluoride charge is compensated by oxygen anions instead of by fluoride ions, because F_i reacts with water vapor:

$$2F_i' + H_2O \rightarrow 2HF + O''$$

The oxygen anion replaces one of the nearest neighbor fluoride ions in the lattice and produces an Er site with trigonal symmetry. The spectrum continues to change as the precipitate is heated to 1000 °C (Fig. 7d). Lines associated with sites labeled G2, G3 and G4 increase in intensity up to 1000 °C but then become weaker again at higher temperatures. These sites are probably the result of additional oxygen incorporation. For example, the site labeled G4 is believed to result from replacement of seven nearest neighbor fluoride ions and the fluoride interstitial charge compensation by four oxygen anions[70]. At very much higher temperatures, the spectrum changes to that of CaO[67].

The sites that are present below 500 °C are of no analytical value. As one lowers the concentration of the rare earth in solution, the line intensities drop non-linearly at a rapid rate until they cannot be detected at a concentration of 1.25 μg/ml. It is assumed that the non-linear behavior is caused by the dissociation of the single pairs of $Er_{Ca}^{\cdot}$ and F_i' at very low concentrations. The lines of the single pairs disappear and are not replaced by spectra from the dissociated pairs because the cubic Er site of a dissociated pair does not have allowed electric dipole transitions. The temperature region between 500° and 700 °C is optimum for an analysis because the site distribution has collapsed into a single site which is intensely fluorescent and is stable against dissociation at very low concentrations. It is particularly advantageous to have only one site because the peak intensity is higher and the system becomes more insensitive to other influences that could change the site distribution.

Any lanthanoid that fluoresces in CaF_2 can be determined by the procedure described. In order to fluoresce, an ion must have excited electronic levels within the $4f^n$ electron configuration (transitions to other configurations have much broader lines because of the additional interactions with the lattice) and must have an excited electronic level whose non-radiative relaxation is slow in comparison with its radiative relaxation[5]. Of the 15 lanthanoid ions, only La, Ce, and Lu do not have excited electronic levels. (Ce actually has one excited level but it is too close to the ground state to be used.) Gd has many excited levels but they lie in the UV beyond 310 nm where it is difficult to obtain convenient tuneable lasers. The non-radiative relaxation rate is determined by the strength of multiphonon processes that convert electronic energy into vibrational energy. The rate for this process depends exponentially upon how much energy an excited level must dissipate in the lattice. If there is another electronic level that has a lower energy than the excited level, a non-radiative transition to the lower level can occur and the energy difference is dissipated as several phonons. Figure 4 describes the relationship between relaxation rate and the energy gap for CaF_2. If the typical radiative transition rate is 10^3 s^{-1}, an energy gap greater than 2600 cm^{-1} is required before a level will generate sufficient fluorescence. All lanthanoid ions having excited electronic levels—Pr^{3+}, Nd^{3+}, Pm^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, Tb^{3+}, Dy^{3+}, Ho^{3+}, Er^{3+}, Tm^{3+}, and Yb^{3+}—also have at least one level that can fluoresce efficiently. We have experimentally demonstrated the feasibility of analyzing all of these ions excepting Pm^{3+}, Gd^{3+}, and Yb^{3+}. Pm is radioactive, while Gd and Yb have electronic levels in a spectral region that is not accessible with our lasers. As will be discussed later, there are methods that can be used for the analysis of those ions which cannot be detected by this method, namely La^{3+}, Ce^{3+}, Gd^{3+}, Yb^{3+}, and Lu^{3+}.

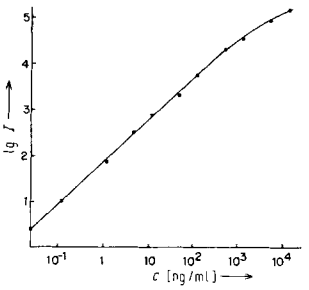


Fig. 8. Fluorescence intensity (I) of a $CaF_2:Er^{3+}$ precipitate as a function of Er^{3+} concentration (c) in the original solution (calibration curve).

The analytical working curve for Er analysis is shown in Figure 8. The concentrations are referenced to the original solution before precipitation. At high concentrations the curve becomes non-linear; at these concentrations additional lines also appear in the spectrum which have been proven to be associated with cluster formation (see later discussions). The spectrum of the cluster site is shown in Figure 9. Note the double line structure that is associated with exchange-splittings between the two lanthanoids. The change in the site distribution accompanying cluster formation causes the non-linearity of the calibration curve (Fig. 8) at high concentrations.

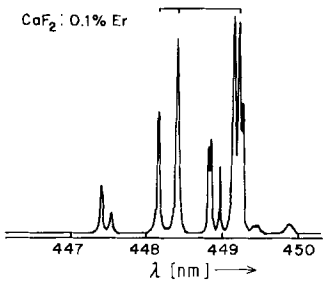


Fig. 9. Excitation spectrum of the $Z \rightarrow H(^4I_{15/2} \rightarrow {}^4F_{5/2})$ transition obtained with wide bandpass monitoring of a CaF_2:0.1 mol-% Er^{3+} precipitate. By comparing this spectrum with that in Figure 7c, the additional lines that are formed at high concentrations are readily recognizable. The three lines from Figure 7c are marked.

The limit of detection for this method depends upon the number of photons available from the laser excitation source. One of the advantages of a pulsed laser is the ability to use time resolution techniques or gating to discriminate between signal and background. The lanthanoids have relatively long fluorescence lifetimes, usually 200 μsec or longer, and discrimination becomes simple. On the other hand, the lifetimes are short enough to allow photomultiplier dark noise fluctuations to be greatly reduced by gating. Thus, the limit of detection is determined more by the excitation source intensity than by the fluctuations in source intensity and by the residual dark noise fluctuations. With currently available instru-

mentation a detection limit of 25 fg/ml (25×10^{-15} g/ml) of Er^{3+} can be achieved, calculated by extrapolation of the signal/noise ratio at 1 pg/ml. The absence of clean-room facilities prevented us from reaching the detection limit of the method experimentally. The instrumentation used by us included a N_2-pumped dye laser with an average power of 1 milliwatt and an uncooled S-20 photomultiplier. With a cooled photomultiplier and a laser power of a modest 50 milliwatts, the detection limit would be 25×10^{-18} g/ml.

The sources of interference in this method can be divided into different classes:

1) formation of other precipitates
2) changes in efficiency of coprecipitation
3) line-broadening
4) changes in site distribution
5) quenching of fluorescence.

The first class of interferences are obvious ones. If we assume the lanthanoid analytes are in solution as we begin the procedure, problems can arise if there are substances present which precipitate when either $Ca(NO_3)_2$ or NH_4F is added. Insoluble fluorides would provide the main problem since most anions that precipitate Ca will have already precipitated the lanthanoid ions. The insoluble fluorides include such compounds as SrF_2, PbF_2, BaF_2, and BiF_3. Generally if such substances are present in concentrations large enough to affect the amount of CaF_2 precipitate that is formed, this will cause more severe interferences of the other classes mentioned above. Interferences of class 2 have not been identified or studied.

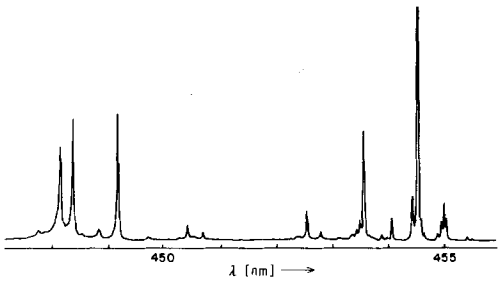


Fig. 10. Excitation spectrum of the $Z \rightarrow H(^4I_{15/2} \rightarrow {}^4F_{5/2})$ transition for a CaF_2:0.1 mol-% Er^{3+} precipitate after addition of 50 ppm of Na^+; for usual conditions see Figure 7c. It can be seen that Na^+ changes the spectrum and therefore acts as an interference.

We have examined examples of each kind of ion that can act as a potential interference. As typical monovalent cations, Li^+, Na^+ and K^+ were added to the lanthanoid-containing solution. Na^+ and Li^+ produce marked changes in the spectrum (Fig. 10). They affect the site distribution by accelerating charge compensation by oxygen anions instead of by fluoride anions. Additional lines appear in the spectrum that are probably associated with lanthanoid-ion sites which are compensated by the monovalent cation.

The spectrum obtained when K^+ is added to the solution is shown in Figure 11. The site distribution is completely changed, the intensity of the lines is dramatically lowered, the lines are broadened, and the background is increased. These changes are very severe and would drastically limit the applicability of the technique if they could not be eliminated. Traces of other ions have also been observed to severely change the site distribution.

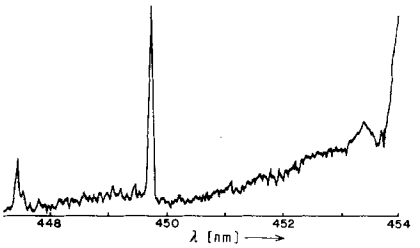


Fig. 11. Excitation spectrum of the $Z \rightarrow H(^4I_{15/2} \rightarrow {}^4F_{5/2})$ transition for a CaF_2:0.1 mol-% Er^{3+} precipitate after addition of 0.1 mol/l of K^+. Comparison with Figure 7c shows the profound influence of K^+.

We believe that these problems are best interpreted in terms of the solid state equilibria in the precipitated microcrystals. Any aliovalent ion that enters the lattice will require a charge compensation and must therefore affect all of the defect equilibria. If all the aliovalent ions are present at trace levels, the position of the defect equilibria can fluctuate as other trace contaminants enter the lattice. The situation is analogous to an unbuffered aqueous solution which can fluctuate in pH as trace quantities of different ions enter the solution. A buffer is required to fix the equilibria positions and remove the sensitivity to traces of other ions. Li and K were chosen to act as the solid state buffer. The solution containing $Ca(NO_3)_2$ and the lanthanoid analytes is treated with $LiNO_3$ and KNO_3 before the precipitation is carried out. The precipitate is heated at as low enough a temperature that only sites of type G1 are formed. This step eliminates the sensitivity of the system to any of the monovalent cations and has been made an integral part of the procedure. All of the results described in the following sections were obtained on adopting this procedure.

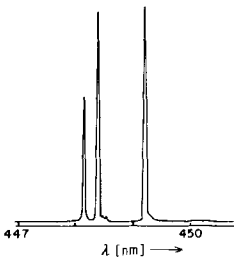


Fig. 12. Excitation spectrum of the $Z \rightarrow H(^4I_{15/2} \rightarrow {}^4F_{5/2})$ transition for a CaF_2:0.1 mol-% Er^{3+} precipitate after addition of 0.005 mol/l of Sr^{2+}. Comparison with Figure 7c shows the line-broadening effect of Sr^{2+} and the additional sites that appear.

Divalent cations do not interfere at low concentrations, but do so at higher concentrations (*ca.* 5×10^{-3} mol/l). An example of a spectrum obtained with $Sr(NO_3)_2$ present in the original solutions is shown in Figure 12. The lines are all broadened and therefore result in a lower measured intensity. Sr ions can enter the lattice substitutionally for Ca and cause disruptions in the lattice order because of their different ionic radii. The lanthanoid ions are therefore present in many different environments, resulting in both broadened lines and a background fluorescence.

Trivalent cations include the lanthanoid ions themselves and many other similar ions. The trivalent cations interfere at concentrations above *ca.* 10^{-5} mol/l by the same clustering mechanism that causes non-linearities in the working curve (see Fig. 8). This interference might be expected, because trivalent cations having properties similar to those of lanthanoid ions should cause a site distribution characteristic

of a higher lanthanoid concentration in the cation lattice. The lanthanoids themselves could cause additional interference by participating in energy transfer processes that quench the fluorescing level. These processes have a particularly strong influence if the two levels lie quite close to each other[66]. However, we have not found any evidence of lanthanoid fluorescence being quenched by other lanthanoids over the entire linear region of the working curve. This lack of interference by quenching means that all of the lanthanoids can be determined in a single sample without any need for prior separation.

Interference by transition metals does not generally occur until concentrations greater than *ca.* 10^{-4} mol/l are reached. Fe^{3+}, however, interferes particularly strongly and its concentration must be kept below *ca.* 4×10^{-6} mol/l. Interferences by transition metals belong to the class 5 interferences (quenching of lanthanoid fluorescence).

We have also examined a number of the common anions such as Br^-, Cl^-, SO_4^{2-}, NO_3^- and PO_4^{3-} and have not found any interference at concentrations below *ca.* 10^{-3} mol/l. We are presently extending our study of interferences to include many other ions. In addition, we are engaged in applying this technique to samples of geological interest in order to test whether interferences will arise which we had not anticipated and to demonstrate the practicability of the method in cases where lanthanoid analysis is important.

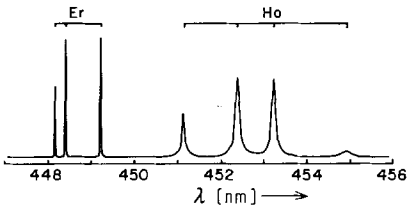


Fig. 13. Excitation spectrum of the $Z \rightarrow H(^4I_{15/2} \rightarrow {}^4F_{5/2})$ transition for a mixed precipitate of $CaF_2:Er^{3+}$, Ho^{3+}. The individual Er^{3+} and Ho^{3+} transitions are indicated. The bandwidth of the fluorescence monitor was sufficiently wide to include both the Ho^{3+} and Er^{3+} fluorescence.

The technique is highly selective regarding the analysis of specific lanthanoid ions. This selectivity is demonstrated for a CaF_2 precipitate containing Ho^{3+} and Er^{3+}, two lanthanoid ions with very similar energy levels. The spectrum in Figure 13 shows that the excitation transitions are close to each other. The fluorescence transitions are also quite close. However, the lines are all sufficiently sharp, so that either Ho or Er can be excited individually. The resulting fluorescence spectrum contains only transitions from the ion excited. The selectivity is ultimately limited by the weak vibronic sidebands that accompany any electronic transition[2,3]. The vibronic sidebands occur because the electronic states of the lanthanoids are loosely coupled to the lattice, and changes in the vibrational state of the lattice can happen simultaneously with an electronic change. Vibronic processes result in the absorption or emission of a lattice phonon. If the experiments are performed at low temperatures, as is usually the case in order to obtain narrow line profiles, then only phonon emission processes need to be considered. Vibronic sidebands are much weaker than the pure electronic transition and their shape reflects the density of phonon states at different energies and the amount of coupling between a phonon of particular symmetry and the electronic levels. The vibronic sideband for a single pure electronic transition in $CaF_2:Eu^{3+}$ is shown in Figure 14. The peak of the sideband is *ca.* 10^3 times weaker than the parent electronic transition shown on the right-hand side in Figure 14. This selectivity is available in both the excitation and fluorescence spectrum

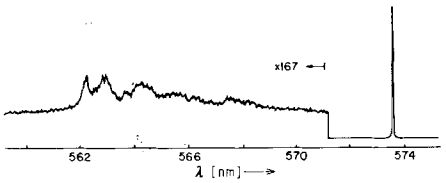


Fig. 14. The structure of the vibronic sideband for the $^7F_0 \rightarrow {}^5D_0$ transition of $CaF_2:Eu^{3+}$. The sensitivity at the lower wavelengths has been increased by a factor of 167 to make the vibronic sideband features visible.

and therefore results in a 10^6 rejection factor between ions that have close lines. If there are lines that lie outside of the region of vibronic sidebands (a region determined by the maximum phonon energy of the lattice; for CaF_2 this is *ca.* 370 cm^{-1}), the rejection factor is larger. This selectivity is more than adequate for performing multiple-ion analysis on samples containing all of the lanthanoids.

3.2. Analysis of Non-fluorescent Trivalent Ions

The clustering behavior that is observed at high lanthanoid concentrations suggests a way for extending the method to other ions that cannot fluoresce. If one wanted to perform a La^{3+} analysis (La^{3+} is a lanthanoid ion that has no excited electronic levels in the $4f^n$ electron configuration), a $CaF_2:Er^{3+}$ precipitate could be formed in the presence of a high Er^{3+} concentration and an unknown concentration of the La^{3+} analyte. Large numbers of Er^{3+} clusters would form, a few of which would also contain a La^{3+} ion. Since La^{3+} has a different ionic radius from Er^{3+}, the Er^{3+} ions in the clusters containing La^{3+} would have slightly different crystal field splittings from those of the Er^{3+} ions in pure Er^{3+} clusters. By selectively exciting the crystal field levels of the La^{3+}-containing clusters, one can obtain a spectrum of only these clusters. This procedure would establish a 1:1 relationship between the non-fluorescent and the fluorescent ion. The sensitivity of the technique depends upon how well one can measure the fluorescent ion. We have already seen that very low detection limits can be achieved by the methods described. The selectivity will depend upon how well the analyte's spectral lines can be resolved from the lines of other sites.

Naturally, this analytical method presents a problem. The success of the method rests upon the ability to discriminate between the weak lines of the clusters containing analytes and the much stronger lines of the pure clusters. Since the separations between the lines are not likely to be very large, one can expect that the lower detection limit is fixed by the selectivity of excitation. This limitation can be overcome by taking advantage of the efficient non-resonant energy transfer that occurs between ions in clusters. The rates of these processes for fluoride compensated clusters can be estimated from Figure 4. The energy mismatch can be estimated by constructing the double ion energy levels which show all the possible energy states for two ions. The double ion levels for Er are shown in Figure 15. The gap below the D level is large

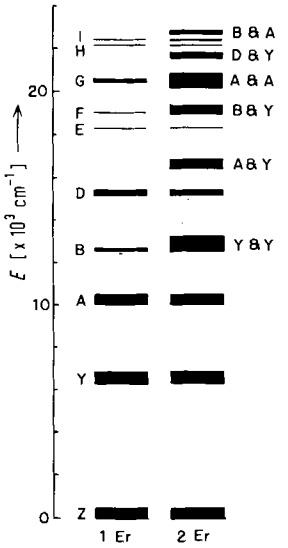


Fig. 15. Left: Electronic energy levels for a single Er^{3+} ion. Right: Possible levels for two Er^{3+} ions ("double ions").

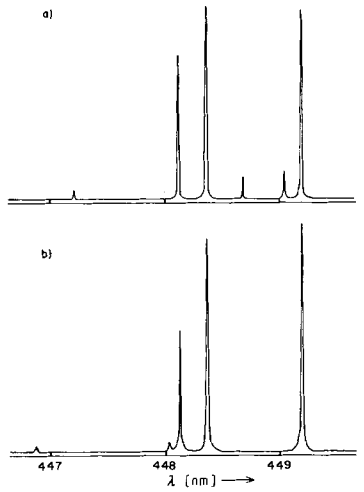


Fig. 16. Excitation spectrum of the $Z \rightarrow H(^4I_{15/2} \rightarrow {}^4F_{5/2})$ transition for a CaF_2 precipitate containing 0.02 mol-% Er^{3+} and a) 0.02 mol-% La^{3+} or b) 0.02 mol-% Ce^{3+}. The lines due to Er-La or Er-Ce clusters are seen by comparison with Figure 7c. A third line from the Er-Ce cluster is hidden by the line at 44.4 nm.

enough for D to fluoresce, while the gap below the E level is too small to allow efficient fluorescence. A cluster that contains two Er^{3+} ions should therefore not exhibit fluorescence from the E level but will fluoresce from the D level. If one of these Er^{3+} ions is replaced by a La^{3+} ion which has no electronic levels, the double ion levels of the Er-La dimer are identical to a single Er^{3+} ion's levels and both the E and D levels can fluoresce. The fluorescence spectrum from the E level can only contain contributions from the Er^{3+} ions that are paired with La^{3+}, while the fluorescence of the pure Er^{3+} cluster will be quenched.

Examples of typical excitation spectra for the detection of La^{3+} and Ce^{3+} are shown in Figure 16 when fluorescence from the E level is monitored with a wide bandpass instrument. Note the absence of lines from pure Er clusters. The relative line positions and intensities are similar to those of the pure Er cluster spectra shown in Figure 9 except that the exchange splittings are not observed and the line positions are shifted. There does not appear to be any simple correlation between the shifts and the ionic radius of the analyte. The technique retains the sensitivity of the direct lanthanoid method and can separate the different analyte peaks nicely by selective excitation. It has been used successfully for the analysis of Sc^{3+}, Y^{3+}, La^{3+}, Ce^{3+}, Gd^{3+}, and Lu^{3+} when Er^{3+} was used to monitor the fluorescence. These ions are the ones that could not be determined directly by the previously discussed method. The ions that can be determined directly will quench the Er^{3+} fluorescence if incorporated into a dimer and thus will not interfere in this method. Thus, this method is complementary to the direct method. All these studies are very new and there are still many factors which must be investigated. We are very pleased with these initial results and expect that the method will be suitable for practical applications.

3.3. Analysis of Non-fluorescent Ions Using Charge Compensation

The idea of achieving a 1:1 association between the analyte and a fluorescent ion, whose fluorescence is modified by the analyte, can be extended to other metal ions if one uses charge compensation to promote an association. In an arbitrary binary compound M_mX_n where the cation M is not trivalent, a trivalent lanthanoid dopant will require a charge compensation. This can be either an intrinsic compensation, such as a lattice vacancy, or an extrinsic compensation. There are several ways of achieving extrinsic compensation. If M is a divalent cation, the charge of the lanthanoid ion can be compensated by replacing another M ion by a monovalent cation. In this case only those monovalent cations are suitable whose ionic radii are close to that of the lanthanoid ion because both are substituting at the M ion lattice site. The charge of the lanthanoid ion can also be compensated by replacing an X ion by another anion that has one unit more negative charge. If M is a tetravalent cation, the lanthanoid ion can be compensated by replacing another M ion by a pentavalent cation with an ionic radius similar to that of the lanthanoid ion or by replacing an X ion by an anion with one unit smaller negative charge.

A less restrictive situation arises when a tertiary compound, $M_mA_nX_p$, is used. If M is again a non-trivalent ion which is replaced by a trivalent lanthanoid ion, the same kinds of charge compensation are possible as in the binary system. In addition, the A ion can be replaced by another ion which has a similar radius. Since the identity of A can be varied widely, the ions of most elements of the periodic systems are potential charge compensators. If M is a divalent cation and A is a cation, the lanthanoid ion can be charge compensated by replacing an A ion by an ion with one fewer positive charges. If M is a tetravalent cation, charge compensation is achieved by replacing A by an ion with one more positive charge.

Both the lanthanoid ion and its charge compensating ion have equal and opposite effective charges relative to the lattice and therefore tend to associate because of their Coulombic attraction. When the charge compensating ion enters the neighborhood of the lanthanoid ion, it changes the crystal fields at the lanthanoid site in a unique way. The new crystal field levels can be selectively excited or monitored in the presence of many other sites. If the charge compensator is an analyte, one can use the line positions to qualitatively indi-

cate the presence of the analyte and the line intensities to quantitatively measure its concentration. This method has been given the acronym SEPIL (*s*elective *e*xcitation of *p*robe *i*on *l*uminescence).

Procedures and guidelines had to be developed to aid the search for proper systems and techniques in order to put these ideas into practice. One of the first problems is the difficulty of carrying out a study of many materials, each of which can be prepared in different ways. Moreover, an arbitrary material generally contains several sites, each having their individual set of lines. Although selective excitation enables the lines in a spectrum to be classified according to the sites, the method requires a great deal of time, especially because one does not know where the lines are. Since the lines are sharp in both fluorescence and excitation, time must be spent at the beginning of studying a material, merely in order to determine the positions of the lines.

The problem of line sorting can be alleviated by using Eu^{3+} as the probe ion. Eu^{3+} has a singlet ground state ($^7F_0$) and a singlet excited state ($^5D_0$)[2]. Only one transition can occur between these two states in either fluorescence ($^5D_0 \rightarrow {}^7F_0$) or absorption ($^7F_0 \rightarrow {}^5D_0$). If one monitors the fluorescence from a material with a very wide bandpass so that all fluorescence can be seen and scans the excitation wavelength of a narrow bandwidth dye laser over the region of the $^7F_0 \rightarrow {}^5D_0$ transition, the resulting excitation spectrum will contain one line from each site. Thus in a single scan, one can obtain all of the information about the sites present in a material and an indication of their concentration. There is the possibility, however, that the lines for two sites accidentally appear at the same wavelength. Such an occurrence can be detected by reference to the many other transitions of Eu^{3+}. Of course it is not necessary to restrict the probe ion to Eu^{3+} after having carried out the initial experiments. A lanthanoid ion can be chosen which gives the best sensitivity and selectivity for the particular analysis.

There are a number of restrictions on the choice of material that can be used in guiding survey experiments to find suitable materials:

1) The short range order about a lanthanoid ion dopant must be sufficiently high that sharp line transitions occur.
2) Both the lanthanoid ion and the analyte ion must be incorporated into the lattice.
3) Both the lanthanoid ion and the analyte ion must be associated with each other.
4) The material must not quench fluorescence from the lanthanoid.

Our preliminary experiments have always been aimed at determining whether the particular material under study meets these requirements. If the material quenches fluorescence, there is little one can do with the material. In the preparation of a sample there are many variables which can affect whether a material meets the other requirements. These variables include the method of sample preparation (precipitation from solution, solid state reaction, cooling of a melt, molten flux reaction, solvent evaporation, *etc.*), the temperature of annealing, the type of reagents used and the valence state of the dopants, the method of incorporating the dopants (coprecipitation, diffusion, solid state reaction), the reaction vessel material used, and the atmosphere above the material during its preparation. Contamination must be carefully guarded against in the initial studies before one knows what ions a given material is sensitive to. Once a method of preparation is found which gives sharp lines and good intensities, different possible analytes are introduced into the material and the $^7F_0 \rightarrow {}^5D_0$ excitation spectrum is obtained to see if new sites are formed as a result of association between the lanthanoid ion and the analyte ion. The preparation variables, particularly the temperature of annealing and the type of reagents used, will also affect the association. The identification and development of suitable materials are therefore involved procedures. It is hoped that once experience has been gained on a number of representative materials, a more efficient method for obtaining suitable materials can be developed.

We have further restricted our survey experiments to materials that can be heated, so as to reduce the number of lattice defects, to permit diffusion of ions into association with each other, and to provide a range of annealing temperatures over which association can take place. We have used materials whose cations have ionic radii similar to those of the lanthanoids, and selected analyte ions whose ionic radii are close to the radius of the lattice ion which they replace.

The first example of a suitable system was $BaSO_4:Eu^{3+}$, PO_4^{3-}. $EuCl_3$ and Na_2SO_4 were added to a solution containing trace concentrations of PO_4^{3-} and $BaSO_4$ was precipitated by adding $BaCl_2$[73]. The Eu^{3+} and PO_4^{3-} coprecipitated with the $BaSO_4$. The excitation spectrum of the undried precipitate is complex and indicates the presence of at least 9 sites. There are two sites in the spectrum that are associated with presence of the PO_4^{3-} ions which compensate the Eu^{3+}-charge. The spectrum is poorly resolved however and cannot be easily used for PO_4^{3+} analysis. If the precipitate is heated, the spectrum and the site distribution change. The sites that correspond to associates with PO_4^{3-} disappear, as do many of the other sites. At higher temperatures between 800—1000 °C, the spectrum becomes sharper and a new, strong line appears that is proportional to the PO_4^{3-} concentration. The excitation spectra of a $BaSO_4$ precipitate ignited at 940 °C without and with the PO_4^{3-} analyte are shown in Figure 17a and b, respectively. The line at 578.2 nm corresponds to the site containing PO_4^{3-}. It should also be noted that the presence of PO_4^{3-} causes other sites to disappear, *e.g.* the site whose line appears at 574.9 nm. This effect is believed to be caused by the shift in the solid state equilibria that must occur when PO_4^{3-} is added (this will be discussed in more detail below).

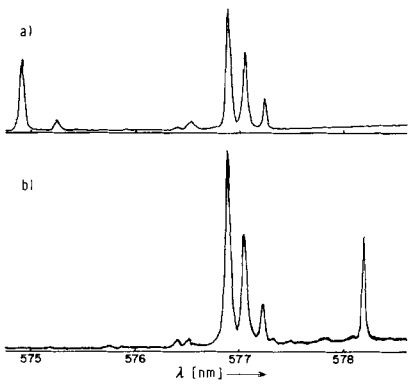


Fig. 17. The excitation spectrum of the $^7F_0 \rightarrow {}^5D_0$ transition of $BaSO_4:Eu^{3+}$ a) without PO_4^{3-} and b) with 4 ppm PO_4^{3-} in the Na_2SO_4 solution.

The methods described earlier in the paper can be used to isolate the transitions of the PO_4^{3-} site from those of the other sites in the spectrum. Remembering that the PO_4^{3-} line at 578.2 nm in Figure 17b represents a $^7F_0 \rightarrow {}^5D_0$ excitation transition that can equally well be observed in fluorescence ($^5D_0 \rightarrow {}^7F_0$), we can tune a monochromator to 578.2 nm and scan the dye laser wavelength over the spectral region of the electronic $^5D_2$-multiplet. The $^5D_2$ state, with $J=2$, will have $(2J+1)$ crystal field levels. The $^7F_0 \rightarrow {}^5D_2$ transition can therefore be expected to have five transitions for each site. The experimentally observed spectrum is shown in Figure 18. It contains exactly five lines, and there are no indications of lines from other sites as might be expected from the well-resolved lines of Figure 17. Thus Figure 18 demonstrates once again the high selectivity of the technique for specific analytes.

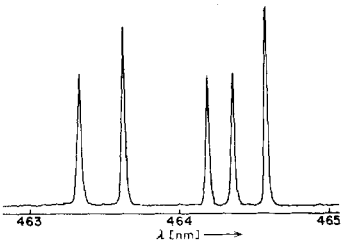


Fig. 18. Single site excitation spectrum of the $^7F_0 \rightarrow {}^5D_0$ transition in $BaSO_4$: EU^{3+}, PO_4^{3-} obtained by monitoring the $^5D_0 \rightarrow {}^7F_0$ transition at 578.2 nm for the PO_4^{3-} site.

Other systems have also been found that are suitable materials for this procedure. Two examples of such materials are shown in Figures 19 and 20: the $^7F_0 \rightarrow {}^5D_0$ excitation spectrum of $Ca_2Nb_2O_7:Eu^{3+}$ both undoped and doped with Zr^{4+}, and of $CdMoO_4:Eu^{3+}$ both undoped and doped with Nb^{5+}. In the spectra new lines appear that are characteristic of the presence of Zr^{4+} and Nb^{5+}, respectively, and can be used for their analysis. Other systems have been found that give analyte lines for Li^+, Na^+, V^{5+}, Ta^{5+}, Cu^+, Ag^+, Bi^{3+}, Sb^{5+}, As^{5+}, Hg^+, and S^{2-}. Work is continuing on these systems.

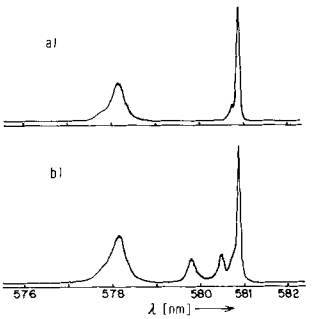


Fig. 19. $^7F_0 \rightarrow {}^5D_0$ excitation spectrum obtained by wide bandwidth monitoring of a $Ca_2Nb_2O_7$ sample containing a) Eu^{3+} and b) Eu^{3+} and Zr^{4+}.

The addition of an analyte ion to a system can have other effects. In many cases, lines characteristic of an analyte-lanthanoid site fail to appear, while lines for an intrinsically compensated lanthanoid site disappear upon adding a charge compensating ion. Such an example is shown in Figure 21 for $PbMoO_4:Eu^{3+}$. If no analyte ions are introduced as charge compensators, the two lines in the $^7F_0 \rightarrow {}^5D_0$ excitation spectrum of Figure 21a indicate there are two major sites intrinsic to the material. If As^{5+} is added for charge

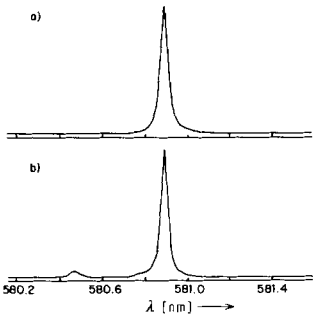


Fig. 20. The $^7F_0 \rightarrow {}^5D_0$ excitation spectrum obtained by wide bandwidth monitoring of a $CdMoO_4$ sample containing a) Eu^{3+} and b) Eu^{3+} and Nb^{5+}.

compensation, the intensity of the main line increases dramatically and the weaker line disappears. Clearly the As^{5+} has an effect on the site distribution—but no new lines are formed.

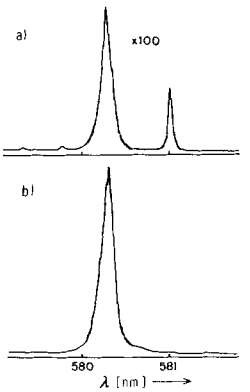


Fig. 21. $^7F_0 \rightarrow {}^5D_0$ excitation spectrum obtained by wide bandwidth monitoring of a $PbMoO_4$ sample containing a) Eu^{3+} and b) Eu^{3+} and As^{5+}.

Even more dramatic changes are observed in the case of $SrSO_4:Eu^{3+}$. Figure 22a shows the spectrum of $SrSO_4:Eu^{3+}$ without extrinsic charge compensation. The Eu^{3+} occupies one intrinsic site. If PO_4^{3-} is added as a charge compensator, a completely new set of lines forms and the intrinsic line disappears (Fig. 22b).

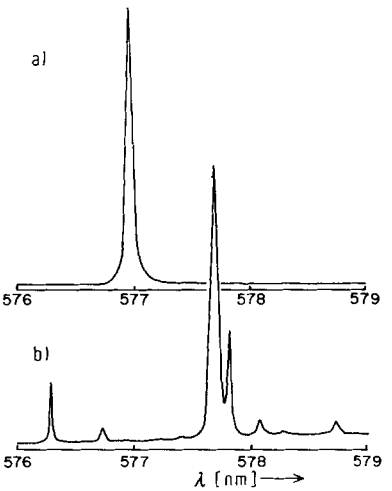


Fig. 22. $^7F_0 \rightarrow {}^5D_0$ excitation spectrum obtained by wide bandwidth monitoring of a $SrSO_4$ sample containing a) Eu^{3+} and b) Eu^{3+} and 5 μg/ml PO_4^{3-}.

All of the examples given are unsuitable for practical applications at the present time because the intensity of the

analyte lines is a non-linear function of concentration. At high concentrations the intensity becomes constant, while at low concentrations it plummets so rapidly that one cannot work below concentrations of about 50 ppb in most cases. If this problem were eliminated, the characteristics of the technique would be very similar to the excellent methods described earlier in Sections 2.1 and 2.2 for lanthanoid analysis.

In order to get an insight into the reasons for the observed behaviors, let us consider the solid state equilibria that should be involved in this problem. Assume we have a binary compound MX, in which M and X are divalent, and that the dominant defects of the compound are the Shottky defects, *i.e.* cation and anion vacancies. A trivalent lanthanoid ion, R^{3+}, and a trivalent anion analyte, A^{3-}, are present as dopants. The relevant equilibria are the following:

$$\begin{array}{lll} \text{MX perfect lattice} \rightleftharpoons & V_M'' & + \; V_X'' \\ & + & + \\ & 2R_M^{\cdot} & + \; 2A_X' \rightleftharpoons 2(R_M \cdot A_X)^x \\ & \downarrow\uparrow & \downarrow\uparrow \\ & (2R_M \cdot V_M)^x & (2A_X \cdot V_X)^x \end{array}$$

where the notation of *Kröger-Vink* has been used[45]. Notice the similarity between these equilibria and the familiar set of EDTA equilibria of analytical importance. The intrinsic vacancies V_M'' and V_X'' play the role of H^+ and OH^- which are formed on dissociation of the H_2O solvent. The $(2R_M \cdot V_M)^x$ species is analogous to the metal hydroxide complexes that form in aqueous solution, while the $(2A_X \cdot V_X)^x$ species is analogous to the different protonated species of the EDTA weak acid. The $(R_M \cdot A_X)^x$ species is the analytically important complex we are interested in observing and is analogous to the metal-EDTA chelate. It is well known that the key to using EDTA as a chelating agent lies in controlling the pH. Too acidic a solution results in an unfavorable conditional formation constant causing dissociation of the chelate, while too basic a solution precipitates the metal hydroxide. One might expect the same ideas would apply to the defect equilibria, where the V_M'' and V_X'' concentrations must be controlled. These concentrations were not controlled in the examples given. Addition of analyte ion would raise the concentration of V_X'' by an amount that depended upon the stability of the $(2A_X \cdot V_X)^x$ pair and, as a result, the concentration of V_M'' would decrease. The $(2R_M \cdot V_M)^x$ species would then tend to dissociate. The addition of analyte ions has two effects in this situation—the shift in defect equilibria and the formation of the analytically interesting $(R_M \cdot A_X)^x$ pairs. An analytical procedure, however, should have the relevant equilibria fixed at optimal values by suitable buffers while the analyte is added. It is believed that the failure to buffer the equilibria is the cause of the non-linear working curves and the plummeting of the intensity at low concentrations. The situation is analogous to the non-linear behavior that has been observed for the fluoride compensated lanthanoid ions in CaF_2; the kind of non-linearity is the same. We are presently studying the control of these equilibria by the atmosphere above the reaction vessel and by addition of other aliovalent ions.

This picture also enables a description of the different behavior observed in materials after addition of the analyte ion A^{3-}. If the equilibrium constant for the formation of $(R_M \cdot A_X)^x$ is much larger than the constants of the other equilibria, the addition of A^{3-} will lead to formation of the species $(R_M \cdot A_X)^x$ and force dissociation of the $(2R_M \cdot V_M)$ species. A behavior such as that shown in Figure 22 would then be observed. If the formation constants for both the species $(R_M \cdot A_X)^x$ and $(2R_M \cdot V_M)^x$ are large, addition of A^{3-} will cause new lines to form without destroying the lines from the intrinsic sites. A behavior such as that shown in Figures 19 and 20 might then be expected. If the formation constants of the $(R_M \cdot A_X)^x$ and $(2A_X \cdot V_X)^x$ species are small, the concentration of V_X'' will be raised as A^{3-} is added to the system; this will lower the V_M'' concentration and cause dissociation of $(2R_M \cdot V_M)^x$. In this case the system might behave similarly as shown in Figure 21.

The picture presented above is quite speculative and is not meant as a definitive explanation of experimental observations. It is certainly oversimplified and omits many important factors such as the interaction with other defects or impurities, the equilibria with atmospheric species and the reaction vessel, the distribution coefficients into the various phases, and the possibility of having several types of defects. It is certainly inadequate for explaining the complex behavior of the $BaSO_4$ system shown in Figure 17. Instead, the picture is meant to focus on the key parts of this method of analysis to provide a framework for organizing previous observations and guiding the ideas of future work. It is a tentative picture at best and can be expected to change appreciably as further work is done in this area.

3.4. Analysis with Pure Lanthanoid Compounds

There are other methods of causing an analyte ion to associate with a fluorescent probe ion. One of the simplest is to form a pure, fluorescent lanthanoid compound in the presence of an analyte ion. Anything that enters the lanthanoid lattice will have to perturb many lanthanoid ions and give rise to new lanthanoid sites which can be identified spectroscopically. Again, selectivity is the key to a successful technique. The site associated with an analyte ion must be measured in the presence of a much larger population of intrinsic sites. There is a severe limitation in the choice of lanthanoid as lattice cation, since rapid exciton migration to quenching ions and energy transfer processes prevent fluorescence from most pure materials[66]. Generally, fluorescence can be obtained from Eu^{3+}, Tb^{3+}, and Yb^{3+} compounds (and occasionally from Gd^{3+} compounds) whose large energy gaps prevent efficient energy transfer.

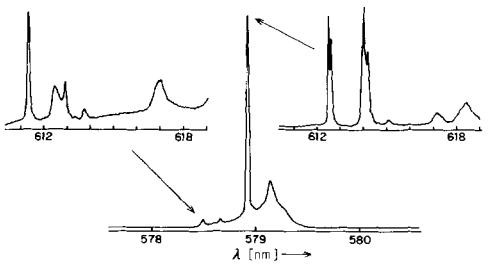


Fig. 23. Bottom: $^7F_0 \rightarrow {}^5D_0$ excitation spectrum of a $Eu_2(SO_4)_3$ sample formed from a solution containing 5×10^{-4} mol/l PO_4^{3-}. Top: Fluorescence spectra that result if the dye laser is tuned to either of the marked lines ($^5D_0 \rightarrow {}^7F_2$ transition).

$Eu_2(SO_4)_3$ (: PO_4^{3-}) was prepared by rapidly evaporating a solution of $Eu_2(SO_4)_3$ in the presence of PO_4^{3-}. The $^7F_0 \rightarrow {}^5D_0$ excitation spectrum of this material is shown in Figure 23 (below). It contains one very intense and sharp line and a band at higher wavelength whose intensity varies from sample to sample. Two additional weak lines appear at short wavelengths with intensities which are proportional to the PO_4^{3-} concentration. Although it would appear difficult to measure these lines at much smaller concentrations because of the very large intensity of the neighboring intrinsic peak, it is possible to selectively excite these lines and obtain fluorescence spectra that are free of fluorescence from the main intrinsic site. This is illustrated in Figure 23 (above left) for the weak line at 578.5 nm; also illustrated (above, right) is the spectrum obtained on excitation of the intrinsic line at 578.1 nm. The selective excitation allows one to follow the fluorescence of this PO_4^{3-} site down to 0.3 ppm PO_4^{3-}, at which point it is obscured by a background fluorescence.

A difficulty that was encountered in this work was the inability to selectively excite the PO_4^{3-} site using other excited levels. For example, if any of the lines occurring in the fluorescence shown in Figure 23 were monitored as an excitation spectrum of the $^7F_0 \rightarrow {}^5D_2$ transition was obtained, all of the excitation spectra would be identical. Excitation anywhere in the $^5D_2$-multiplet results in exactly the same fluorescence spectrum. This behaviour suggests that rapid energy transfer can occur from either the $^5D_2$ or $^5D_1$ excited states to the Eu^{3+} site which has the lowest $^5D_0$ energy, where it becomes trapped and must fluoresce. The lower part of Figure 23 shows that the PO_4^{3-} sites have $^5D_0$ states whose energy is higher than that of the other intrinsic sites (since they appear at shorter wavelength). Therefore they can transfer energy to the intrinsic sites. If the $^5D_0$ state is excited directly, this energy transfer between sites does not occur, probably because the density of phonon states available at these small energy differences is too small to allow efficient non-resonant energy transfer. This explanation immediately suggests that if the introduction of an analyte ion produces a Eu^{3+} site with a lower $^5D_0$ state than the intrinsic sites, energy transfer to this site should be very efficient and would greatly enhance the fluorescence intensity for such a site. Such a system might be of great analytical interest.

3.5. Analysis of Complexing Agents

Another method of achieving an association between a lanthanoid probe ion and an analyte ion is to form complexes of the two ions in aqueous solutions. One is again restricted in the choice of lanthanoid ions that can be used for such experiments since the high vibrational energies of water strongly favor multiphonon processes. Only the ions with very large energy gaps, such as Eu^{3+}, Tb^{3+}, and Gd^{3+}, can fluoresce.

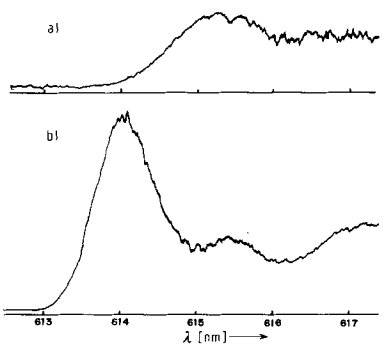


Fig. 24. $^5D_0 \rightarrow {}^7F_2$ fluorescence spectrum of a) a $Eu(NO_3)_3$ solution and b) of a $EuCl_3$ solution.

Figure 24a shows the $^5D_0 \rightarrow {}^7F_2$ fluorescence spectrum of a $EuCl_3$ solution while Figure 24b shows the $^5D_0 \rightarrow {}^7F_2$ fluorescence spectrum of a $Eu(NO_3)_3$ solution. Although the lines are quite broad, the $Eu(NO_3)_3$ fluorescence can be distinguished from the fluorescence of the uncomplexed Eu^{3+}. Figure 25 shows the $^7F_0 \rightarrow {}^5D_2$ excitation spectra of uncomplexed and complexed Eu^{3+}. Again the lines are broad but separated sufficiently enough to distinguish between complexed and uncomplexed Eu^{3+}. Thus despite the large linewidths of Eu^{3+} in solution, it is still possible to obtain good selectivity for NO_3^- because of the large separations of its lines in both the excitation and fluorescence spectra.

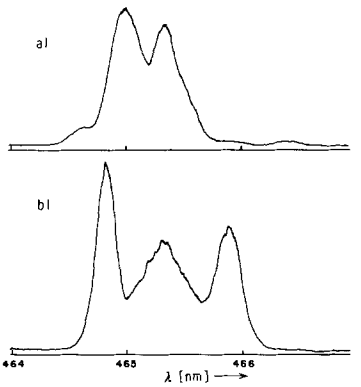


Fig. 25. $^7F_0 \rightarrow {}^5D_2$ excitation spectrum of a) a $EuCl_3$ solution and b) a $Eu(NO_3)_3$ solution.

4. Conclusions

In this paper, we have shown how the laser excitation techniques provide a way of obtaining direct information about the microscopic details of the clustering processes in fluorite materials. EPR methods have failed in this respect—for reasons which are still unknown. The many different bulk measurements that have been made require theoretical modeling in order to glean microscopic information, and they lack the selectivity required to study the many different kinds of sites. The selective excitation of lanthanoid probe ions offers a new approach to the problem. The sensitivity and selectivity of laser excitation methods provide a way of examining sites in a material whose concentrations differ by several orders of magnitude. It is expected that these advantages will result in laser and lanthanoid spectroscopy playing a far greater role in the quest to understand the basic chemical processes which control the solid state chemistry of a material.

We have also outlined a very different method of performing chemical measurements at the trace level. The direct excitation of a lanthanoid ion has resulted in the ability to detect 25 parts in 10^{15} of a lanthanoid in aqueous solution with very high selectivity for the specific lanthanoid of interest. We have shown how non-fluorescent ions can be measured with a similar sensitivity and selectivity by forcing the system

to dimerize and causing a 1:1 association between the non-fluorescent analyte ion and a fluorescent lanthanoid probe ion. Extension of this idea to other ions of the periodic system can be accomplished by using charge compensation to cause the 1:1 pairing between analyte ion and fluorescent lanthanoid ion. The procedures for lanthanoid analysis work quite nicely and we believe they presently constitute one of the best ways of performing analytical measurements on lanthanoids. There is still much work that needs to be done before practicable methods for the real analytical determination of other ions in the periodic system are available, but the method has great promise.

This paper has outlined two applications of the idea of using lanthanoid probe ions with selective laser excitation methods to study complex materials. We believe there are many applications that remain to be tried. The spectra of the lanthanoids provide information at the atomic level about the short range environments of a material, indeed with a sensitivity and selectivity that are difficult to match with other techniques. These are the very properties that modern researchers need in their effort to understand fundamental processes and to further improve the limits of detection.

This research was supported by the National Science Foundation under grants CHE74-24394 A-1 and DMR77-07765.

Received: July 31, 1978 [A 289 IE]
German version: Angew. Chem. *91*, 765 (1979)

[1] *J. Becquerel*, Z. Phys. *58*, 205 (1929).
[2] *G. H. Dieke:* Spectra and Energy Levels of Rare Earth Ions in Crystals. Interscience, New York 1968.
[3] *B. G. Wybourne:* Spectroscopic Properties of Rare Earths. Interscience, New York 1965.
[4] *R. B. Chesler, J. E. Geusic* in *F. T. Arecchi, E. O. Schulz-Dubois:* Laser Handbook I. North-Holland, Amsterdam 1972, p. 325.
[5] *L. A. Riseberg, M. J. Weber*, Prog. Opt. *14*, 90 (1976).
[6] *B. DiBartolo:* Optical Interactions in Solids. Wiley, New York 1968.
[7] *C. W. Rector, B. C. Pandey, H. W. Moos*, J. Chem. Phys. *45*, 171 (1966).
[8] *R. H. Heist, F. K. Fong*, Phys. Rev. *B1*, 2970 (1970).
[9] *R. E. Bradbury, E. Y. Wong*, Phys. Rev. *B4*, 690, 694, 702 (1971).
[10] *Yu. K. Voron'ko, A. A. Kaminskii, V. V. Osiko*, Sov. Phys. JETP *23*, 10 (1966).
[11] *A. A. Kaplyanskii, S. A. Basoon, V. A. Rachin, R. A. Titov*, Pisma Zh. Eksp. Teor. Fiz. *21*, 438 (1975).
[12] *A. A. Kaplyanskii, S. A. Basoon, V. A. Richin, R. A. Titov*, Fiz. Tverd. Tela *17*, 3661 (1975).
[13] *K. F. Renk, J. Deisenhofer*, Phys. Rev. Lett. *26*, 764 (1971).
[14] *W. E. Bron, W. Grill*, Phys. Rev. *B16*, 5303, 5315 (1977).
[15] *R. S. Meltzer, J. E. Rives*, Phys. Rev. *B15*, 2442 (1977).
[16] *P. M. Selzer, W. M. Yen*, Phys. Rev. Lett. *38*, 858 (1977).
[17] *Yu. K. Voron'ko, A. A. Kaminskii, V. V. Osiko*, Sov. Phys. JETP *22*, 501 (1966).
[18] *Yu. K. Voron'ko, A. A. Kaminskii, V. V. Osiko, A. M. Prokhorov*, JETP Lett. *1*, 120 (1965).
[19] *D. R. Tallant, J. C. Wright:* Proceedings of the 11th Rare Earth Research Conference 1974.
[20] *D. R. Tallant, J. C. Wright*, J. Chem. Phys. *63*, 2074 (1975).
[21] *L. Dubicki, J. Ferguson, G. A. Osborne, I. Trabjerg:* Spectroscopie des Éléments de Transition et des Éléments Lourds dans les Solides. No. 255. CRNS, Paris 1977.
[22] *W. Van Gool:* Principles of Defect Chemistry of Crystalline Solids. Academic Press, New York 1966.
[23] *W. Hayes:* Crystals with the Fluorite Structure. Clarendon Press, Oxford 1974.
[24] *N. B. Hannay:* Treatise on Solid State Chemistry. Plenum Press, New York 1975.
[25] *C. N. R. Rao:* Solid State Chemistry. Marcel Dekker, New York 1974.
[26] *J. B. Goodenough, M. S. Whittingham:* Solid State Chemistry of Energy Conversion and Storage. American Chemical Society, Washington 1977.
[27] *A. D. Franklin*, J. Nonmetals *1*, 27 (1972).
[28] *A. K. Cheetham, B. E. F. Fender, D. Steele, R. I. Taylor, B. T. M. Willis*, Solid State Commun. *8*, 171 (1970).
[29] *A. K. Cheetham, B. E. F. Fender, M. J. Cooper*, J. Phys. *C4*, 3107 (1971).
[30] *D. Steele, P. E. Childs, B. E. F. Fender*, J. Phys. *C5*, 2677 (1972).
[31] *J. Makovsky*, Phys. Rev. Lett. *15*, 953 (1965).
[32] *I. B. Aizenberg, M. S. Orlov, A. L. Stolov*, Sov. Phys. Solid State *15*, 1240 (1973).
[33] *P. P. Yaney, D. M. Schaeffer, J. L. Wolf*, Phys. Rev. *B11*, 2460 (1975).
[34] *N. E. Kask, L. S. Kornienko, M. Fakir*, Sov. Phys. Solid State *6*, 430 (1964).
[35] *Kh. S. Bagdasarov, Yu. K. Voron'ko, A. A. Kaminskii, L. V. Krotova, V. V. Osiko*, Phys. Status Solidi *12*, 905 (1965).
[36] *Yu. K. Voron'ko, A. A. Kaminskii, V. V. Osiko*, Sov. Phys. JETP *22*, 295 (1966).
[37] *J. Fontanella, C. Andeen*, J. Phys. *C9*, 1055 (1976).
[38] *A. Edgar, H. K. Welsh*, J. Phys. *C8*, L336 (1975).
[39] *J. H. Chen, M. S. Donough*, Phys. Rev. *185*, 453 (1969).
[40] *C. Burely, F. Gonzales-Jimenez, P. Imbert, F. Varret*, J. Phys. Chem. Solids *36*, 683 (1975).
[41] *M. R. Mustafa, W. E. Jones, B. R. McGarvey, M. Greenblatt, E. Banks*, J. Chem. Phys. *62*, 2700 (1975).
[42] *E. L. Kitts, M. Ikeya, J. H. Crawford*, Phys. Rev. *B8*, 5840 (1973).
[43] *A. Edgar, C. A. Freeth, G. D. Jones*, Phys. Rev. *B15*, 5023 (1977).
[44] *C. Andeen, D. Lonk, J. Fontanella*, Phys. Rev. *B16*, 3762 (1977).
[45] Throughout the paper, we will use the notation of *Kröger-Vink* [22]. The subscript indicates the lattice site, the symbol represents the type of occupancy of that site, and the superscript indicates the effective charge relative to the lattice where ′ is negative, • is positive, and x is neutral.
[46] *F. K. Fong*, Prog. Solid State Chem. *3*, 135 (1966).
[47] *R. H. Heist, F. K. Fong*, Phys. Rev. *B1*, 2970 (1970).
[48] *M. J. Weber, R. W. Bierig*, Phys. Rev. *A134*, 1492 (1964).
[49] *U. Ranon, J. S. Hyde*, Phys. Rev. *141*, 259 (1966).
[50] *E. Secemski, W. Low*, J. Chem. Phys. *64*, 4240 (1976).
[51] *J. M. O'Hare, T. P. Graham, G. T. Johnston*, J. Chem. Phys. *64*, 4242 (1976).
[52] *F. K. Fong*, J. Chem. Phys. *64*, 4243 (1976).
[53] *A. D. Franklin, S. Marzullo*, Proc. Brit. Ceram. Soc. *19*, 135 (1971).
[54] *A. D. Franklin*, U.S.N.T.I.S. AD Rep. 748259 (1971).
[55] *J. M. O'Hare*, J. Chem. Phys. *57*, 3838 (1972).
[56] *G. K. Miner, T. P. Graham, G. T. Johnston*, J. Chem. Phys. *57*, 1263 (1972).
[57] *M. R. Brown, K. G. Roots, J. M. Williams, W. S. Shand, C. Grater, H. F. Kay*, J. Chem. Phys. *50*, 891 (1969).
[58] *A. D. Franklin*, J. Chem. Phys. *64*, 1509 (1976).
[59] *C. R. A. Catlow*, J. Phys. *C9*, 1859 (1976).
[60] *D. R. Tallant, M. P. Miller, J. C. Wright*, J. Chem. Phys. *65*, 510 (1976).
[61] *D. R. Tallant, D. S. Moore, J. C. Wright*, J. Chem. Phys. *67*, 2897 (1977).
[62] *J. C. Wright:* Spectroscopie des Éléments de Transition et des Éléments Lourds dans les Solides No. 255. CRNS, Paris 1977.
[63] *M. D. Kurz, J. C. Wright*, J. Lumin. *15*, 169 (1977).
[64] *M. P. Miller, J. C. Wright*, J. Chem. Phys. *68*, 1548 (1978).
[65] *J. B. Fenn, J. C. Wright, F. K. Fong*, J. Chem. Phys. *59*, 5591 (1973).
[66] *J. C. Wright:* Radiationless Processes in Molecules and Crystals. Vol. 15. Springer, Berlin 1976.
[67] *F. J. Gustafson, J. C. Wright*, Anal. Chem. *49*, 1680 (1977).
[68] *G. M. Zverev, A. I. Smirnov*, Sov. Phys. Solid State 9, 1586 (1968).
[69] *A. F. Leung*, J. Phys. *C6*, 2234 (1973).
[70] *C. Yang, S. Lee, A. J. Bevelo*, Phys. Rev. *B12*, 4687 (1975).
[71] *T. Rs. Reddy, E. R. Davies, J. M. Baker, D. N. Chambers, R. C. Neumann, B. Uzbay*, Phys. Lett. *A36*, 231 (1971).
[72] *J. M. Baker, E. R. Davies, T. Rs. Reddy*, Contemp. Phys. *13*, 45 (1967).
[73] *J. C. Wright*, Anal. Chem. *49*, 1690 (1977).

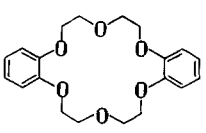
Multidentate Acyclic Neutral Ligands and Their Complexation

By Fritz Vögtle and Edwin Weber[*]

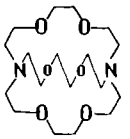
The properties of cyclic crown ethers are approximated by acyclic neutral ligands (podands), which are compared and contrasted with open-chain bioionophores and acidic chelating agents in this article. Variations of the *endo*-polarophilicity/*exo*-lipophilicity balance, complex stability, ion selectivity can often be accomplished more easily, with greater versatility, and at less expense with acyclic polyethers than with their cyclic counterparts; complexation and decomplexation are generally faster in acyclic systems; and the pseudocavity usually has greater conformational flexibility. Acyclic crown ethers and open-chain cryptands stiffened by rigid "terminal groups" containing donor atoms readily form crystalline complexes of alkali and alkaline earth metals. Some open-chain neutral ligands form helical conformations in their crystalline complexes. The observed coordination numbers and geometries are of theoretical interest. Attractive terminal group interactions lead to pseudocyclic species occupying a position intermediate between cyclic and acyclic ligands. It has recently proved possible to isolate crystalline complexes of alkali and alkaline earth metal ions with weakly donating oligo(ethylene glycol ethers) and with glycols; such complexes have also been obtained with sugars. Acyclic neutral ligands can serve as simple models of nigericin-type bioionophores and be used analytically in microelectrodes. The recently discovered crystalline stoichiometric complexes formed by some acyclic neutral ligands with guest molecules such as urea, thiourea, and water provide a fresh insight into weak interactions between neutral molecules and for the development of urea receptors.

1. Introduction[1]

Induced by formation of alkali metal ion complexes by dibenzo[18]crown-6 *(1)*[2], the range of available synthetic crown ethers[1] was first extended by variation of ring size and of donor atoms in the monocyclic representatives[3] and by the preparation of bi- [*e.g. (2)*] and oligocyclic cryptands[4][**]:

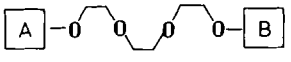


(1)

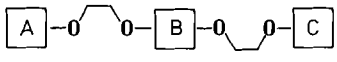


(2)

The *open-chain* bioionophores such as nigericin *(5)*[5] (see Table 1) which like the cyclic bioionophores nonactin and valinomycin[6] can complex alkali metal ions with a remarkable degree of selectivity[7] prompted the study of acyclic oligoethers. The exceptional properties of the cyclic crown ethers offer the only explanation for the dearth of work performed with simple acyclic neutral ligands of types *(3)* and *(4)* (A, B, C are any structural units, *vide infra*). The latter have the advantage of facile synthesis, which requires use of neither dilution principle[8] nor template effect[9] and is therefore inexpensive[10], of versatility of ligand structure[1b,1e], and of fast complex formation (see Section 4.2.5).



(3)



(4)

In order to demonstrate the importance of open-chain ligands of crown ether type (podands), we shall first consider corresponding natural ionophores and, for purposes of demarcation, the alkali metal ion complexes of "acidic" chelate-forming ligands.

2. Acyclic Ionophoric Antibiotics

Ionophoric antibiotics are lipid-soluble natural products which form complexes with alkali or alkaline earth metal ions and can thus influence the transport of ions through membranes[11]. They can be divided into several groups on the basis of structural features[6,7,12]:

a) *Peptides*[13], *acyclic* ionophoric antibiotics (gramicidin[14]; alamethicin[15]) with up to 20 amino acid units, and also *cyclic* ones (antamanide[16]);

b) *Polyenes*[17] and *polyethers,* including the *open-chain* nigericin antibiotics, nigericin *(5)*[5], grisorixin *(6)*[18], dianemycin *(7)*[19], monensin *(8)*[20], X-206 *(9)*[21], X-537 A *(10)*[22] (see Table 1), and *cyclic* macrolide *esters* of the actin series (nonactin to tetranactin)[23];

c) *Depsipeptides*[12] (valinomycin, enniatin, monamycin, beauvericin), *i.e.* ester amides. They usually have cyclic structures, frequently with unusual ring sizes, which may contain uncommon amino acids.

Most of the acyclic (or pseudocyclic, *vide infra*) ionophores have a polyether structure. Of physiological[24] and clinical importance[25] are their selectivities for various cations[7]:

[*] Prof. Dr. F. Vögtle, Dr. E. Weber
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, 5300 Bonn (Germany)

[**] We propose the following rule in the interest of systematic use of the terms crown ether, coronand, cryptand, and podand: *coronands* are taken to mean medio- and macro*mono*cyclic compounds with any heteroatoms. *Cryptands* are *bi-* and *poly*cyclic compounds with any heteroatoms, *podands* are acyclic coronand and cryptand analogs with any heteroatoms. The term *crown ether* is used for coronands having only oxygen as heteroatom.

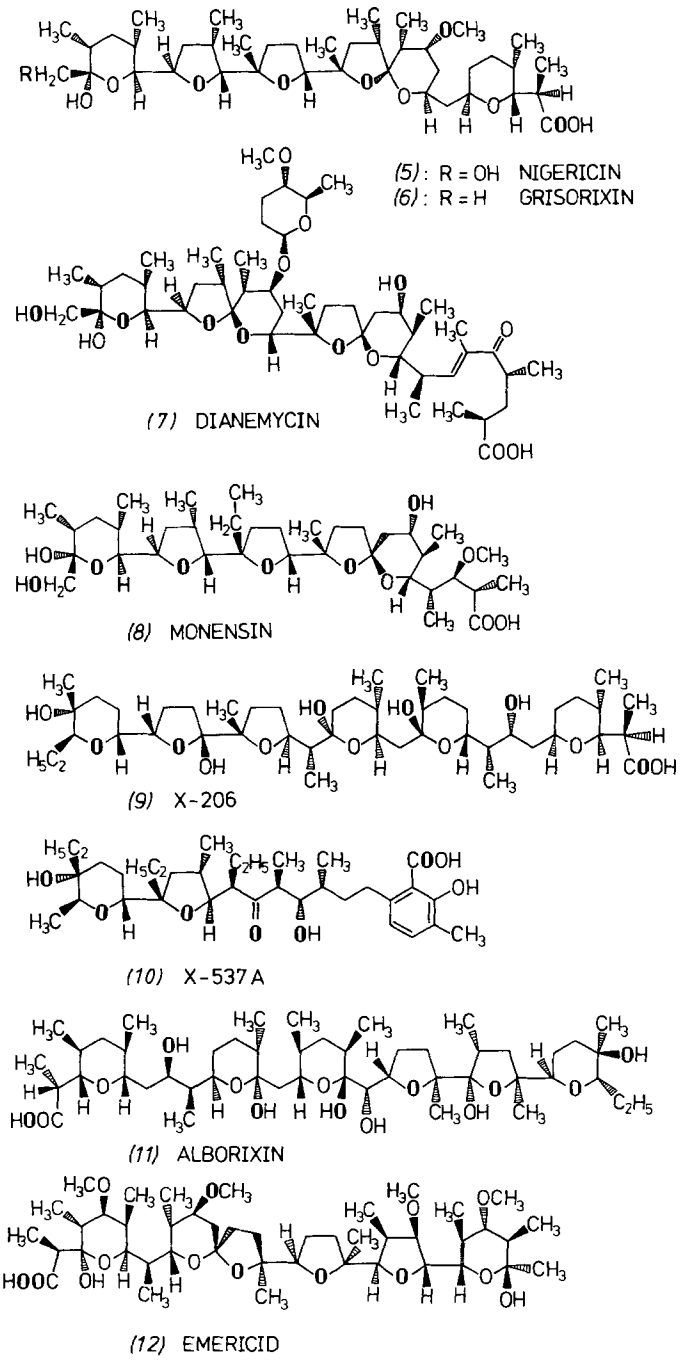
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0753 $ 02.50/0*

While the open-chain nigericin *(5)* (like most cyclic ionophores) shows a preference, *e.g.* for $K^{\oplus}$ over $Na^{\oplus}$[26], the order $Na^{\oplus} > K^{\oplus}$ applies to monensin *(8)*, also in biological systems[26,27].

On complexation, acyclic antibiotics (*e.g.* nigericin) wrap themselves around the cation like a *pseudocyclic* species. As with cyclic ligands[28], this enclosure of the ions occurs in such a way that polar regions (ether, carbonyl oxygens) of the ligands are directed inward (*endo*-hydrophilic or *endo*-polarophilic) towards the cation; the periphery of the complex therefore consists of lipophilic regions (CH_2 groups, alkyl groups, aliphatic rings) making the complex *exo*-lipophilic and thus soluble in lipophilic media (organic solvents, biological membranes). The generally flexible open-chain bioionophore changes its conformation on complexation; it usually becomes less mobile. This affects, *e.g.* the rate of complexation and of the dissociation of the complex into its components[12]. In the case of monobasic acids, the pseudocyclic species are stabilized by terminal group interactions, in the complex and in the free ligand[29,30]. In the latter case, the pseudocavity is usually occupied by an additional water molecule[6,12].

Monensin *(8)*[20], nigericin *(5)*[5], grisorixin *(6)*[18], X-537 A *(10)*[22], alborixin *(11)*[31], and emericid *(12)*[32] (Table 1) are well characterized carboxylic antibiotics. They all possess an acyclic primary structure but may adopt cyclic tertiary structures as a result of hydrogen bonding. X-ray structure analyses[20b] show the free acid monensin *(8)* to exist in a cyclic arrangement with two intramolecular H bonds between the C=O group and a water molecule which holds the two ends of the chain together (Fig. 1a). Complexation of an $Ag^{\oplus}$ ion leads to differing H bonding[33]; however, the C=O does not coordinate the central ion according to X-ray structure analyses[20c] (see Fig. 1b). In the free ligands, the water molecules bound by H bonds appear to play an important role in complexation, in that they affect the hydration sphere of the central ion[12].

Table 1. Important acyclic ionophoric antibiotics. Coordinated oxygen atoms are shown in bold type.



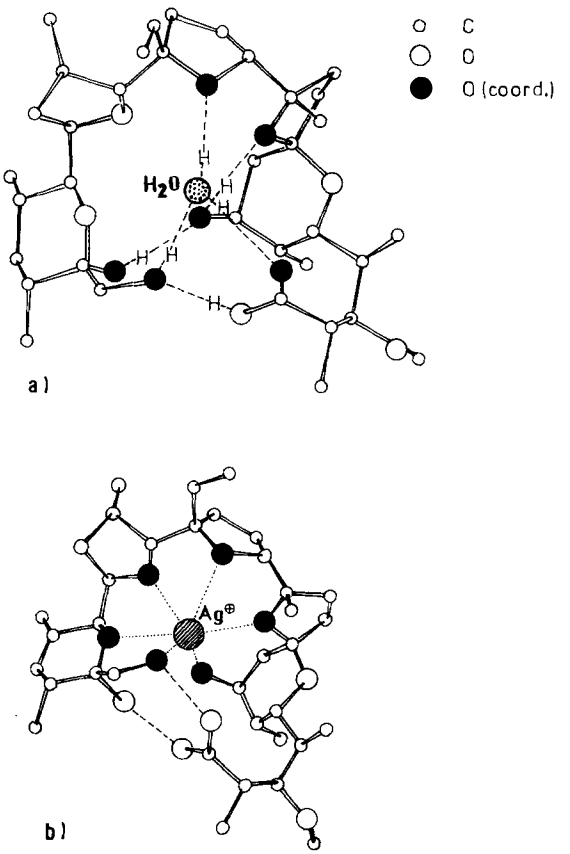


Fig. 1. a) Structure of monensin *(8)*-monohydrate. H-bonds shown as dashed lines. b) Fine structure of the monensin-$Ag^{\oplus}$ complex. Metal/oxygen contacts shown as dotted lines. Two H bonds (dashed) are responsible for the pseudocyclic ligand conformation [28].

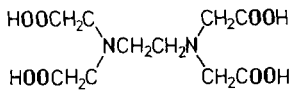
The silver salts of the ionophoric antibiotics nigericin *(5)*[5b] and grisorixin *(6)*[18b] resemble the monensin-$Ag^{\oplus}$ salt[20c], except that the silver ion is coordinated by the C=O group.

The $Ba^{2\oplus}$ complex of X-537 A *(10)* crystallizes as an aggregate of two molecules of antibiotic, one $Ba^{2\oplus}$ ion, and one molecule of water of solvation[34]. Six oxygen atoms of one ionophore molecule and two of the other coordinate the cation. In the dimeric $Ag^{\oplus}$ complex of X-537A, the $Ag^{\oplus}$ ions are enclosed in almost cylindrical fashion by the ligands, with each ion being fixed to five oxygen atoms and one phenyl ring[22b]. As in monensin, the C=O groups are not joined directly to the $Ag^{\oplus}$ ion.

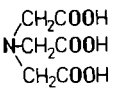
3. Chelates: Alkali Metal Complexes of (Potentially) Acidic Acyclic Ligands

In contrast to the "classical" heavy metal complexes[35], stable coordination compounds of Group I and II elements with synthetic acyclic *neutral* ligand molecules were apparently unknown until the sixties. Crystalline products of alkali metal hydroxides and alkoxides and 1,3-diketones, *o*-nitrophenol, and salicylaldehyde all have chelate structures[36].

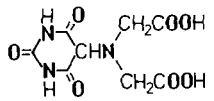
A climax was reached in the complex chemistry of protic "chelating agents"[37] on preparation of "complexones" [ethylenediaminetetraacetic acid (EDTA) *(13)*, nitrilotriacetic acid (NTA) *(14)*, *etc.*][38], which preferentially bond to alkaline earth metal ions. Uramildiacetic acid *(15)* can also form stable complexes with univalent metal ions in aqueous solution (stability sequence: $K^{\oplus} < Na^{\oplus} < Li^{\oplus} < Tl^{\oplus} < H^{\oplus}$)[39]. However, $M^{2\oplus}$ ions (except $Be^{2\oplus}$) are complexed better by EDTA than by uramildiacetic acid. Complexones having heterocyclic ether oxygen[40] or amine nitrogen donor centers[41], such as *(16)* and *(17)*, permit further variation in the stability sequence.



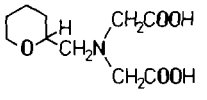
(13)



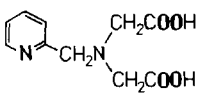
(14)



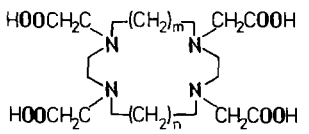
(15)



(16)



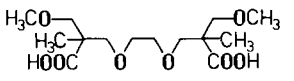
(17)



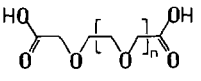
(18a–c): n,m = 2,3

Among the four-armed ligands of the same type as tetraazacycloalkane-*N,N',N'',N'''*-tetraacetic acid *(18)*[42], whose complexing properties depend on ring size, *(18a)*, $n=m=2$, having a pK value of 15.85, is the strongest complexing agent known for $Ca^{2\oplus}$. In the case of *(18b)*, $n=2$, $m=3$, the stability of the $Sr^{2\oplus}$ complex (pK = 11.70) is very noticeable, while *(18c)*, $n=m=3$, is able to discriminate between $Mg^{2\oplus}$ and $Ca^{2\oplus}$.

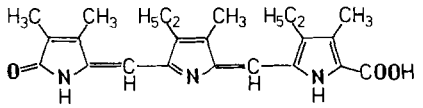
In the presence of pyridine or triphenylphosphane, 2,9-bis(methoxymethyl)-2,9-dimethyl-4,7-dioxa-1,10-decanedioic acid *(19)* forms crystalline dimeric chelates with $Cu^{2\oplus}$ ions; the ether oxygen atoms play an important role in their formation[43]. Unsubstituted oligo(ethylene glycol) dicarboxylic acids *(20)* are found by pH titrimetry to show various stability sequences with alkaline earth metal ions, depending upon the number of ether oxygen atoms present ($n=0$–3)[44].



(19)



(20): n = 0-3



(21)

Sodium chloride and some other alkali metal halides could be precipitated from aqueous solution as coordination compounds with *rac-p,p'*-diamino-2,3-diphenylbutane[45]. Furthermore, the $NH_4^{\oplus}$, alkali metal, alkaline earth metal, and heavy metal "salts" of oxotripyrrene-2-carboxylic acid *(21)* have also been ascribed chelate character[46].

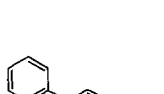
Alkali metal complexes with phosphane oxides as ligands have been examined by X-ray structure analysis[47]: in the NaBr complex of *P,P'*-methylenebis(diphenylphosphane oxide) the $Na^{\oplus}$ ion is located in a trigonal-prismatic environment of six oxygen atoms of the phosphane oxide[48]. IR studies suggest partly electrostatic bonding between $Na^{\oplus}$ and O. The smaller Li atom is accordingly coordinated by a tetrahedral arrangement of only four oxygen atoms in the LiI-triphenylphosphane oxide complex[49]. Analogous arsenic ligands form complexes of only modest stability with alkali and alkaline earth metal halides[48].

A roughly octahedral environment of O coordination sites is found in the $NaClO_4$ complex of bis[*N,N'*-ethylenebis(salicylideniminato)copper(II)][50]: two O donors are contributed by the chelating $ClO_4^{\ominus}$ ion and two by each of the tetradentate ligands in the Cu complex, which are fixed in sandwich fashion above and below the $Na^{\oplus}$ ion. Chelation of the $Na^{\oplus}$ ion is again regarded as the principal feature of the bonding in this complex.

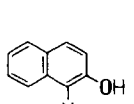
8-Hydroxyquinoline *(22)*, isonitrosoacetophenone *(23)*, and 1-nitroso-2-naphthol *(24)*, on the other hand, can probably form *true* (*i.e.* nonprotic) coordination compounds[51].



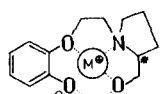
(22)



(23)



(24)



(25)

Another acidic complex ligand is a chiral dihydroxy compound, called "semicrown" by *Wudl*, which forms complex salts of type *(25)* with alkali metal ions[52]; it yields a stable crystalline salt with $Li^{\oplus}$. The optically active ligand exhibits cation-specific ORD curves, suggesting that the $Li^{\oplus}$ and $Na^{\oplus}$ ions are probably enclosed; this appears impossible with larger ions.

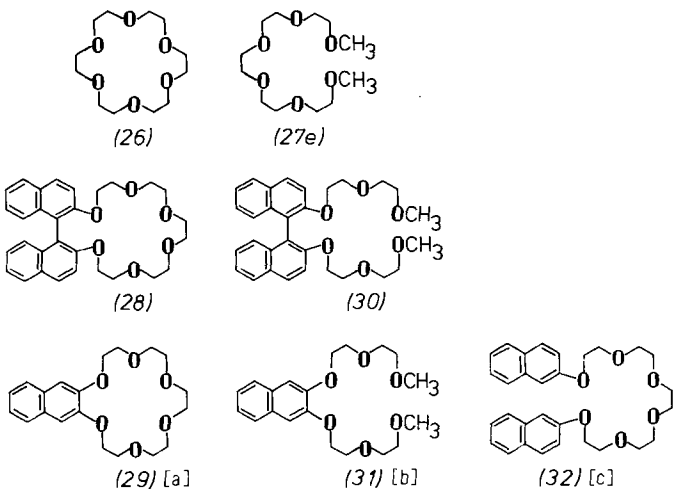
4. Synthetic Acyclic Neutral Ligands (Podands)

4.1. Classical Glyme Compounds (Oligoethylene Glycol Dimethyl Ethers) and Their Relatives

On going from cyclic [18]crown-6 *(26)* to open-chain, and yet also hexadentate, pentaethylene glycol dimethyl ether ("pentaglyme") *(27e)* (Table 2) an approximately 10^4-fold drop in stability (complexation constant K_s[1b,4]) is observed for complexation of $K^{\oplus}$ ions (*ca.* 10^3 for $Na^{\oplus}$)[53]. This corresponds to a drop in the enthalpy of complexation ΔG^0 of *ca.* 25 kJ/mol (6 kcal/mol)[54].

This tendency is also observed for *tert*-butylammonium as guest ion in cyclic crown ethers *(28)* and *(29)* and the corresponding glyme analogues *(30)*—*(32)*[55].

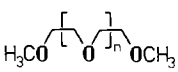
Table 2. Comparison of some crown ethers and their acyclic analogues.



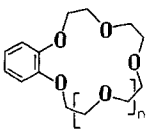
[a] $K_E = 26$ (with tBuNH$_3^{\oplus}$ClO$_4^{\ominus}$). [b] $K_E = 0.026$ (with tBuNH$_3^{\oplus}$ClO$_4^{\ominus}$), 4.5 (with tBuNH$_3^{\oplus}$PF$_6^{\ominus}$). [c] $K_E = 0.0738$ (with tBuNH$_3^{\oplus}$PF$_6^{\ominus}$).

The extraction constants K_E (solvent $CDCl_3/D_2O$) show that *(29)* complexes *ca.* 10^3 more strongly with tBuNH$_3^{\oplus}$ than with *(31)* whose donor centers only partly converge. Compound *(31)* has complexation properties some $10^{1.5}$ better than *(32)* with terminal naphthyl groups since there are no longer any (mutually linked) rigid groups able to enforce convergence of donor atoms. The difference in complex stability between the cyclic compound *(28)* and its acyclic analog (360:40) seems remarkably small compared with *(26)*/*(27e) (vide supra)*; apparently, the binaphthyl hinge permits extensive perturbation of planarity (and convergence) of individual coordination sites. Thus it may be concluded that enforced convergence of the binding sites in these simple systems, *i.e.* a stiffening of the ligand backbone favoring coordination, considerably increases complex stability. The modest difference between the cyclic compound *(28)* and the acyclic analogue *(30)* also suggests that a detailed examination of the readily preparable open-chain neutral ligand might be a rewarding object of study.

The difference in complex stability which can result on ring closure—retaining the nature and geometry of donor atoms—is denoted as the *"macrocyclic effect"*[4,53a,56]. Although this effect was originally explained in terms of entropy factors which oppose complete enclosure of cations by acyclic polyethers[56], studies on macrocyclic tetramine[57] and tetrasulfide systems[58] showed that thermodynamic parameters (ΔH), coupled with ligand solvation effects, often play a greater role in the origin of the macrocyclic effect[59]. Polarographic determinations of $\log K_s$, ΔH, and ΔS for the interaction between heavy metal ions such as $Pb^{2\oplus}$ with [18]crown-6 *(26)* or tetraglyme *(27d)*, $n = 3$, in aqueous solution showed the cycle *(26)* to be some 10^4 times more stable than the open-chain ligand[60]. The macrocyclic effect was attributed largely to entropy effects in this case. Measurement of complex stability constants of some oligoethylene glycol dimethyl ethers *(27)* of various chain lengths for $Na^{\oplus}$, $K^{\oplus}$, $Cs^{\oplus}$, $Tl^{\oplus}$[61] (potentiometric and conductometric, in CH_3OH) revealed that an increase in the number of coordination sites (ether O atoms) raises the stability constants and the $K^{\oplus}/Na^{\oplus}$ selectivity; replacement of the two methoxy chain ends by primary carboxamide groups or ester groups impairs the complexation properties of the ligands.



(27a)-*(27i)*: n = 0-8
(27k): n = 21



(33a): n = 1
(33b): n = 2

In keeping with the low stability constants—even in low-polarity organic solvents—*crystalline alkali metal complexes* of such "simple" acyclic oligoethylene glycol ethers *(27)*, the glymes, were unknown until very recently[62]; this also applies to ligands containing polyether chains of up to ten oxygen atoms which are bent by and also partly stiffened by inclusion of *ortho*-substituted aryl groups[61].

The stoichiometries and specific structures of the resulting ion pair/glyme compounds were determined in tetrahydrofuran (THF) by titration of difluorenylbarium with glymes of various chain lengths[63]. Like [18]crown-6 *(26)* and monobenzo[18]crown-6 *(33b)*, glyme-7[64] *(27f)*, $n = 5$, and glyme-9 *(27h)*, $n = 7$, give 1:1 complexes between the ligand and difluorenylbarium. It can be shown from the optical spectra that these complexes are mixed intimate/loose ion pairs of the type fluorenyl$^{\ominus}$Ba$^{2\oplus}$/glyme/fluorenyl$^{\ominus}$[65]. The ability of glyme-5 *(27d)*, $n = 3$, like monobenzo[15]crown-5 *(33a)* to form a stable 2:1 complex with difluorenylbarium suggests that a ligand such as glyme-10 *(27i)*, $n = 8$, should have adequate bonding sites for construction of an entirely separate 1:1 ion pair complex. Such an ion pair also results on coordination of difluorenylbarium with glyme-23 *(27k)*; two $Ba^{2\oplus}$, $(\text{fluorenyl})_2^{2\ominus}$ units may possibly be complexed to this glyme.

Numerous publications have already appeared concerning the synthesis and structure of crystalline glyme complexes with transition metal ions, *e.g.* $Fe^{2\oplus}$, $Mn^{2\oplus}$, $Co^{2\oplus}$, $Ni^{2\oplus}$, $Cu^{2\oplus}$[66], and with mercury[67] and cadmium salts[68], including some X-ray structure analyses[69]. While several molecules of *dimethoxyethane (27a)* (monoglyme) are usually required (generally three[66,69]) for complexation, dinuclear complexes are also formed by suitably long polyether chains[67c]. X-ray structure analysis[67a] of the complex of *tetraethylene glycol dimethyl ether (27d)* (TGM) with $HgCl_2$ (1:1 stoichiometry) indicates the following ligand conformation[70]:

CH_3–O–CH_2–CH_2–O–CH_2–CH_2–O–CH_2–CH_2–O–CH_2–CH_2–O–CH_3 *(27d)*

ap sc ap ap (−)sc ap ap sc ap ap (−)sc ap

All the H_2C–O bonds are thus antiperiplanar *(ap)*, and the CH_2–CH_2 bonds in the adjacent unit alternately synclinal *(sc)* and (−)-synclinal [(−)*sc*]. The ligand is fixed in a circular geometry but does not form a closed circle (see Fig. 2a). The five oxygen atoms, which are almost coplanar and all directed inward, closely embrace the $Hg^{2\oplus}$ ion (2.78—2.98 Å).

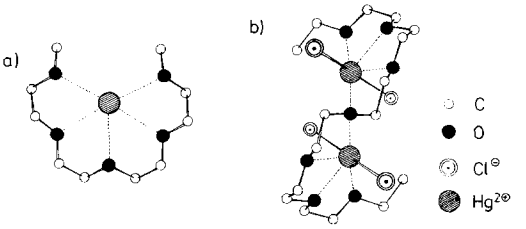


Fig. 2. Interactions between the O and Hg atoms in the $HgCl_2$ complexes of (a) TGM *(27d)* and (b) HGE *(27l)* [67a, c].

In the corresponding *tetraethylene glycol diethyl ether* (TGE)/$HgCl_2$ complex[67b] very similar Hg—O distances and angles are found in the interior of the chain. An *sc* arrangement occurs at only one end of the chain, thus avoiding steric hindrance of the ethano groups in the *ap/ap* conformation.

Hexaethylene glycol diethyl ether (27l) (HGE) can utilize its seven coordination sites to bond two $Hg^{2\oplus}$ ions at relatively short distance (Hg—O, 2.66—2.91 Å); the HGE molecule exhibits the following conformation in the complex[67c]:

CH_3–CH_2–O–CH_2–CH_2–O–CH_2–CH_2–O–CH_2–CH_2–O–

ap ap sc ap ap (−)sc ap ap sc sc sc

–CH_2–CH_2–O–CH_2–CH_2–O–CH_2–CH_2–O–CH_2–CH_3

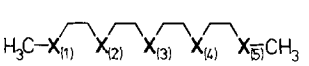
sc ap ap (−)sc ap ap sc ap ap *(27l)*

The adjacency of two *sc/sc* sequences at the central O atom is remarkable; it effects a separation into two coordination moieties of four coplanar oxygen atoms, each occupied by one $Hg^{2\oplus}$ ion. The central O atom is involved in coordination to both Hg ions (see Fig. 2b).

Similar structural units are found in the complex of tetraethylene glycol dimethyl ether *(27d)* (TGM) with $CdCl_2$[68]. However, owing to the smaller number of donor sites available (five per glyme molecule) additional Cl bridging ligands are required; each bridge holds together two ligands over a total of four $Cd^{2\oplus}$ ions.

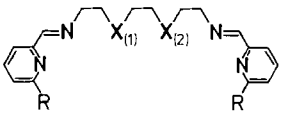
While glyme complexes of $Hg^{2\oplus}$ salts are relatively easy to obtain the preparation of corresponding coordination compounds with the softer[71] $Hg^{\oplus}$ ions runs into difficulties owing to disproportionation to Hg^0 and $Hg^{2\oplus}$[72]. However, a crystalline complex of composition $Hg_2(diglyme)_2(NO_3)_2$ has recently been isolated; it can be kept for some time under a protective gas but on heating (65 °C) the organic ligand *(27b)* is completely eliminated[73]. Corresponding $Hg^{\oplus}$ complexes of sulfide ligands proved to be more stable[74].

New combinations of sulfur and oxygen donor centers in oxathiapentadecanes of general type *(34a)* should be particularly suitable for complexation of heavy metal ions, especially $Ag^{\oplus}$, $Hg^{2\oplus}$[75].



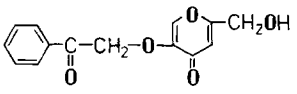
(34a): $X_1, X_2, X_3, X_4, X_5 = O, S$

(34b): $X_1, X_5 = N; X_2, X_4 = S; X_3 = O$



(35): $X_1, X_2 = O, S$; $R = H, CH_3$

Complexation of transition metal ions ($Cu^{2\oplus}$, $Ni^{2\oplus}$, $Co^{2\oplus}$, $Zn^{2\oplus}$, $Pd^{2\oplus}$ and $Ag^{2\oplus}$) with the open chain sulfur-, oxygen-, and nitrogen-containing ligand 8-oxa-5,11-dithia-2,14-diazapentadecane *(34b)* has also been studied[76]. Alkali metal complexes of this "heteroglyme" appear—as expected from the low tendency of the soft sulfur atom to coordinate the hard Group I elements[77]—to play only a subordinate role. The same applies to the many open-chain multidentate Schiff base ligands *(35)* which readily form complexes with Fe, Co, Cu, Pd, Pt, Ru, *etc.*[78].



(36)

More than 25 years ago, *phenacyl kojate (36)* was found to form crystalline 2:1 complexes with sodium halides in methanol[79]. Their structures[80] (see Fig. 3) resemble those of the [18]crown-6 complexes of the corresponding sodium salts[81]: six oxygen donor centers (from two phenacyl kojate units) are grouped in planar fashion around the sodium ion; in contrast to the crown ether complex, however, four of them come from a carbonyl group. The crystal structure is held together by H bonds between CO and OH groups and by H...O interactions. The Na···O distances lie between 2.56 and 2.68 Å[82].

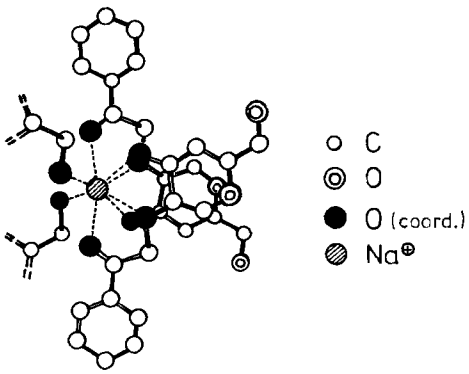
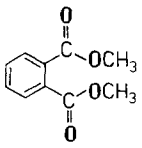


Fig. 3. Crystal structure of the complex formed by phenacyl kojate *(36)* with NaCl[80].

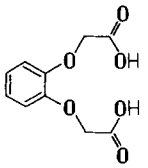
Alkali metal salts have been known for some time to form complexes with 1,4-*dioxane*[83]; however, these complexes

have poor thermal stability and exhibit high dioxane vapor pressures even at 300 K. Although some of them are isolable in crystalline form from aqueous solution they generally lose their dioxane to the air. The coordination compounds of $NaClO_4$, $NaBF_4$, NaI with dioxane, like the $AgClO_4$ complex, possess a cubic structure with the metal ion in an octahedral environment of dioxane oxygen atoms at distances of 2.43—2.46 Å. The perchlorate ion at the center of the unit cell can undergo free rotation, and the dioxane molecules rotate about their O—O axes. Ions of the higher alkali metals are too voluminous to form stable crystal structures.

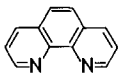
Dimethyl phthalate (37) acts as a bidentate neutral ligand towards various divalent cations such as $Mg^{2\oplus}$, $Ca^{2\oplus}$, $Mn^{2\oplus}$, $Fe^{2\oplus}$, $Co^{2\oplus}$, $Ni^{2\oplus}$, and $Zn^{2\oplus}$[84]. In the resulting complexes, the metal ions are each bonded by three dimethyl phthalate molecules *via* the carbonyl groups, with the coordinating carbonyl oxygens forming a regular octahedron. It is important for these complexes to have a large counterion (*e.g.* $InCl_4^{\ominus}$); they decompose completely in the presence of water.



(37)



(38)



(39)

A remarkably stable 2:1 complex is formed by *O,O'-catecholdiacetic acid (38)* and KCl[85]. It has a complicated layer structure stabilized by H bonds in which the $K^{\oplus}$ ions are enclosed in sandwich fashion by ten O atoms (four ether and six carbonyl oxygens) in an irregular pentagonal-antiprismatic arrangement (Fig. 4).

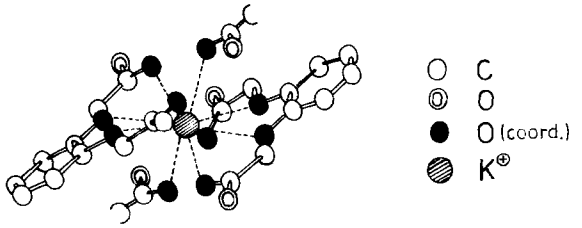


Fig. 4. Structure of the complex of *O,O'*-catecholdiacetic acid with KCl [85].

No such coordination compounds can be obtained with Li, Na, Cs, and NH_4 salts. The observed "precipitation selectivity" towards $K^{\oplus}$, which exceeds that of $NaB(C_6H_5)_4$, is unusual since all the other known precipitation reagents for $K^{\oplus}$ also respond to $NH_4^{\oplus}$, $Cs^{\oplus}$, and $Rb^{\oplus}$[86].

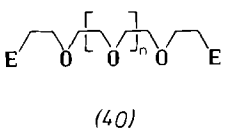
Work by *P. Pfeiffer*, who isolated crystalline complexes of *1,10-phenanthroline (39)* with, *e.g.* $LiClO_4$, $NaClO_4$, $AgNO_3$, $TlNO_3$, $Ca(ClO_4)_2$, $Sr(ClO_4)_2$, and $Ba(ClO_4)_2$ as long ago as 1938[87], seems to have been forgotten. The complexes are precipitated from aqueous/alcoholic solution and can be recrystallized without decomposition. The Li complex forms particularly readily, while the Na salts show little tendency to undergo complexation and no corresponding K compound could be obtained at the time. The results were recently reconsidered and an interpretation based on the influence of the counterion and on protonated intermediates proposed[88a]. At roughly the same time, alkali metal complexes of phenanthroline and of *bipyridine*, including some with potassium salts, were obtained in independent studies[88b].

The tendency of certain heterocycles to favor $Li^{\oplus}$ over ions of the higher alkali metals is also apparent from the solubility series of the chlorides of $Na^{\oplus}$, $K^{\oplus}$, $Rb^{\oplus}$, and $Cs^{\oplus}$ in *pyridine*, in which all these salts except LiCl are practically insoluble[89]. The situation can be modified by stepwise addition of water. This is the basis of a separation of lithium ions from other alkali metal ions and from $Ba^{2\oplus}$ which was developed as long ago as 1908[90].

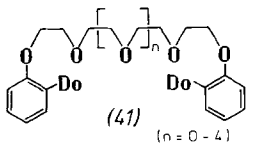
4.2. Acyclic Crown Ethers and Coronands

4.2.1. Terminal Group Concept

Attachment of rigid (*e.g.* aromatic) *terminal groups* (*E*) bearing donor centers (Do) [cf. *(40)*] to oligoethylene glycol units ("terminal group concept")[91] affords neutral ligands *(41)* which readily form stable crystalline complexes with alkali and alkaline earth metal ions[92] in the same way as the cyclic crown ethers. Apart from complexes of Na, K, Ca, *etc.*, it is also possible to obtain such compounds of lanthanoids, uranyl, Zn, Hg, Mg, and Ag salts, as well as ammonium ion complexes.

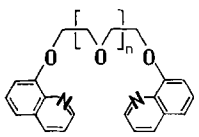


(40)

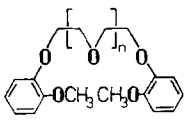


(41)

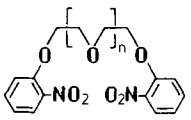
Suitable terminal groups (*E*) are 8-quinolyloxy, *(42)*, *o*-methoxyphenoxy *(43)*, *o*-nitrophenoxy groups *(44)*, among many others[91,92].



(42a–g): n = 0–6



(43a–d): n = 0–3



(44a–d) n = 0–3

Synthesis of unsymmetrical open-chain ligands such as *(45)* permits almost any intramolecular combination of weak and strong donor terminal groups.

The terminal groups function as anchoring points with locally fixed donor centers on which the cation can take hold; a certain number of donor sites remains a prerequisite for complex formation. Structures such as *(47)* in which the terminal groups are isolated from one another by a polymethylene chain show only limited ability to form crystalline alkali metal complexes although the distance between the quinolyl units was modified by variation of *n*[92,93a].

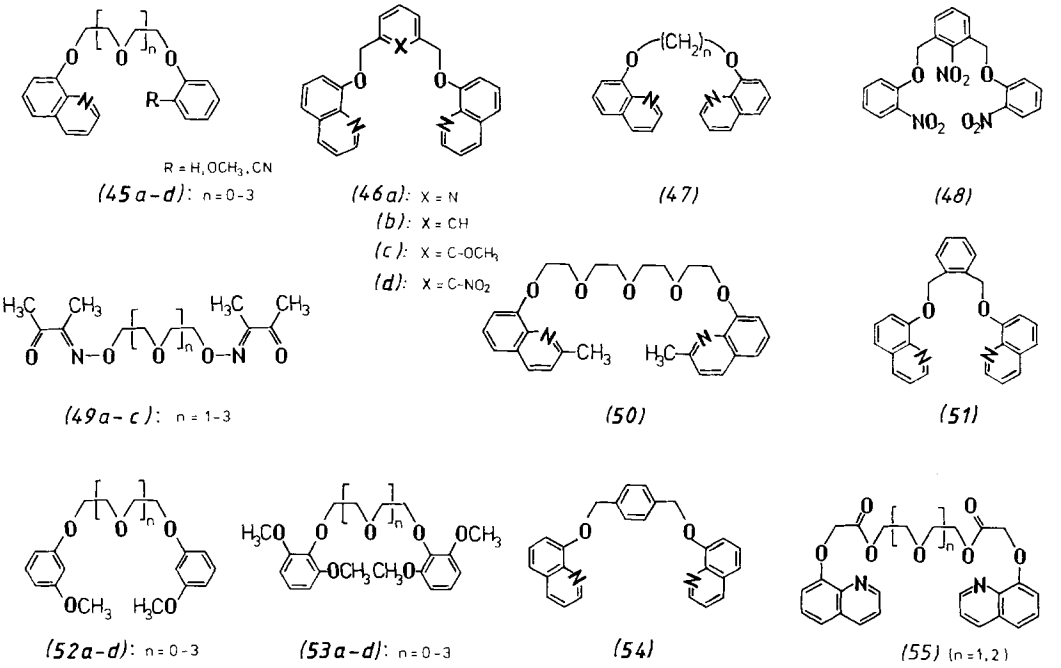
Apart from the terminal group donor effect, geometrical and steric factors also play a role[91,92]: the compounds *(46c)*, X = C—OCH_3, *(46d)*, X = C—NO_2, and *(48)* bearing an adequate number of proven donor atoms neither form crystalline complexes with alkali metal salts nor do they transfer alkali metal permanganates into organic phases. Complexation

is apparently blocked by substituents (which in principle are capable of coordination[93b]) projecting into the pseudocavity.

Among the neutral ligands having diacetylmonoxime terminal groups *(49)*[94], the *E* configuration of the oxime appears to interfere with the formation of crystalline complexes.

tion is also retained on recrystallization of the complex (from methanol/ethyl acetate).

The tetrasubstituted ligand *(53)* forms not only 1:1 complexes[95a]: transition from 1:1 stoichiometry in the *(53a)*-$LiClO_4$ complex to 3:2 stoichiometry (ligand:salt) in the *(53a)*-sodium complex can be rationalized in terms of the greater radius of the sodium ion, which precludes complete



On the other hand, no steric hindrance of crystalline complex formation by the methyl groups is observed in the quinaldine compound *(50)*; this is easily rationalized in terms of the helical structure of the ligand in the complex (see Section 4.2.3). The *ortho*-phenylene compound *(51)* can also form stable complexes of the ligands *(43)*, *(52)* (with positionally isomeric methoxy terminal group), and *(53)*, which contain only oxygen as donor centers; only the *o*-methoxy derivatives give crystalline alkali metal salt complexes under comparable conditions[95a].

Terminal groups can also be attached by way of ester groups instead of ether functions [cf. *(55)*]; in some cases, transesterification was observed on attempted isolation of crystalline alkali metal complexes in methanol as solvent[95b].

4.2.2. Stoichiometry of the Crystalline Complexes

Stable crystalline complexes are obtained not only with Group I and II metals[91,92,95a] but also with transition metal ions ($Zn^{2\oplus}$, $Cd^{2\oplus}$, $Hg^{2\oplus}$, $Ag^{\oplus}$, $Co^{2\oplus}$, $Ni^{2\oplus}$) and lanthanoid and actinoid ions ($Pr^{3\oplus}$, $Nd^{3\oplus}$, $UO_2^{2\oplus}$) and with ammonium salts[92,95b]: however, many cations remain to be studied.

In spite of less strictly stipulated "cavity geometry", complexes of exactly stoichiometric composition are generally formed—even in the presence of a large excess of one component of the complex[92]. For example, the ligand *(42d)* always gives a 1:1 complex with KSCN regardless of whether the molar ratio of ligand to salt is 2:1 or 1:2. This composienclosure by a single ligand molecule. The fact that the *(53b)*-sodium and *(53b)*-potassium complex also exhibit 2:1 stoichiometry requires a different explanation, particularly since the ligand *(43b)*, which bears a single *o*-substituent on each side, forms a 1:1 sodium complex. In this case, mutual steric hindrance in the 1,2,6-positions rules out the availability of the methoxy groups in the optimum cation region—as manifested, *e.g.*, by chemical shift differences in the ^{1}H-NMR spectra of the complexes—with the result that a further ligand molecule is required for occupation of the free coordination sites on the metal ion.

The proposed structures are also supported by features of the IR spectra of these complexes. In general, interpretable changes in the IR absorptions of crown ether complexes relative to the free ligands are conspicuous in the region of the mostly strong bands of the original salt[2,96]. Above all, these include the absorptions of inorganic anions such as $NO_3^{\ominus}$, $SCN^{\ominus}$, $ClO_4^{\ominus}$, $BF_4^{\ominus}$, and also those of complexed ammonium ion[97]. This also applies to complexes of open-chain crown ethers[95].

Some of the complexes contain H_2O in stoichiometric proportions[91,92], as revealed by the appearance of more or less sharp OH bonds in the IR spectra[95]. The question whether the H_2O molecules are in coordinational contact with the complexed cation or exist as free water of crystallization in the crystal lattice[98] will only be conclusively settled by X-ray structure studies *(vide infra)*. This also applies to the extent of participation of anions in coordination[99], which has been explained in such a way for some complexes.

4.2.3. X-Ray Structure Analyses of Crystalline Complexes

Right at the start of our investigations[92], model considerations of the structure of the ligand *(42d)*, $n=3$, equipped with 8-quinolyloxy terminal groups, suggested that on participation of all seven heteroatoms in coordination of the metal ion a screw-shaped, and thus chiral, arrangement of the ligand skeleton should result; mutual hindrance of the α- and β-hydrogen atoms on the quinoline ring is the reason for the lack of coplanarity of the donor centers. The ability of ligand *(42d)* to effectively wrap around a "fitting" cation in helical-chiral fashion is demonstrated by a consideration of space-filling atomic and spherical ion models[100]. In this respect, *(42d)* is a model substance for acylic ionophores, *e.g.*, for open-chain gramicidins and nigericins (cf. Section 2).

An X-ray structure analysis has been performed on the *(42d)*-RbI complex[101] which crystallizes in beautiful platelets. It confirms the expected participation of all seven heteroatoms (5O, 2N) in complexation and affords the first proof of a *helical-chiral* arrangement of a synthetic open chain ionophore around an alkali-metal ion (Fig. 5b): plus and minus helices are present in equal amounts. However, the iodide ions are not included in the coordination sphere of the central ion; nor are they in direct contact with any heteroatoms of the quinolyl ether.

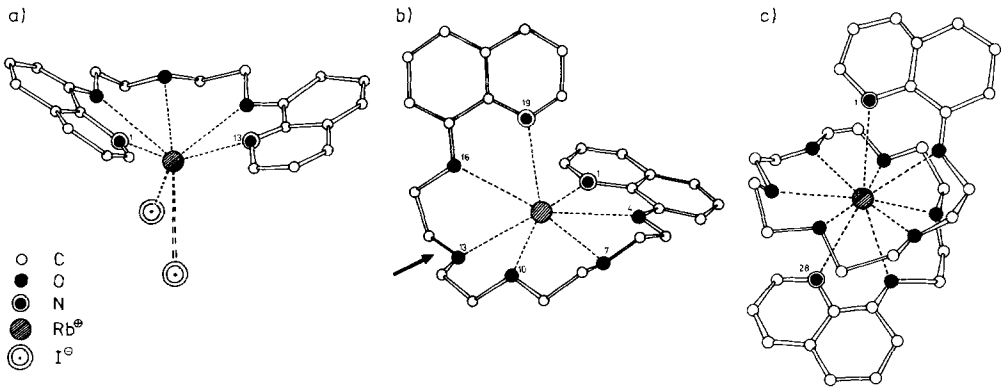


Fig. 5. Structures of some $Rb^{\oplus}$ complexes of open-chain neutral ligands: (a) *(42b)*-RbI with planar wrapping around the cation; (b) *(42d)*-RbI with helical wrapping of ligand around the cation; and (c) *(42g)*-RbI with spherical wrapping around the cation.

The bond lengths and angles between the heteroatoms (O, N) and the $Rb^{\oplus}$ ion admittedly deviate from one another but can nevertheless be regarded as approximately symmetric with regard to an axis shown joining the $Rb^{\oplus}$ ion and the O(10) atom in Figure 5b. Whereas the $Rb^{\oplus}\ldots O$ distances in the dibenzo[18]crown-6-RbSCN complex (2.861—2.939 Å) largely correspond to the sum of atomic and ionic radii (2.87 Å)[102], the bond lengths in the *(42d)*-RbI complex show some remarkable differences: the $Rb^{\oplus}\ldots O(10)$ distance of 2.88 Å closely approaches the ideal value (2.87 Å); the distances $Rb^{\oplus}\ldots O(7)$ and $Rb^{\oplus}\ldots O(13)$ of 2.99 and 2.94 Å, respectively, show considerable extension. Even greater extension is observed with the bond lengths between $Rb^{\oplus}$ and O(4) and O(16), which have values of 3.07 and 3.09 Å. The most likely cause of such deviations in bond lengths lies in the differing donor strengths of aliphatic or aromatic oxygen atoms, rather than contributions by steric hindrance of the polyether chain. In contrast, the $Rb^{\oplus}\ldots N$ distances of 2.91 Å for N(1) and 2.96 Å for N(19) are very close to the value of 2.97 Å calculated from the atomic and ionic radii.

The angle formed by two adjacent donor sites with $Rb^{\oplus}$ as apex can be divided into three categories (see Fig. 5b): $O\ldots Rb\ldots O$ angles having values of 54—59° are determined by the conformational arrangement, *i.e.* the specific geometry of the $O-CH_2-CH_2-O$ fragments within the polyether chain. The $N\ldots Rb\ldots O$ angles of 52 and 53 are laid down by the atomic arrangement in the 8-quinolyloxy group while the angle of 77° between $Rb^{\oplus}$ and the two quinoline N atoms results from the acyclic structure of the ligand.

In the complexes of cyclic crown ethers the oxygen atoms coordinated around the metal ion are usually coplanar; in the ideal case, the complexed cation is located in this plane at the center of the ring[28]. If the relative sizes of cation and cavity are less favorable then the metal ion may be displaced somewhat from the "crown ether plane"[103].

In *(42d)* the chain bearing the oxygen and nitrogen donors is too long to enclose the $Rb^{\oplus}$ in a plane. Nevertheless, the major part of the donor atoms is fixed in a plane in this complex (Fig. 5b). This applies to atoms N(1), O(4), O(7), O(10), and O(13). In this region of the ligand the conformational angles at the C—C bonds are expectedly synclinal *(sc)* and those at the C—O bonds antiperiplanar *(ap)*. In order to avoid collision of the two terminal quinoline units, the dihedral angle at bonds C(12)—O(13)—C(14)—C(15) is *sp* instead of *ap* (see arrow in Fig. 5b). As a result, the heteroatoms O(16) and N(19) are displaced, together with the attached quinolyl group, from the plane formed by the other five donor sites, and the $Rb^{\oplus}$ ion is shifted by 0.748 Å towards the other quinolyl group; this imparts the particular (helical) structure to the complex.

The helical arrangement of the *(42d)*-RbI complex is replaced in the RbI complex of the ligand *(42b)*, $n=1$, shorter by two oxyethyl units, by an approximately *planar* arrangement (folded like a butterfly) having mirror symmetry (Fig. 5a)[104]. X-ray structure analysis of the RbI complex shows this neutral ligand to be pentadentate. Differences in O—Rb distances can also be seen here. However, the coordinative bonds of the ether oxygen atoms to the central ion are even longer than in *(42d)*-RbI and deviate considerably in the extreme case for the central O atom (3.18 Å) from the calculated value of 2.87 Å. The Rb...N distances of 2.98 Å closely

approach the calculated value of 2.97 Å. The coordination sphere of the $Rb^{\oplus}$ which, in contrast to the case of *(42d)*, is not saturated by five donor sites, is filled alternately by two iodine atoms per ligand unit participating in complexation.

Spherical wrapping around a rubidium ion was ascertained in the RbI complex of the *decadentate* linear polyether *(42g)*, $n=6$, by X-ray structure analysis (Fig. 5c)[105a]: All the heteroatoms lie approximately on the surface of a sphere of radius *ca.* 3 Å, whose poles are occupied by the two quinoline nitrogen atoms. Starting from one of the nitrogen donor sites, the ligand chain runs to the equator of the sphere which it encircles and then proceeds to the other pole. The $Rb^{\oplus}$ ion is tenfold coordinated if the $Rb^{\oplus}\ldots N$ and $Rb^{\oplus}\ldots O$ contacts of 3.371 and 3.147 Å are included. Similar values are known for highly coordinated $Rb^{\oplus}$ but other $Rb^{\oplus}$-polyether complexes with smaller ligands show normal values (cf. Fig. 5a, b). The iodide ions lie in cavities between the "spheres" of the $Rb^{\oplus}$ complexes where they are held by weak van der Waals forces. For this reason they are statistically twofold disordered.

X-ray structure analysis of the *(50)*-RbI complex[104] revealed a significant difference in the ligand conformation, compared with the *(42d)*-RbI complex (Fig. 5b). While a discontinuous helix having a somewhat bent but coordinated quinoline terminal group is present in the latter, the likewise heptadentate diquinaldine ligand *(50)* is arranged as a *continuous* helix in its complex (see Fig. 6a). This can be explained by assuming the methyl groups of the quinaldine units to sterically hinder planar inclusion of the cation at the terminal group, thus inducing a helical wrapping which then continues. In the analogous quinoline ligand *(42d)*, on the other hand, a planar geometry is sterically feasible at one of the quinolyloxy termini which remains coplanar until steric hindrance occurs on addition of the second quinolyl group so that this latter group is kinked (see Fig. 5b).

ion chain structures (Fig. 6c)[104]: the two carbonyl groups of any one ligand molecule do not coordinate the potassium ion held tightly by the five intramolecular ether oxygen donor centers but instead the potassium ion of the preceding and the following ligand. This observation is compatible with the high entropy of complexation found for the sodium ion *(vide infra)* which can be interpreted both as cyclization and as polymerization entropy.

As shown by the X-ray structure analysis of the complex of phenylglycine ethyl ester-hydrotrifluoromethanesulfonate with the double phosphane oxide *O,O'*-(3-oxapentamethylenedioxy)bis(triphenylphosphane oxide) (Fig. 7), the phosphane oxide moiety can be utilized both as donor terminal group and as a structural unit enhancing the lipophilic properties of podands[107].

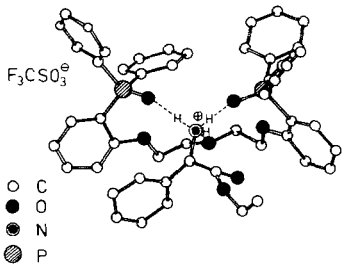


Fig. 7. Stereochemistry of the phenylglycine ethyl ester-hydrotrifluoromethanesulfonate complex of *O,O'*-(3-oxapentamethylenedioxy)bis(triphenylphosphane oxide).

4.2.4. NMR Studies on Complexation in Solution

The line shape and position of the signals in the ^{1}H-NMR spectra of complexing agents are generally modified by their contact with metal ions[108a]. In the case of acyclic ligands, too, ^{1}H-NMR spectroscopy proved extremely useful[65] for

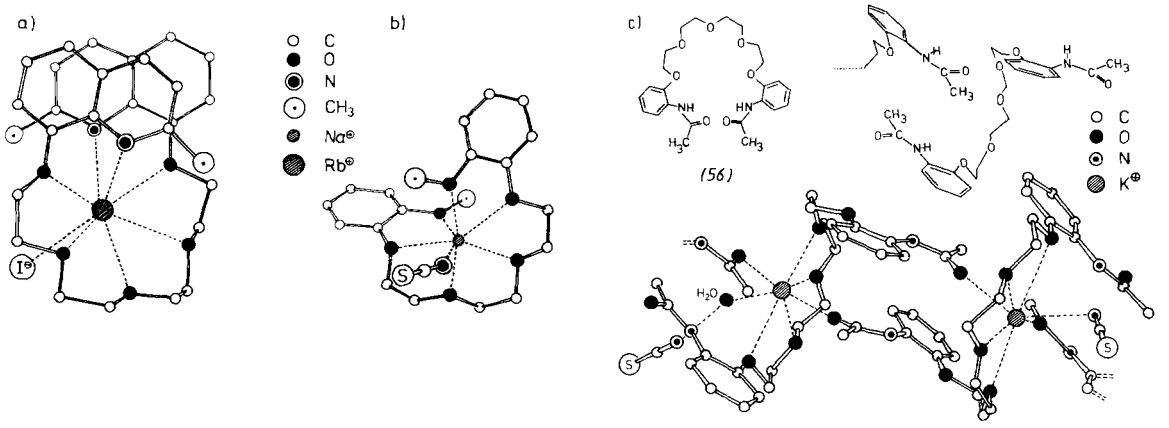


Fig. 6. Geometry of the alkali metal ion complexes of the open-chain ligands (a) *(50)*, (b) *(43c)*, and (c) *(56)*.

The ligand also forms a continuous helix in the *(43c)*-NaSCN complex[106], with a OCH_3 group above or below the other benzene ring[104]. The central sodium ion coordinates to all six oxygen atoms and to the $SCN^{\ominus}$ ion lying above the helix (see Fig. 6b).

X-ray structure analysis of the 1:1 KSCN complex of the amide ligand *(56)* unexpectedly shows polymeric ligand-cat-

recognizing complexation at certain bonding sites[108b] and for analysis of ion pair equilibria in solution, particularly when complexation has no effect on the optical spectra[109].

For example, in a 1:1 mixture of fluorenyllithium and ethylene glycol dimethyl ether (DME) *(27a)* in deuterated benzene, the signals of the CH_2 protons are shifted upfield by 1.22 pm and those of the CH_3 groups by 0.76 ppm[110]. A

similar situation is observed when higher glymes or crown ethers complex with fluorenyl ion pairs[111]. Differences in the NMR spectra are also observed when glymes form complexes with paramagnetic ion pairs[109].

In the ^{1}H-NMR spectra of the complexes of podands with stiffened terminal groups, pronounced changes are observed in the splitting pattern and in the chemical shifts of the aromatic part[92,95,112]: the 8-quinolyloxy unit of ligand *(42d)* absorbs in three separate characteristic signal groups around $\delta = 7.40$, 8.10, and 8.90[92]. In the $K^{\oplus}$ complex the shape of these resonance signals has changed considerably; even more noticeable is their pronounced upfield shift ($\delta = 0.52$ ppm) which affects mainly the pyridine protons and indicates participation of the quinoline nitrogen in coordination of the $K^{\oplus}$ ion. The absorptions of the methylene protons are generally affected much less by complexation (increasingly less towards the center of the chain); apart from further splitting of the multiplet structure, the absorptions of methylene protons close to the ends of the chains merely experience a slight partial upfield shift. The heptadentate helical structure of the RbI complex of *(42d)* (cf. Fig. 5b) established by X-ray crystal structure analysis is in full accord with the upfield shift found for the heterocyclic terminal groups[100].

The RbI complex of the quinoline ligand *(42b)* containing two oxyethyl units less fails to show any sign of helicity in its NMR spectrum[112]. Containing a total of five donor atoms, the ligand is too short to overlap in a helical fashion in solution or in its crystals (see Fig. 5a).

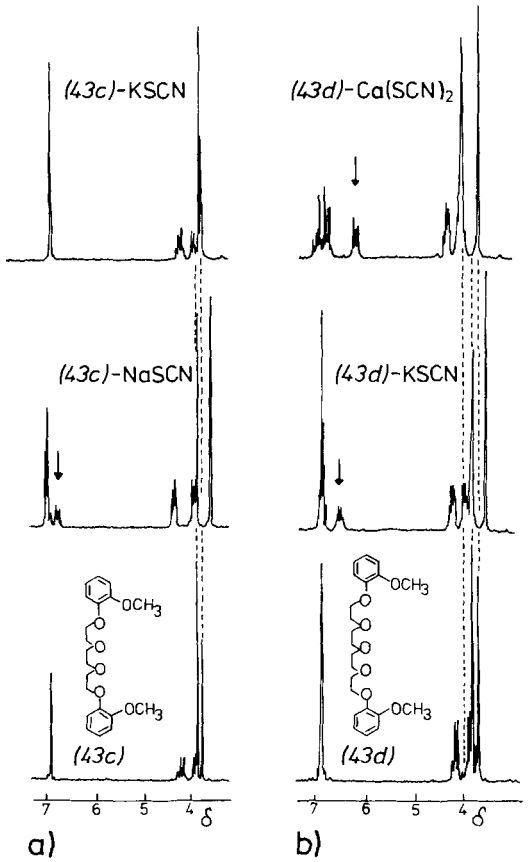


Fig. 8. ^{1}H-NMR spectra (sections) of the free ligands *(43c)* and *(43d)* and of some of their complexes. The OCH_3 region is dashed; arrows mark upfield shifts of aromatic protons.

The OCH_3 group in the ligands *(43)* and *(53)* which possess methoxyphenyl terminal groups is even better suited as an NMR probe for determining the structure of the complex in solution[95a] (see Fig. 8): while the OCH_3 protons generally exhibit an upfield shift in the $Na^{\oplus}$ complexes of *(43c)*, owing to partial overlap of the two aromatic terminal groups, the $K^{\oplus}$ ion leads to disappearance of overlap (cf. Fig. 8a). No upfield shift is observed since the larger $K^{\oplus}$ ion is no longer sufficiently enclosed by the inadequately long ligands in order to form a helix.

However, in the ligand *(43d)* containing one oxyethyl unit more, not only the $Na^{\oplus}$ ion but also the larger $K^{\oplus}$ ion leads to helical overlapping of the terminal groups (see Fig. 8b). The small ion $Ca^{2\oplus}$ permit an even closer enclosure of the cation with a helical structure showing more pronounced overlapping than in the potassium complex.

The helical complexes of type *(46a)* having central pyridine unit and aromatic or heteroaromatic terminal groups exhibit temperature dependent ^{1}H-NMR and ^{13}C-NMR spectra[113]. In the case of the NaSCN complex of the quinaldine analogue of *(46a)*, lowering of the temperature leads to broadening of the CH_2 absorption, which can be interpreted in terms of slowing down of the racemization (fast at room temperature) of the plus to the minus helix and *vice versa* (cf. Fig. 9). A free enthalpy of activation of $\Delta G_c^{\ddagger} \approx 41$ kJ/mol (≈ 9.8 kcal/mol) is calculated for this racemization process.

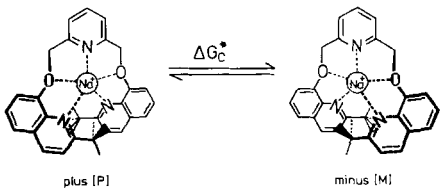


Fig. 9. Configurational interconversion [P]⇌[M] of the complex of NaSCN with the quinaldine analogue of *(46a)*.

The $Mg(ClO_4)_2$ complex of this ligand shows considerable broadening of the OCH_2 signals at room temperature as a consequence of its tighter helical structure (small cation with high charge density).

Measurements of ^{13}C-NMR shifts and spin-lattice relaxation times are attracting increasing interest in the study of alkali metal ion complexation by open chain neutral ligands[114].

In the future, a better understanding of complexation/decomplexation processes and their temperature dependence should result from NMR spectroscopy of the complexed cations, *e.g.* with the aid of ^{23}Na nuclear magnetic resonance[115] *(vide infra)*.

4.2.5. Thermodynamics and Kinetics of Complexation in Solution

Because they have model character for the transport of cations through biological membranes[116], the thermodynamics and kinetics of the complexation of $Na^{\oplus}$, $K^{\oplus}$, $Rb^{\oplus}$, $Cs^{2\oplus}$, and $Mg^{2\oplus}$ ions have been examined for various podands[117,118]. Changes in UV absorption of the two linear quinolyl ethers *(42d)*, $n = 3$, and *(46a)* (in methanol) on continuous addition of metal ions reveal the existence of two

nonequivalent bonding sites for alkali metals ions, with stability constants between 10^3 and 10^4 l mol^{-1} for K_1 and between 10^2 and 10^3 l mol^{-1} for K_2[117]. Stepwise bonding of $Na^{\oplus}$ and $K^{\oplus}$ ions induces a hypso- and hypochromic shift of the absorption maximum of the ligands. In methanol, the 1:1 and 1:2 complexes of the quinoline ligands *(42d)* with $Na^{\oplus}$ and $K^{\oplus}$ exhibit comparable stability. The stability constants are largely independent of ionic radius, as is apparent from the relatively small discrimination factor $K_1(Na^{\oplus})/K_1(K^{\oplus})=0.5$; this is a consequence of the flexibility of the tetraethylene glycol chain which can readily adapt to the various ions (cf. Fig. 10a). Introduction of a bridging pyridine ring into the ether chain increases the rigidity of the system, as is manifested in a greater cation selectivity [$K_1(Na^{\oplus})/K_1(K^{\oplus})=12$] of ligand *(46a)* (Fig. 10b).

In order to gain further information about the specific contribution of the 8-quinolyloxy terminal groups to complexation, studies were conducted on the coordination behavior towards $Mg^{2\oplus}$ since it has long been known that 8-hydroxyquinoline *(22)* forms stable chelates with $Mg^{2\oplus}$[119] whereas the classical oxygen-containing crown ethers show little tendency to complex $Mg^{2\oplus}$ ions[1a, 7a, 53, 120]. Stoichiometric titrations show that *(42d)* has four bonding sites for $Mg^{2\oplus}$ and that *(42d)*-$Mg^{2\oplus}$ complexes are considerably more stable in methanol than complexes of corresponding alkali metal ions. The four bonding sites are apparently non-equivalent, and the conformation of the polyether molecule changes several times on successive complexation.

Far lower K_s values are found for nitro groups in *(44d)*, $n=3$, with poor selectivity towards $Na^{\oplus}$ and increasing selectivity towards $Rb^{\oplus}$ (Fig. 10c), as well as the unsymmetrical compound *(45d)*, $n=3$, with phenyl (R = H) and quinoline at the ends of the chains (Fig. 10a). Atypical behavior is seen with *(79b)*, $n=1$ (see Section 4.3.3) with pronounced peak selectivity for $K^{\oplus}$ and very low tendency to complex other ions, as well as with the acidic ligand *(61a)* (see Section 4.2.8) with plateau selectivity towards $K^{\oplus}$ and $Rb^{\oplus}$ ($\log K_2 \approx 3$) and very low stability of the $Cs^{\oplus}$ complex.

The *meta*- and *para*-phenylene system, *(46b)* and *(54)*, respectively, having 8-quinolyloxy terminal groups, was compared with the corresponding ligand *(46a)* containing pyridine as central units: whereas *(46a)* exhibits high peak selectivity for $Na^{\oplus}$ ions at comparably high complex stability *(vide supra)*, the complexes of the two phenylene compounds with all ions show much lower K_s constants.

The fluorescence spectrum of *(54)* contains a pronounced band at *ca.* 300 nm whose intensity can be selectively modified by cations: $Rb^{\oplus}$ ions with optimum adaptation of host and guest[121] have a strong quenching effect on this fluorescence band. Thus an electronic interaction of the *para*-phenylene π-electron system can be deduced with the cation[122].

The *changes in entropy* (ΔS^0) on complexation of the open-chain ligands with several cations are, *e.g.*, -170 for *(42d)* with $Li^{\oplus}$, and -59 J K^{-1} mol^{-1} for $Na^{\oplus}$. ΔS *increases* sharply with increasing ionic size from $Li^{\oplus}$ to $Cs^{\oplus}$ while ΔH decreases along the same series. The ionic radius-dependent increase in entropy can be interpreted as being due to differing conformational changes on complexation of variously sized ions, since the rise in the ΔS curve apparently opposes expulsion of solvent molecules from the solvation sheath of the ions—which should lead to the opposite sequence of ΔS with increasing ionic size.

This finding appears all the more remarkable in view of the *decrease* in ΔS with increasing ionic radius observed with crown ethers such as [18]crown-6 *(26)* or [2.2.2]cryptand *(2)*[123]. This appears to reflect the replacement of the solvent molecules by the ligand, while the increase in entropy with open-chain ligands suggests entropy-controlled complexation.

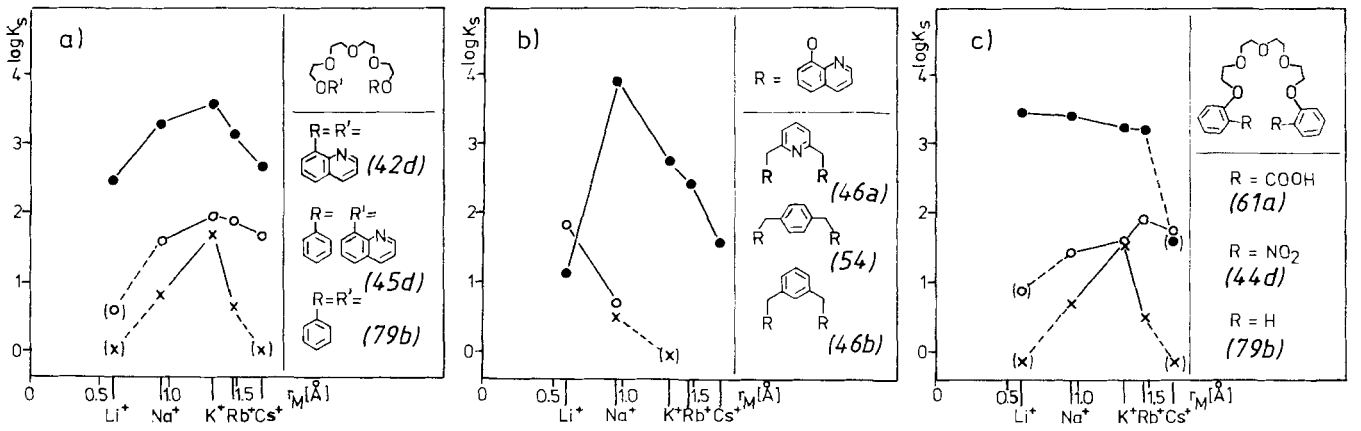


Fig. 10. Stability constants ($\log K_s$) of various podand-alkali metal ion complexes as function of ionic radius. (a) Stepwise loss of donor terminal groups; (b) ligands with stiffened chain; (c) variation of terminal group.

^{23}Na-NMR studies on the thermodynamics of complexation of the open-chain ligand *(56)* with $Na^{\oplus}$ in pyridine as solvent afforded $\Delta H^0=-17$ kcal/mol (-71 kJ/mol), $\Delta S^0=-48$ cal K^{-1} mol^{-1} (-201 J K^{-1} mol^{-1})[124]. The strongly negative ΔS^0 value suggests an entropy of cyclization or/and polymerization (see Fig. 6c for X-ray structure analysis). Complexation compells the ligand to adopt a particular conformation in which most or all of the oxygen donor centers form bonds to the included $Na^{\oplus}$ ion, accounting for the relatively large change in enthalpy. Complexation of *(56)* in solution is enthalpy-driven. It is seen from ^{23}Na-NMR studies that the interaction is best described by a successive

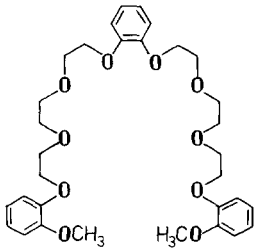
wrapping of the heptadentate ligand *(56)* around the sodium ion.

Kinetic data for the complexation/decomposition equilibria of $K^{\oplus}$ ions with *(42d)* and of $Na^{\oplus}$ ions with *(46a)* in methanol were obtained[117,118] from temperature jump relaxation experiments[125], which initially showed the occurrence of a simple reaction $A + B \rightleftharpoons AB$. The experimentally determined rate constants $k_{1,2}$ for recombination between $Na^{\oplus}$ and *(46a)*, and of $K^{\oplus}$ with *(42d)*, of 4×10^8 and 1×10^8 $mol^{-1}\ s^{-1}$, respectively, are relatively high[125]; nevertheless, they are more than one power of ten lower than the value of 5×10^9 $mol^{-1}\ s^{-1}$ expected for diffusion-controlled recombination of alkali-metal ions with uncharged monodentate ligands in methanol[126,127]. The reduced rate of complex formation can be rationalized as a consequence of stepwise displacement of solvent molecules from the inner coordination sphere of the metal ion by coordinating oxygen atoms of the polydentate ligand. In order to account for the high overall rate, each individual substitution process must occur at a rate of about $10^9\ s^{-1}$. Values of this order have been reported for the recombination of alkali metal ions with acidic chelating agents such as ethylenediaminetetraacetic acid *(13)* and nitrilotriacetic acid *(14)*[128].

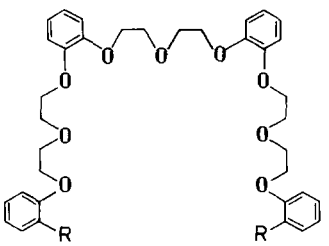
That the sum of the individual substitutions is the rate-determining step of complexation is underlined by comparison of $k_{1,2}$ for *(42d)* and *(46a)*: the flexible heptadentate ligand *(42d)* complexes $Na^{\oplus}$ and $K^{\oplus}$ four times as slowly as the more rigid pyridine-containing ligand *(46a)* which has only five coordination sites and accordingly cannot embrace a metal ion so completely. Overall, however, complexation in both cases is sufficiently fast to satisfy the demands formulated by *Eigen et al.*[129] for a carrier molecule[12].

4.2.6. Long-Chain Multidentate Acyclic Ligands

Long-chain multidentate podands of types *(57)* and *(58)*[130] are of interest because they might be able to form helical *endo*-polarophilic/*exo*-lipophilic "ion channels". Such multiply wound spiral structures which participate in ion transport through membranes[131] by the channel or pore mechanism[11,13] have been detected for several biomolecules such as gramicidin[132]. Model studies on synthetic channel-forming ionophores should provide an insight into possible transport mechanisms.



(57)



(58a): R = OCH_3
(58b): R = NO_2

All the ligands *(57)* and *(58)* qualitatively show pronounced solid/liquid phase transfer for inorganic salts; $KMnO_4$ is readily transferred into organic phases. That salts such as NaSCN, KSCN, NH_4SCN, $UO_2(NO_3)_2$ are complexed, follows from shifts and splitting of signals in the ^1H-NMR spectra; as with the shorter chain and more rigid ligands (cf. Section 4.2.4) this suggests helical structures. A number of crystalline alkali and alkaline earth metal salt complexes, including some with 1:2 ligand/salt stoichiometry, have been isolated[130]; an X-ray structure analysis has been published for the complex of *(58b)* with KSCN (Fig. 11)[105b]: in contrast to spherical wrapping of the decadentate ligand *(42g)* around the $Rb^{\oplus}$ ion[105a], the polyether *(58b)* is wrapped in an S-shaped manner in the *dinuclear* KSCN complex with a $K^{\oplus}SCN^{\ominus}$ ion pair located in each half-loop[105b]. The arrangement of the ligand in the complex is stabilized by coordination to $K^{\oplus}$, with double coordination of O(17) (cf. $Hg^{2\oplus}$-HGE complex, Section 4.1) and O(1), O(18), probably playing an important role. Interestingly, the nitro group is rotated relative to the phenoxy group by $-42\,°C$. Partial rotation through $-13°$ can be explained as due to steric repulsion between an oxygen atom of the nitro group and the *ortho*-situated ether oxygen atom; any twisting in excess of this figure is possibly due to an improvement of coordination of the nitro-oxygen atoms with $K^{\oplus}$. Formation of a dinuclear complex appears to be generally favored by double coordination of the terminal nitro groups. For example, a 1:1 complex of $K^{\oplus}$ could be isolated with the analogous ligand having 2,6-dimethoxyphenoxy in place of *ortho*-nitrophenoxy groups, while the smaller $Na^{\oplus}$ ion gave a 1:2 complex[130].

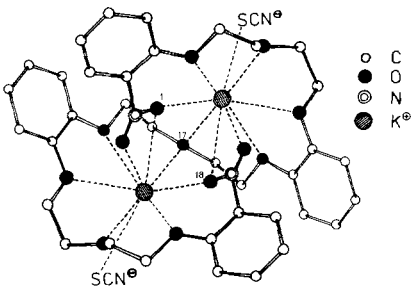


Fig. 11. Structure of the dinuclear KSCN complex of *(58b)*.

We have no detailed knowledge about the structure of the 1:1 complexes of these ligands; however, it can be assumed that helices with several turns may be present[133] which could comply with the pore concept of ion transport through membranes[11].

4.2.7. Neutral-Molecule Complexes of Acyclic Ligands

In 1970, *Pedersen* discovered that crown ethers not only complex metal ions but also enter into "coordinative" interaction with neutral molecules such as urea and thiourea[134]. Owing to the sometimes complicated stoichiometry, the complexes were initially regarded as adducts of the channel inclusion type[135]. Meanwhile, however, numerous substrate complexes of cyclic crown ethers have been found to have uniform stoichiometry, for example those with dimethyl acetylenedicarboxylate[136a] or CH-acid compounds such as CH_3CN[136b,136d], malononitrile[136c], and others[136d], or with NH-acid compounds such as benzenesulfonamide[137a] or phenylhydrazines[137b] as guest molecules.

We found that open-chain ligands like *(42d)* and *(43d)* are capable of forming stable crystalline 1:1 adducts with neutral guest molecules[138]. Crystalline urea and thiourea complexes can be formed, *e.g.* simply by uniting methanolic solutions of the substrates and an acyclic crown ether such as *(42d)*. The colorless adducts can be recrystallized unchanged from acetone. Elemental analyses confirm an exact 1:1 stoichiometry; it is also obtained when the dissolved components are mixed in various stoichiometric ratios. It may be concluded from the stoichiometry that we are not dealing with inclusion adducts in which the urea molecules form a crystalline host lattice with channel-like cavities[135], because such channel adducts are always found to have stoichiometries corresponding to five to six thiourea or urea molecules for one guest molecule (such as paraffins, *etc.*)[139].

X-ray structure analysis[140] of the crystals formed by *(42d)* and thiourea establishes the presence of crown-ether type 1:1 complexes (Fig. 12a): the NH terminal groups of the thiourea remarkably coordinate with all seven donor sites of the acyclic ligand, involving bifurcated H bonds.

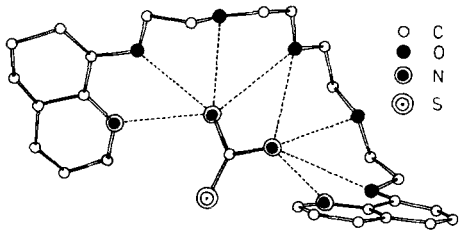
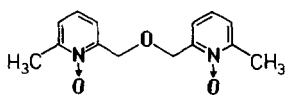


Fig. 12a. Crystal structure of the complex of *(42d)* with thiourea.

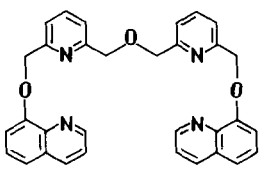
An analogous 1:1 complex is formed between thiourea and the heptadentate neutral ligand *(43d)*; an X-ray analysis has been performed[104].

It is characteristic that the non-crown type compound *(47)* shows deviating behavior; the 1:2 stoichiometry common for quinoline[141] is found with one thiourea molecule per heteroarene. The podands *(60)*, which contain two pyridine rings as central unit and are therefore fairly rigid, form crystalline complexes of alkali, alkaline earth, and transition metal ions, and also of urea and thiourea, with unusual ease[142]. The clearly observable, upfield shifts in the ^{1}H-NMR spectra indicate strong face-to-face overlapping of the end groups.

In this context it was found that classical neutral transition metal ligands such as phenanthroline *(39)* form crystalline stoichiometric 1:1 complexes with alkali metal salts[88b] and with urea[88c].



(59)



(60)

An interesting 1:2 complex of the double pyridine *N*-oxide *(59)* and water has also been isolated[142]; X-ray structure analysis (Fig. 12b)[104] showed that two of the ligand molecules are pseudocyclized *via* two H_2O molecules (H bonding) with the *N*-oxide oxygen atoms, while in the resulting pseudocavity two other water molecules are linked, again by H bonds, to each other and to the pyridine *N*-oxide oxygen atoms. Both the pseudocyclization *via* bridging water molecules and the coordination of water in the cycle show a remarkable analogy to H_2O bonding in bioionophores (Fig. 1a) and in cyclodextrins[143].

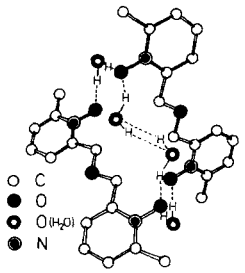


Fig. 12b. Pseudocyclization and H bonding in the H_2O complex of the podand *(59)*.

Thus it has been demonstrated that podands, like the coronands, are suitable for complexation of neutral substrate molecules and therefore also have the character of receptor models[144]; in the case of urea as guest molecule this is of great clinical interest owing to the possibility of accelerating dialysis. The design of improved urea receptors will utilize the kind of bonding first observed in podand-urea complexes.

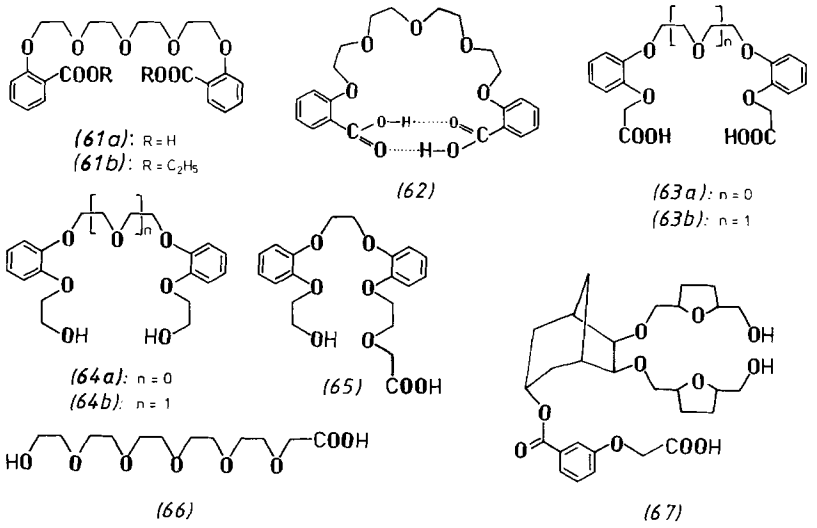
4.2.8. Interaction between Terminal Groups

The dicarboxylic acid *(61a)*[91] differs from the ligands having neutral donor terminal groups described so far in several properties: in spite of the comparatively high acidity, the carboxy protons have not been removed in the crystalline KSCN and $Ca(SCN)_2$ complexes, a fact substantiated by IR spectroscopy and interpreted with the aid of an attractive intramolecular terminal group interaction of the kind shown in *(62)*[91].

In this respect, *(61a)* can serve as a model for biotic acyclic carboxylic ionophores[12,116], in which the ligand conformation is enforced in pseudocyclic manner by similar strong intramolecular H bonds, partly *via* interposed water molecules[145]. Antibiotics belonging to the nigericin group (see Section 2) are very appropriate examples.

The open-chain dicarboxylic ligand *(63b)*[146a] behaves analogously. It also forms a series of crystalline alkali metal ion complexes, *e.g.* with KCl, KBr, KI, NaBr, RbSCN, Na- and K-picrate, in which the acid acts as neutral ligand. A crystal structure analysis is available for the K-picrate complex[146a] (see Fig. 13).

Contrary to expectation, no head-to-tail H bonds are observed. Instead, the principal feature is the dimeric centrosymmetric structure of the complex cation. In this structure, each individual ligand is arranged spirally and its conformation is fixed by one $K^{\oplus}$ ion each. One carbonyl oxygen of the monomer [O(17), O(17')] serves as bridging atom and is further coordinated to a second $K^{\oplus}$ ion (see Fig. 13). In this way, irregular eightfold coordination of potassium is achieved, with K...O distances between 2.29 and 2.93 Å; the two $K^{\oplus}$ ions are separated by 4.74 Å in the dimeric complex.



Significantly modified torsional angles are observed at the O(31) atom (see Fig. 13) (152 and 75°; normal values, 180 and 60°, respectively); this is responsible for the helical pitch of the ligand. The picrate ions do not participate in coordination of $K^{\oplus}$ but are bonded to one carboxy H each of the dimer *via* H bonds (not shown) and are also close to a benzene ring of a second complex unit.

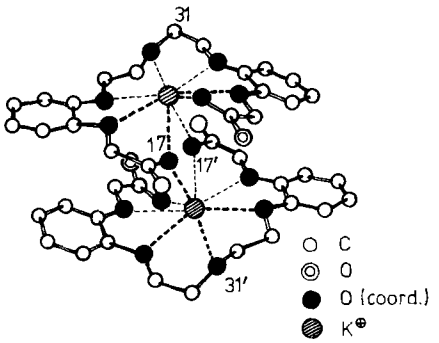
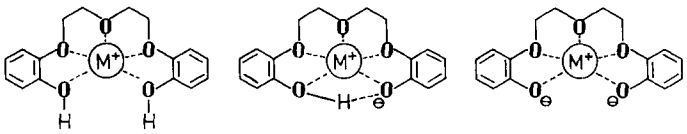


Fig. 13. Crystal structure of the complex of *(63b)* with K-picrate.

On reduction of the carboxy ligand *(63a)*, the open-chain polyether diol *(64a)* results which forms a crystalline 1:1 complex with NaSCN and a 2:1 complex with KSCN[146b]. Crystal structure analyses of the two complexes revealed heptadentate coordination of $Na^{\oplus}$ in the sodium complex and decadentate coordination of $K^{\oplus}$ on the potassium complex. In the dimeric 1:1 NaSCN complex, one of the two hydroxy oxygen atoms of ligand *(63a)* bonds alternately to the adjacent metal ion. The seventh coordination site is occupied by the $SCN^{\ominus}$ ion. In the 2:1 KSCN complex, two ligand units are grouped around one $K^{\oplus}$ ion in such a way that a pseudo-twofold symmetry axis is generated. Five of the total of six oxygen atoms of each ligand make up the tenfold coordination of the central ion. Specific H bonds are apparently one reason for the difference in the structures. While H bonds exist between the $SCN^{\ominus}$ ions and the two hydroxy groups of *one* ligand in the NaSCN complex, two hydroxy groups (one of which is uncoordinated) from *different* ligands are linked by H bonds in the KSCN complex.

Pseudocyclization by *intramolecular* H bonds is postulated for the complexes of the "acidic" ligands *(65)* and *(66)* on the basis of their ability to transport alkali metal ions through a liquid membrane of 1-hexanol[147]. That *(65)* permits considerably better transport than *(66)* is interpreted by assuming the benzene ring to permit greater stability of the pseudocyclic conformation in the complex (cf. Section 4.1) and to lead to better solubility of the salts in 1-hexanol. Moreover, *(64a)*, which does not contain a carboxy group, also transports alkali metals only poorly. The carboxy group therefore seems to be essential for ion transport (see also Section 4.3.2).

It was recently shown that open-chain ligands having tetrahydrofuran units such as *(67)* effect efficient transport of $Ca^{2\oplus}$ across lipophilic layers[148].



(68) *(69)* *(70)*

Acyclic "neutral" ligands with "acid" phenolic terminal groups can form several kinds of alkali and alkaline earth metal salt complexes[149]: complexes *(68)* neutralized by inorganic counterions, such as arise from open-chain crown ethers, and—after loss of one or both protons—acid complexes *(69)* and *(70)*, in which the ligands serve as mono- and dianions, respectively.

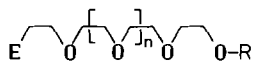
Special interactions between terminal groups are to be expected when nucleic bases such as adenine, thymine, *etc.* are attached to the ends of oligoethylene glycol ethers[150].

4.3. Weakly Complexing Acyclic Neutral Ligands

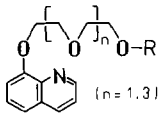
There is still a lack of systematic studies in the transition region between glymes *(27)* and open-chain crown ethers *(40)*, *i.e.* on those podands which bear just *one strong* donor group at the end of one chain or *several weaker* donor terminal groups.

4.3.1. Oligoethylene Glycol Ethers Bearing only One Strong Terminal Group

In ligand skeletons *(71)* having one strong donor terminal group (*E*), the other end of the chain can be weakly coordinated without the complex loosing its crystallinity[151].

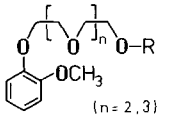


(71)



(n = 1, 3)

(72a): R = 1-Naphthyl
(72b): R = Phenyl
(72c): R = Methyl



(n = 2, 3)

(73a): R = 1-Naphthyl
(73b): R = Phenyl
(73c): R = Methyl

Thus the tetra- to hexadentate neutral ligands *(72a)*—*(72c)*[151] containing a good coordinating group such as an 8-quinolyloxy group on the one side and a poor coordinating group such as naphthoxy, phenoxy, or methoxy group on the other still give readily crystalline complexes with various salts. Just a single effective terminal group also permits isolation of crystalline alkali metal ion complexes of *(73a)*—*(73c)*[151]. The short chain of the oligoethylene glycol moiety is remarkable—as with the ligands having two strong donor terminal groups[91,92,95], it need only have $n>1$ and possess four donor atoms.

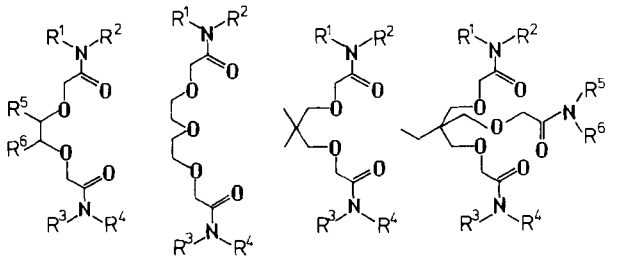
The flexible chain segment attached to the rigid donor terminal group (*E*) in *(71)* is apparently able to wrap around the cation after anchoring to the metal ion in a favorable planar arrangement; a second donor terminal group is then no longer necessary for formation of crystalline complexes. However, such an additional group may well enhance its stability and, above all, raise its complex constant.

Information about the geometry of the donor-free ends of the chains of the complexes in solution is provided by comparison of the ^{1}H-NMR spectra of the naphthyl ether *(72a)*, $n=2$, and the phenyl ether *(72b)*, $n=2$[151]: while the former exhibits a strong upfield shift of the α- and β-quinoline protons on transition from the free ligand to the complex, only the signal of the α-quinoline proton shows an upfield shift in the complex of *(72b)*. Since spatial proximity of the naphthyl/phenyl and quinolyl group can be deduced in both cases from the chemical shift, the difference should be related to the greater anisotropic region of the naphthalene ring; a change in the mutual orientation of the ends of the chains might also be responsible for the difference[152].

Suitable choice of donor terminal groups (*E*) on the one side and lipophilic chain termini on the other side of a ligand skeleton should open the way to further ligand/complex topologies with almost infinitely variable lipophilic/hydrophilic balance and complex stability constants and complexation kinetics[118], which is important for some applications[25].

4.3.2. Ionophores of Dioxasuberamide Type with Lipophilic Chain Termini

The acyclic compounds *(74a)* and *(74b)*[153] of the same type as dioxasuberamide and its homologue *(75)*, $R^1=R^2=R^3=R^4=C_6H_5$[154], are suitable sensors for potentiometric activity determinations of $Na^{\oplus}$, $Ba^{2\oplus}$, $Ca^{2\oplus}$, and of other ions of Groups IA and IIA[155]. The cation selectivity is dependent mainly upon molecular structure (nature and number of coordination sites, nature of the chain termini, *etc.*)[7b,156], apart from the choice of measuring medium. In



(74) *(75)* *(76)* *(77)*

(74a), $R^1=R^2=R^3=R^4=CH_2C_6H_5$, $R^5=R^6=H$
(74b), $R^1=R^3=$ Propyl, $R^2=R^4=$ Neopentyl, $R^5=R^6=H$
(74c), $R^1=R^2=R^3=R^4=C_6H_5$, $R^5=R^6=H$
(74d), $R^1=R^3=CH_3$, $R^2=R^4=H_3CCH_2OOC(CH_2)_{11}$–, $R^5=R^6=CH_3$
(74e), $R^1=R^2=R^3=R^4=$ Propyl, $R^5=R^6=H$
(74f), $R^1=R^2=R^3=R^4=$ Propyl, R^5—R^6 = —$(CH_2)_4$—

general, divalent cations are increasingly preferred over monovalent cations with increasing dielectric constant of the membrane phase[156]. An increase in the polarity of the ligand skeleton has a similar effect, with the result that small cations are preferred over bulkier ones of the same charge[7a,7b,153,157].

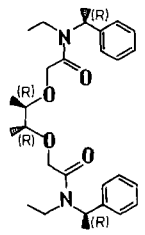
For example, the following selectivity sequences are found for the ligands *(74c)* and *(74d)* by potentiometry on liquid membrane electrodes[158]:

(74c): $Ba^{2\oplus}>Sr^{2\oplus}\gtrsim Ca^{2\oplus}>Mg^{2\oplus}$;
$Na^{\oplus}\gtrsim K^{\oplus}>Rb^{\oplus}>NH_4^{\oplus}>Cs^{\oplus}>Li^{\oplus}$
(74d): $Ca^{2\oplus}>Sr^{2\oplus}>Ba^{2\oplus}>Mg^{2\oplus}$;
$Li^{\oplus}>Na^{\oplus}\gtrsim Cs^{\oplus}>Rb^{\oplus}\gtrsim K^{\oplus}\gtrsim NH_4^{\oplus}$

Comparative measurements in the dioxasuberamide series with ligand-impregnated PVC membranes show *(74a)* to be a $Na^{\oplus}$-selective ionophore[155a], *(74b)* a $Ca^{2\oplus}$-selective ionophore[7b], and *(75)* a $Ba^{2\oplus}$-selective ionophore[156]. It recently also proved possible to tailor a ligand of similar structure for $Li^{\oplus}$, *viz.* *(76)*, $R^1=R^3=CH_3$, $R^2=R^4=$ heptyl[159]. Paying due attention to the coordination number/donor atom relation[160], the same kind of ligand could also be adapted to fit the $Na^{\oplus}$ ion by addition of another donor arm ("tripod", cf. Section 5.2). This $Na^{\oplus}$ ionophore *(77)*, $R^1=R^3=R^5=CH_3$, $R^2=R^4=R^6=$ heptyl[161] discriminates against $K^{\oplus}$ ions considerably more strongly ($K^{Pot}_{NaK}=4.4\times10^{-3}$ in *o*-NPOE[161]) than the $Na^{\oplus}$-selective ligand *(74a)* ($K^{Pot}_{NaK}=2\times10^{-1}$, in DBE[156], PVC matrix) and can therefore be used for intracellular studies under physiological conditions[162].

Ion carriers such as *(78)* having C_2 symmetry, which possess four centers of chirality, exhibit enantiomer-selective electromotive properties on incorporation into suitable mem-

branes[163] and accumulate one enantiomer, *e.g.* of α-phenylethylammonium ions, on transport across membranes[164].



(78)

Although these comparatively lipophilic ligands are conceived as ion carriers for liquid membrane sensors[165] and therefore do not have high K_s values, but require fast complexation kinetics in the interest of fast equilibration[154,166], the complex stabilities nevertheless suffice for formation of some crystalline complexes of alkali- and alkaline earth metal salts[158]. The isolated complexes usually require additional water molecules for construction of a stable crystal lattice. Coordinative participation of the carbonyl oxygen atoms[167], which could be substantiated by ^{13}C-NMR spectroscopy for the dissolved state[114a,c], could also be established for the solid state by IR spectroscopy and by crystal structure analyses recently carried out on the $CaCl_2$ and $MnBr_2$ complexes of the ligands *(74e)* and *(74f)*[168]: in both cases the metal ion is coordinated to four ether oxygen atoms and four carbonyl groups of a pair of symmetrically equivalent ligands (Fig. 14). In spite of differing demands of the two metal ions [$r(Ca^{2\oplus})=0.99$ Å, $r(Mn^{2\oplus})=0.80$ Å] the coordination geometries are essentially similar. A trigonal dodecahedron is present in both cases, with the four ether oxygens and the four carbonyl oxygens respectively at the corners of a distorted square. The measured O-metal ion distances are longer for the ether oxygens than for the carbonyl groups, with the latter actually shorter than the calculated ion/atom contacts. The O...Ca distances in the *(74e)*-$CaCl_2$ complex (Fig. 14a) are 2.462 and 2.364 Å (sum of ionic radii 2.39 Å), and

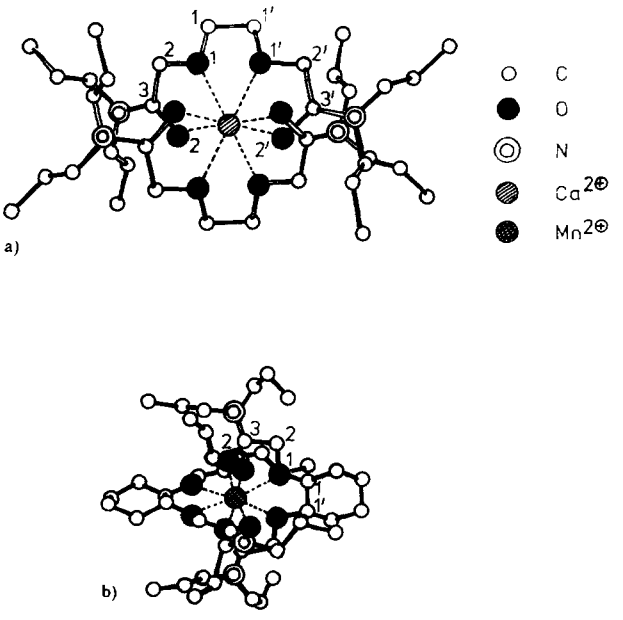


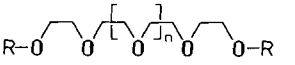
Fig. 14. Geometry (a) in the complex of *(74e)* with $CaCl_2$ and (b) in that of *(74f)* with $MnBr_2$ [168].

the O...Mn distances in the *(74f)*-$MgBr_2$ complex (Fig. 14b) are 2.370 and 2.185 Å (additive value 2.20 Å). The torsional angles show the atomic sequences C(1'), C(1), O(1), C(2), C(3), and O(2) of both ligands to be almost planar.

In contrast to the crystals of *(74e)*-$CaCl_2$ (2:1 stoichiometry), there are two kinds of $Mn^{2\oplus}$ in different geometrical sites in the packing of the crystals of *(74f)*-$MnBr_2$ (1:1 stoichiometry). One kind is coordinated pairwise by ligand molecules while the other is surrounded by a square plane of bromide ions.

4.3.3. Glyme Analogues with Donor-Free Rigid Ends

The simplification of "open-chain crown ethers" *(40)*[91,92] by stepwise worsening of the donating properties of the chain ends in *(71)*[151] raises the question whether podands devoid of donor terminal groups—such as *(79)*—might not also form crystalline complexes with alkali and alkaline earth metal salts (for heavy metal complexes, see Section 4.1).



(79a): R = 1-Naphthyl (n = 1 - 4)
(79b): R = Phenyl

Careful crystallization experiments with the polyethers *(79a)* and *(79b)* having two donor-free but rigid aryl groups as the chain termini and at least five ether oxygen atoms ($n \geq 1$) indeed afforded a series of crystalline complexes with alkaline earth, and also alkali metal ions[169].

As with the ligands bearing donor terminal groups[92], the formation of a pseudocycle or a helix during complexation in solution can be deduced from the upfield shift observed in the ^{1}H-NMR spectra for the aromatic and aliphatic protons[169] (cf. Section 4.2.4 and 4.3.1). Given a sufficiently long chain (above six CH_2CH_2O units), complexation can only be recognized from the upfield shift of the aliphatic protons. In these cases the aryl ether oxygen atoms may possibly no longer participate in coordination of the metal ion.

If the chain of *(79a)* and *(79b)* is shortened to just four or less CH_2CH_2O units, then no crystalline complexes are obtained under the experimental conditions employed, in accord with previous findings[2,92]. Thus the ligands *(79a)* and *(79b)* mark the limits of crystallizability of crown ether-type complexes. These ligands (with short chains) belong to the simplest and most inexpensive ligands available[10].

Recently, even the long-known *oligoethylene glycol dimethyl ethers* (glymes) *(27)* (Section 4.1) without rigid terminal groups but having a certain minimum number of chain members, *e.g.* hexaglyme *(27f)*, $n=5$, heptaglyme *(27g)*, $n=6$, have been found to form crystalline complexes with alkali/alkaline earth metal ions[169]. Previous attempts to prepare such compounds had all failed[2,92]. Thus it has been demonstrated that glymes not only interact with solvents and cations (solvation/association effects)[65] but also form stoichiometric crystalline complexes whose study (X-ray structure analysis) appears of fundamental importance.

Similar stoichiometric 1:1 neutral complexes with alkali and alkaline earth metal salts have meanwhile also been isolated[172] with the corresponding non-alkylated oligoethylene

glycols[170] and even with *ethylene glycol* itself[171]. Compounds having free OH groups do not seem to require a complexing central portion in order to form crystalline complexes.

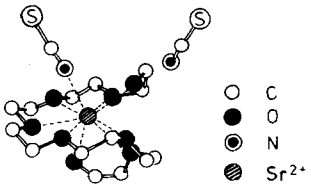
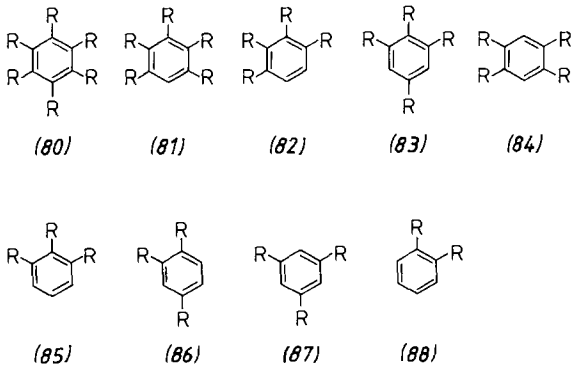


Fig. 15. Structure of the complex of heptaethylene glycol with $Sr(SCN)_2$.

An X-ray structure analysis is available for the heptaethylene glycol-$Sr(SCN)_2$ 1:1 complex (Fig. 15); it reveals an interesting coordination geometry[173]: all eight oxygen atoms of the glycol coordinate to the metal ion; in addition, one of the two $SCN^{\ominus}$ ions is also bonded to $Sr^{2\oplus}$ *via* a nitrogen atom. As in other podands having a similar number of donor atoms (see Section 4.2.3) the ligand chain in this complex is wrapped in helical fashion around the central ion. The Sr...O bond lengths vary between 2.56 and 2.73 Å, with the terminal oxygen atoms showing the shortest Sr...O distances.



(a), R = n-$C_4H_9(OCH_2CH_2)_3SCH_2$; *(b)*, R = $CH_3(OCH_2CH_2)_2SCH_2$; *(c)*, R = CH_3SCH_2; *(d)*, R = n-$C_4H_9SCH_2$; *(e)*, R = n-$C_{12}H_{25}SCH_2$; *(f)*, R = $C_6H_5SCH_2$; *(g)*, R = 2,6-$(CH_3)_2C_6H_3SCH_2$; *(h)*, R = $C_6H_5CH_2SCH_2$; *(i)*, R = β-Naphthyl-SCH_2; *(k)*, R = $C_6H_5OCH_2$; *(l)*, R = *o*-CHO—C_6H_4—OCH_2; *(m)*, R = *o*-CH_3CO—C_6H_4; *(n)*, R = C_6H_5—N=N—*p*-C_6H_4—OCH_2; *(o)*, R = 8-Quinolyl-OCH_2; *(p)*, R = 8-Quinolyl-$OCH_2CH_2COOCH_2$; *(q)*, R = C_6H_5S

ring by way of sulfur atoms[174]. These compounds, which are reminiscent of octopi, exhibit striking phase transfer properties towards metal ions (cf. Fig. 16). *(80a)* transfers a large proportion of alkali metal picrate (Mg, Ca, Sr, Ba) from, *e.g.*, 10^{-4} N aqueous solution into dichloromethane; almost all the salt is transferred into the organic phase in the case of alkali metal picrate solutions (Li, Na, K, Rb, Cs)[175].

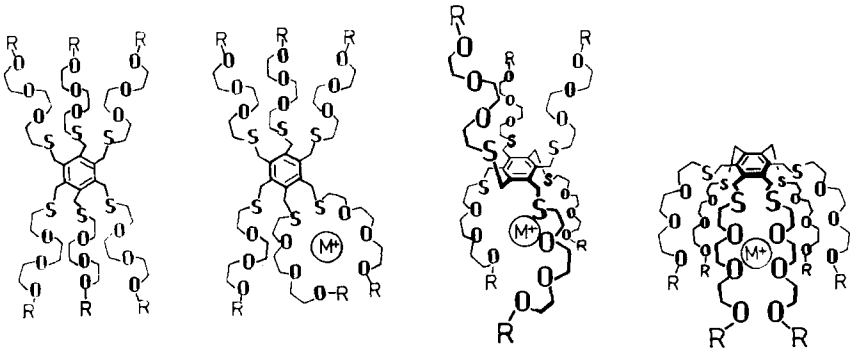


Fig. 16. Interaction between octopus-like ligands *(80a)* and cations $M^{\oplus}$.

5. Acyclic Neutral Ligands Having Many Arms (Oligo/Polypodands)

5.1. Ligands without Donor Terminal Groups

Many-armed neutral ligands—polypodands[*]—are of interest for several reasons[1]: the high number of donor atoms holds promise of powerful and versatile complexation; there is also a possibility of discovering novel stereochemical arrangements and complex geometries. Such molecular skeletons should also permit a wide range of variation of lipophilic/hydrophilic balance of both ligands and complexes.

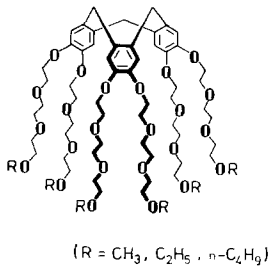
The first compounds described were *(80)*—*(88)* which bear several donor-containing "tentacles" attached to a benzene

Phase transfer is greatly restricted on reduction of the number of donor sites, whether by shortening of the tentacles as in *(80b)* or by reduction of their number as in *(81)*—*(88)*.

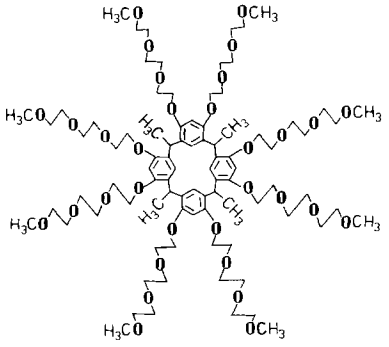
Similar phase transfer properties are shown by the hexapodands *(89)*[176] derived from cyclotriveratrylene. While *(89)* can form an "octopus-like" complexation cavity, the conformationally more rigid *(90)*[176] is unable to do so; its phase transfer activity is therefore very modest.

The oxygen-free hexasubstituted benzenes *(80c)*—*(80g)*[177] examined for sake of comparison are naturally unable to act as ligands towards metal ions[174]. However, as was subsequently demonstrated for various examples [*(80h)*, *(80k)*, *(80q)*[178]; *(80l)*—*(80p)*[179]], they form a new type of stoichiometric inclusion compound by acting as host molecules ("hexahosts") for neutral organic molecules such as acetone, dioxane, diglyme, trichloroethanol, dimethylformamide, dimethylacetamide, tetramethylurea, hexamethyl-

[*] Having already denoted podands as open-chain analogs of coronands and cryptands (see Footnote [**] on p. 753), we classify them as *di-*, *tri-*, *tetra-*, ... *poly*-podands according to the *number* of donor "arms".



(89)



(90)

phosphoric triamide, pyridine, lutidine, collidine, toluene, styrene, cyclohexane, and other hydrocarbons[135d, 178]; their precise structure has yet to be elucidated. Since decomposition of the adducts, which are stable at room temperature, is greatly accelerated by a drop in pressure, a channel structure would appear likely[178]. An X-ray structure analysis has been performed on the CCl_4 clathrate of the host molecule *(80q)* containing fewer benzylic CH_2 groups (Fig. 17)[180]. As is typical of hexasubstituted benzenes[181], the SC_6H_5 side arms point alternately upwards and downwards out of the plane of the central benzene ring and give rise to three-dimensional *inter*molecular cavities in the crystal lattice which are occupied by the CCl_4 guest molecules (1:2 stoichiometry). CCl_3CH_3 and CCl_3SCl can also be incorporated into host lattice in the same ratio, whereas CCl_3Br and CCl_3NO_3 give 1:1 adducts[180, 182].

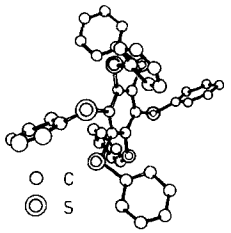
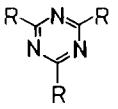


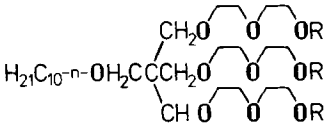
Fig. 17. Geometry of the "hexahost" *(80q)* in the CCl_4 clathrate [180].

A remarkable degree of *guest selectivity* is found for the hexahosts on recrystallization from solvent mixtures (*e.g. o*- and *p*-xylene in equimolar amounts)[183]. Which of the two isomers is preferentially complexed depends primarily on the structure of the host[135e]. *(80h)* and *(80i)* favor inclusion of *p*-xylene, while *(80f)* and *(80k)* take up more of the *o*-isomer. An *o/p* ratio of 90:10 is found for hexakis(phenylthiomethyl)benzene *(80f)*.

Interest also attaches to adduct formation between some "octopus molecules" bearing donor terminal groups with crown ethers such as [12]crown-4, [15]crown-5, [18]crown-6, and crown ether-cation complexes (cascade complexing)[179]. X-ray structure analyses should reveal whether these are intramolecular compounds or whether the guest molecules are accommodated in cavities in the crystal lattice.

Open-chain crown ether fragments without donor end groups have been attached to the triazine system *via* N atoms, and the resulting tri- and hexapodands *(91)* examined with respect to their phase-transfer behavior[184] (cf. Section 6). Once again, phase transfer depends upon the number of polyether arms and upon the length of the terminal alkyl groups (cf. [174]). Corresponding modifications have been performed on *pentaerythritol* as links for polyether "tentacles" *(92)*[184].





(91a): R = (n-C_4H_9O)$_2$N-

(91b): R = (n-C_8H_{17}O)$_2$N-

(91c): R = n-C_4H_9O-

(91d): R = n-C_8H_{17}O-

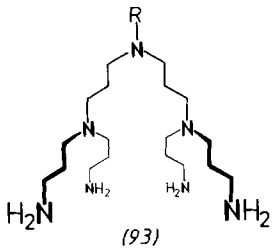
(92a): R = H

(92b): R = CH_2CH_2OH

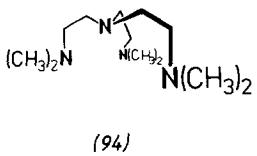
(92c): R = n-C_8H_{17}-

(92d): R = n-$C_8H_{17}OCH_2CH_2$-

Oxygen-free polyamines of the many-armed "cascade molecule" type *(93)*[185] are of interest as chelating agents in metalation reactions[186] or as polyfunctional hydrolysis catalysts[187]. Crystalline stoichiometric alkali metal salt complexes of permethylated polyamines such as *(94)* are known[186].

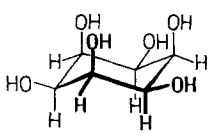


(93)

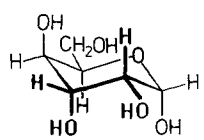


(94)

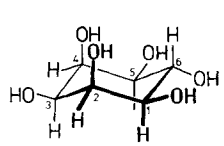
Complexation of *carbohydrates* (cyclitols, sugars) with alkali metal ions has been studied by paper electrophoresis[188] and by NMR spectroscopy[189]: the electrophoretic investigations carried on from the observation that many polyols migrate towards the cathod on paper electrophoresis in supporting electrolytes containing acetates of various metals[190]. Among the polyols examined, *cis*-inositol *(95)* showed the greatest mobility in solutions of all the metal acetates used, the effect being most pronounced in the presence of $Ca^{2\oplus}$, $Sr^{2\oplus}$, and $Ba^{2\oplus}$ ions[189]. This is not very surprising in view of



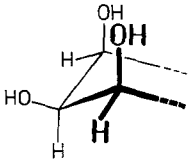
(95)



(97)



(96)



(98)

the four potential complex bonding sites—three jointly acting axial OH groups and three *a-e-a* arrangements of O atoms. *epi*-Inositol *(96)* having only an *a-e-a* orientation of OH groups, exhibit only about one third of the mobility of *cis*-inositol under comparable conditions.

Other cyclitols and sugars, *e.g.* α-gulose *(97)* having an OH group arrangement resembling that of *(98)*, behave correspondingly. Worthy of note is the specificity difference between the series $Ca^{2\oplus}$, $Sr^{2\oplus}$, $Ba^{2\oplus}$, $La^{3\oplus}$, which are suitable for both *cis-(95)* and *epi*-inositol *(96)*, and small ions ($r = 0.6$—0.8 Å) such as $Mn^{2\oplus}$, $Fe^{3\oplus}$, $Ni^{2\oplus}$, $Co^{2\oplus}$, $Cu^{2\oplus}$, $Zn^{2\oplus}$, $Mg^{2\oplus}$, which are effective only in solutions of *cis*-inositol[189a]. This suggests that the latter cations coordinate only to the three axial OH groups of *(95)*. Even smaller cations ($Be^{2\oplus}$, $Al^{3\oplus}$, $Li^{\oplus}$) have no effect at all on electrophoretic mobility.

Addition of $CaCl_2$ to a solution of *epi*-inositol *(96)* effects significant changes in the NMR spectra[189a,b]: all signals are shifted downfield, with that of H(3) being shifted most (0.32 ppm in 2 M $CaCl_2$). The diamagnetic shifts are dependent upon the charge of the complexed cation and its bond strength. $La^{3\oplus}$ ions accordingly cause larger shifts and $Na^{\oplus}$ smaller shifts than $Ca^{2\oplus}$ ions[191]. The stability constants of the complex formed can thus be roughly estimated from the shift data[189a,b].

The stereochemistry was elucidated by X-ray structure analysis of some hydrated $CaBr_2$ complexes (see Fig. 18) which could be isolated in crystalline form by evaporation of equimolar amounts of the components in aqueous solution[192]; in these complexes the $Ca^{2\oplus}$ ions are located in a square-antiprismatic environment of eight oxygen atoms contributed to varying extents by several ligand molecules (three in the case of galactose, two for inositol) and by water participating in coordination (3 to 4 molecules).

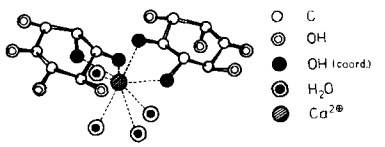
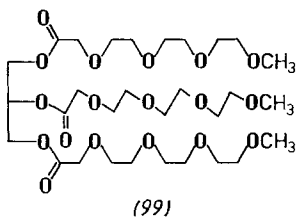


Fig. 18. Coordination sphere of the $Ca^{2\oplus}$ ion in the inositol-$CaBr_2$ complex [192a].

Several bonding and torsional angles show characteristic deviations relative to those in uncomplexed sugars. Such changes in conformation may be involved in biological $Ca^{2\oplus}$ transport[193] or in the reversible fixation of $Ca^{2\oplus}$ ions in carbohydrate compartments in membrane surfaces[194].

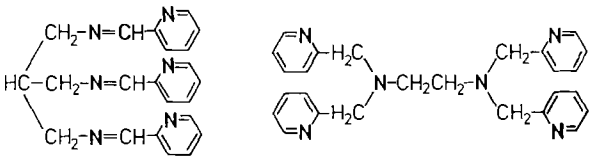


(99)

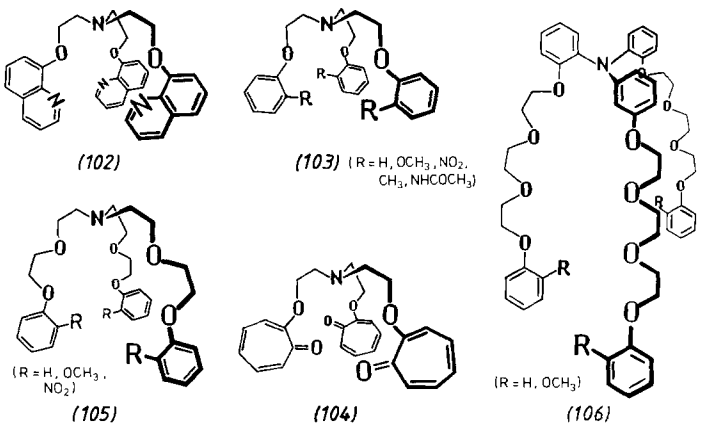
In this connection, there would appear to be a variety of interesting applications for the recently synthesized "hydrophilic lipids" of type *(99)*, in which the fatty acid residues are replaced completely or partly by oligoethylene glycol ether chains; given a sufficient number of ether oxygen atoms, these substances become so hydrophilic that they dissolve in water[195].

5.2. Polypodands Having Donor Terminal Groups (Acyclic Cryptands, Tetrapodands)

Although many-armed ligand skeletons with neutral coordinating terminal groups *(100)*[196], *(101)*[197] have long been known[78a], particularly for complexation of heavy metal ions, acyclic ligands having cryptand properties for elements of Groups I and II have only recently become available[198] by combination of the polypodand (octopus molecule)[174] and terminal group concepts[91,92].



(100) *(101)*



(102) *(103)* *(105)* *(104)* *(106)*

These neutral ligands *(102)*—*(105)*, which have been designated *open-chain cryptands*, do indeed exhibit cryptand-analogous complexation and phase transfer behavior[198]: $KMnO_4$ and aqueous Na- and K-picrate are more readily taken up in organic phases than with dibenzo[18]crown-6 *(1)*. A series of crystalline complexes can be isolated with salts such as NaSCN, KSCN, RbI, NH_4SCN, $Ni(ClO_4)_2$, H_2PtCl_6, BaI_2, $Th(NO_3)_3$, $Cu(ClO_4)_2$, *etc.*[118,198].

The KSCN complex of the three-armed, decadentate neutral ligand *(105)*, $R = OCH_3$, which is the first alkali metal complex of an open-chain cryptand to be examined by X-ray structure analysis, exhibits a novel complexation geometry (Fig. 19)[104]: all ten donor centers including the three OCH_3 terminal groups participate in coordination of the metal ion, which is located at the center of the pseudocavity. In order to attain this coordination, the three arms wrap around the cation in a propeller-like fashion. Owing to the complete screening of the cation, there is no point of attack for the anion. The $SCN^{\ominus}$ ion is therefore outside the lipophilic periphery of the cation complex, as in the bicyclic cryptands.

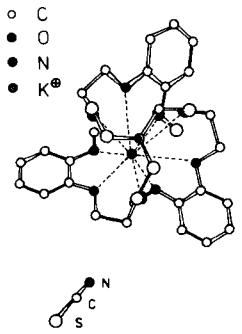


Fig. 19. Structure of the KSCN complex of *(105)*, R = OCH_3 ("open-chain cryptand").

Of all the acyclic ligands studied so far[198], *(102)* exhibits the highest complex constant for alkali metal ions (in methanol/water); not only its preference for $Na^{\oplus}$ ($\log K = 2.7$) over $K^{\oplus}$ ($\log K = 2.0$) and $Li^{\oplus}$ ($\log K < 2$) but also its high selectivity for divalent cations, especially $Ba^{2\oplus}$ ($\log K = 3.2$) and $Sr^{2\oplus}$ ($\log K = 2.7$), warrant mention. The even higher complex constant of the pseudocryptand *(104)*, having three tropolone ether terminal groups, for these divalent cations (*e.g.* $\log K(Ba^{2\oplus}) = 3.6$, $\log K(Sr^{2\oplus}) = 3.3$, but $\log K(K^{\oplus})$ and $\log K(Na^{\oplus}) < 2$) is also striking. Accordingly, we were able to prepare a BaI_2 complex, but no KSCN complex, of *(104)*. On the other hand, the complex stabilities with the smaller ions $Li^{\oplus}$ (<2) and $Ca^{2\oplus}$ (<2) are significantly lower. These ligand selectivities can be rationalized with the aid of space-filling models, and apparently arise from the inability of the pseudocavity to contrast sufficiently to ensure ubiquitous intimate contact with the small cations owing to steric constraints. Only *(102)* shows a $\log K$ value >2 for $Mg^{2\oplus}$. Parallels between ligand cavity size and complexation strength can also be deduced from the ^{1}H-NMR spectra of the complexes (anisotropic upfield shift)[198].

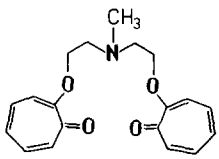
The reaction of tris(chloroethyl)amine with salicylate ions does not lead to the expected ether, as in the dipod system [cf. *(61a)*[91]], but instead, as shown by preliminary results of X-ray structure analyses[104], to the tris(salicyclic ester) having free phenolic OH groups which forms colored neutral complexes soluble in organic media, even with heavy metal ions.

The benzo-annelated tripodand *(106)*, R = OCH_3[199], has been found to give 1:1 complexes with KI, RbI, and BaI_2, and a 1:2 complex with $Ba(SCN)_2$; corresponding complexation experiments with *(106)*, R = H, were unsuccessful, thus underscoring the favorable effect of the terminal groups in this system too. For constant chain length but different terminal groups the contribution of the terminal groups to complexation in the tripodand series *(105)* was found to increase in the following order[199]: phenyl < 2-NO_2-phenyl ≤ CH_3 ≤ 2-CH_3O-phenyl ≤ 8-quinolyl.

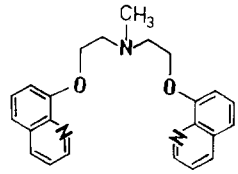
The complex stabilities measured for the tetrapodands *(107)* and *(108)* with various terminal groups were generally somewhat lower than for the analogous tripodands *(102)* and *(104)*[200]. The four large terminal groups probably offer steric hindrance to complexation of small cations.

The ethylenediamine system and the tropolone end group in *(108)* appear to complement each others particularly well[200]: in methanol/water (88:12), a value of $\log K_s = 2.5$ is found for $Na^{\oplus}$ ions and 2.7, 3.0, and 3.1 for $Ca^{2\oplus}$, $Sr^{2\oplus}$, and $Ba^{2\oplus}$ ions (cf. [198]).

Also of interest in this connection is a comparison of the tropolone compound *(108)* with the corresponding dipodand *(109)*. Although the latter is a stronger complex ligand than the dipodand molecule *(110)* with quinoline terminal group, it is significantly weaker than the corresponding tetrapodand *(108)*[200].

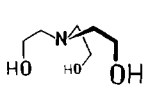


(109)

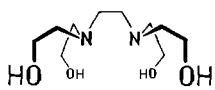


(110)

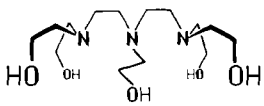
Further studies will show whether the attachment of *additional* tentacles (pentapodands ... octapodands) gives rise to a further (selective) enhancement of complexing ability (*e.g.* towards divalent ions). It may be that a *lengthening* of the arms of the polypodands proves more favorable on account of the less extensive steric hindrance.



(111)



(112)



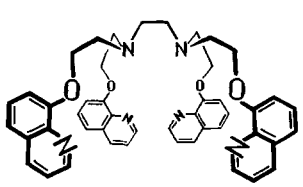
(113)

The strict 1:1 stoichiometry recently found for the alkali/alkaline earth metal complexes of nitrilotriethanol *(111)* and of the corresponding tetra- and pentapodands *(112)* and *(113)*[201] is worthy of note: these are examples of fundamental, facile recognition and selectivity processes on a molecular level[144].

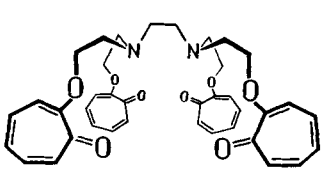
6. Use of Open-Chain Neutral Ligands for Phase Transfer Catalysis

While the phase transfer properties of cyclic crown ethers and cryptands have found wide application in chemical synthesis[202], only few results of this kind have so far been reported for open-chain neutral ligands.

The phase transfer efficiency of open-chain neutral ligands of type *(42d)* and *(80a)* was compared with that of cyclic and bicyclic crown ethers and cryptands[175a] with the aid of the standardized phase transfer reaction of benzyl chloride with potassium acetate in acetonitrile as solvent. It was found that each ligand generates a *naked anion* characteristic for its particular system. Further investigations will show to what extent this result, obtained for $K^{\oplus}$ and acetonitrile as solvent, is valid for other systems.



(107)



(108)

Comparison with the noncatalyzed reaction shows that equilibria with characteristic product yields are attained in all cases. They vary between several percent and almost 100%. The time of equilibration also depends upon the type of ligand, varying between a few hours and several days.

This and similar substitution reactions with other potassium salts (in acetonitrile or benzene) have also been carried out with glymes of various chain lengths *(27)* and analogous compounds[10]: it was found that the efficiency of the oligoethylene glycol dimethyl ethers increases with concentration, that at the same concentration (in mol/l) the longer-chain ethylene glycol ethers are more effective than the shorter chain ones, and that a certain minimum chain length is necessary for significant catalytic properties. Diglyme *(27b)* and triglyme *(27c)* therefore exhibit only slight effects. At equal concentration, the open chain ethers are somewhat inferior to the macrocyclic crown ethers, *e.g.* [18]crown-6. This can be compensated by increasing the concentration.

In the *triazine* series *(91)*, phase transfer activity peaks at *(91b)* and falls on shortening of the alkyl group [*(91a)*] or if the number of arms is reduced to three [*(91c)*, *(91d)*][184]. Compound *(91b)* resembles typical trialkylphosphonium catalysts in its phase transfer efficiency[203] and is hardly inferior to the alkyl-substituted cryptands[204]. Whereas *(91b)* proved to be a good phase transfer catalyst in all the reactions studied, the efficiency of the pentaerythritol derivatives *(92)* is highly dependent upon the kind of reaction being catalyzed[184].

During the etherification of glycols or mixtures of glycols of various degrees of oligomerization or polymerization with methyl chloride or dimethyl sulfate in a solid/liquid two phase system (sodium hydroxide/benzene; light petroleum or xylene were used in some cases), the glycol appears to initially act like a phase transfer catalyst by enclosing the sodium ion; as the reaction proceeds it is released by the resulting ether[205]. Anion transfer from solid to solution is promoted to a greater extent by triethylene glycol than would be expected from a potentially tetradentate ligand.

Non-linear relationships between the chain length of oligoethylene glycol ether *(27)* and the complex stability were also observed on complexation of aryldiazonium ions[206]: the complex stability increases with the number of donor atoms up to a certain length (heptaglyme) and then falls abruptly at *octaglyme (27h)*. A further increase in the number of ether oxygen atoms leads to a renewed rise in complex stability. Since the complex constant of [18]crown-6 towards the same diazonium ion is only about five times greater than that of the dimethyl ether of Carbowax-1000[207], the possibility opens up of using this less expensive glyme mixture as phase transfer catalyst in the reaction of aryldiazonium salts[206b]. Aryldiazonium salts experience photochemical stabilization on complexation with glymes (and crown ethers)[206a]. Interestingly, triglyme *(27c)* exerts a stabilizing effect comparable with that of [15]crown-5.

7. Outlook

A new chapter of complex chemistry with neutral organic ligands has begun. Parallel to the cyclic and polycyclic series attempts should be made in the case of podands to create pseudocavities, by means of specifically interacting terminal groups, which resemble those in bioionophores. These cavities may possibly simulate the ionic channel structure and the bactericidal properties of the bioionophores. The incorporation of chiral structural elements into oligopodands also appears a rewarding aim. Such molecules could also be of interest as chiral additives for enantioselective syntheses[208]. Helical enclosure of metal ions such as $Li^{\oplus}$ by chiral ligands in organolithium compounds may effect a higher optical induction than the reagents examined so far[209].

The synthesis of new topologies of acyclic crown ethers and cryptands— also for simple glycols—and their testing as phase transfer catalysts in chemical reactions with ions is just a matter of time[210]. There is no lack of expectation, some rather speculative, in chemistry and other branches of science and technology, such as photography, vulcanization techniques, petroleum engineering, electroplating, reaction engineering[211]. The comparatively low price of open-chain crown compounds should further their large-scale commercial utilization[10]. Considerable progress has already been made in the construction of multielectrode systems doped with open-chain neutral ligands for simultaneous determination of the concentration of several cations, *e.g.* in blood and serum[25].

Mutually comparable physico-chemical studies (ΔH, ΔG, ΔS, ΔK_s, k) of host-guest interactions between simple ligands and simple guest ions or molecules could contribute much to our understanding of passive and active ion transport[11,12,116,131], the mode of action of biological ionophores[7c], and drug/receptor, enzyme/substrate, and antigen/antibody interaction[144,212]. Since the salt balance is of vital importance for organisms (blood coagulation, sugar balance, muscle contraction, kidney function, *etc.*)[24a] and specific modifications play an important role in pathological concentration changes (cancer, gout, *etc.*) and the action of drugs (*e.g.* digitalis)[213], further research into neutral ligand complexation appears of general interest and practical value in numerous fields of application.

We are indebted to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for support of our own work. Thanks are also due to Ms. B. Jendrny for her assistence.

Received: May 30, 1978;
supplemented: August 30, 1979 [A 291 IE]
German version: Angew. Chem. *91*, 813 (1979)

[1] Reviews: a) *J. J. Christensen, D. J. Eatough, R. M. Izatt*, Chem. Rev. *74*, 351 (1974); b) *F. Vögtle, E. Weber*, Kontakte (Merck) *1/77*, 11; c) *R. M. Izatt, J. J. Christensen:* Synthetic Multidentate Macrocyclic Compounds. Academic Press, New York 1978; d) Progress in Macrocyclic Chemistry. Vol. 1. Wiley, New York 1979; e) *F. Vögtle*, Chimia *33*, 239 (1979); f) *F. Vögtle, E. Weber* in *S. Patai:* The Chemistry of the Ether Linkage. Wiley, London, in press.

[2] *C. J. Pedersen*, J. Am. Chem. Soc. *89*, 7017 (1967).

[3] Review: *C. J. Pedersen, H. K. Frensdorff*, Angew. Chem. *84*, 16 (1972); Angew. Chem. Int. Ed. Engl. *11*, 16 (1972).

[4] Review: a) *J.-M. Lehn*, Struct. Bonding *16*, 1 (1973); b) Acc. Chem. Res. *11*, 49 (1978); c) Pure Appl. Chem. *50*, 871 (1978).

[5] a) Isolation: *R. L. Harned, P. H. Hidy, D. J. Cornus, K. L. Jones*, Proc. Indiana Acad. Sci. *59*, 38 (1959); *T. Kubota, S. Matsutani, M. Shiro, H. Koyama*, Chem. Commun. *1968*, 1541; b) structure elucidation (Ag salt): *L. K. Steinrauf, M. Pinkerton, J. W. Chamberlin*, Biochem. Biophys. Res. Commun. *33*, 29 (1968); *M. Shiro, H. Koyama*, J. Chem. Soc. *B 1970*, 243.

[6] Review: *K. O. Hodgson*, Intra-Sci. Chem. Rep. *8*, 27 (1974).

[7] Reviews: a) *W. E. Morf, W. Simon,* Helv. Chim. Acta *54*, 2683 (1971); b) *W. Simon, W. E. Morf, P. Ch. Meier,* Struct. Bonding *16*, 113 (1973); c) *B. C. Pressman,* Annu. Rev. Biochem. *45*, 501 (1976).

[8] Review: *F. Vögtle,* Chem.-Ztg. *96*, 396 (1972), and references cited therein.

[9] Review: *M. De Sousa Healy, A. J. Rest,* Adv. Inorg. Chem. Radiochem. *21*, 1 (1978).

[10] Cf. Kontakte (Merck) *1/77*, 29; *H. Lehmkuhl, F. Rabet, K. Hauschild,* Synthesis *1977*, 184; *D. Balasubramanian, P. Sukumar, B. Chandani,* Tetrahedron Lett. *1979*, 3543.

[11] Reviews: *P. B. Chock, E. O. Titus,* Prog. Inorg. Chem. *18*, 287 (1973); *E. Bamberg, R. Benz, P. Läuger, G. Stark,* Chem. unserer Zeit *8*, 33 (1974); *D. E. Fenton,* Chem. Soc. Rev. *6*, 325 (1977).

[12] Review: *W. Burgermeister, R. Winkler-Oswatitsch,* Top. Curr. Chem. *69*, 91 (1977).

[13] *C. H. Hassall, W. A. Thomas,* Chem. Br. *7*, 145 (1971), and references cited therein.

[14] *R. Sarges, B. Witkop,* Biochemistry *4*, 2491 (1965); review: [12].

[15] Improved structural proposal: *D. R. Martin, R. J. P. Williams,* Biochem. J. *153*, 181 (1976).

[16] *T. Wieland, G. Lüben, H. Ottenheym, J. Faesel, J. X. de Vries, W. Konz, A. Prox, J. Schmid,* Angew. Chem. *80*, 209 (1968); Angew. Chem. Int. Ed. Engl. *7*, 204 (1968); details in [12].

[17] *E.g.* amphotericin-B: *A. C. Cope, U. Axen, E. P. Burrows, J. Weinlich,* J. Am. Chem. Soc. *88*, 4228 (1966); *W. Mechlinski, C. P. Schaffner, P. Ganis, G. Avitable,* Tetrahedron Lett. *1970*, 3873.

[18] a) Isolation: *P. Gachon, A. Kergomard, H. Verschambre,* Chem. Commun. *1970*, 1421; b) structure ($Ag^{\oplus}$ salt): *M. Alleaume, D. Hickel, ibid. 1970*, 1422.

[19] Structure: *E. W. Czerwinski, L. K. Steinrauf,* Biochem. Biophys. Res. Commun. *45*, 1284 (1971).

[20] a) Isolation: *A. Agtarap, J. N. Chamberlin,* Antimicrob. Agents Chemother. *1967*, 359; b) structure: *W. K. Lutz, F. K. Winkler, J. D. Dunitz,* Helv. Chim. Acta *54*, 1103 (1971); c) $Ag^{\oplus}$ salt: *A. Agtarap, J. W. Chamberlin, M. Pinkerton, L. K. Steinrauf,* J. Am. Chem. Soc. *89*, 5738 (1967); *M. Pinkerton, L. K. Steinrauf,* J. Mol. Biol. *49*, 533 (1970).

[21] Structure: *J. F. Blount, J. W. Westley,* Chem. Commun. *1971*, 927.

[22] a) Isolation: *J. Berger, A. I. Rachlin, W. E. Scott, L. H. Sternbach, M. W. Goldberg,* J. Am. Chem. Soc. *73*, 5295 (1951); *J. W. Westley, R. H. Evans, Jr., T. Williams, A. Stempel,* Chem. Commun. *1970*, 71; b) Structure ($Ag^{\oplus}$ salt): *C. A. Maier, I. C. Paul, ibid. 1971*, 181.

[23] *J. Beck, H. Gerlach, V. Prelog, W. Voser,* Helv. Chim. Acta *45*, 620 (1962) and earlier work; *K. Ando, Y. Murakami, Y. Nawata,* J. Antibiot. *24*, 418 (1971).

[24] Reviews: a) *H. Vahrenkamp,* Chem. unserer Zeit *7*, 97 (1973); b) see also *H. Zähner,* Angew. Chem. *89*, 696 (1977); Angew. Chem. Int. Ed. Engl. *16*, 687 (1977); c) *J. C. Ellroy, V. L. Lew:* Membrane Transport in Red Cells. Academic Press, New York 1977.

[25] Reviews: *J. G. Schindler,* Biomed. Tech. *22*, 235 (1977); *J. G. Schindler, R. Dennhardt, W. Simon,* Chimia *31*, 404 (1971); *F. Scheller, D. Pfeiffer,* Z. Chem. *18*, 50 (1978); recent examples: *H. Maier, A. Röckel, A. Heidland, D. Schneider, Ch. Steffen, O. Aziz, R. Dennhardt, H.-O. Lindt, J. G. Schindler,* Res. Exp. Med. *172*, 75 (1978); *Ch. Steffen, J. G. Schindler, O. Aziz,* Biomed. Tech. *21*, 188 (1976).

[26] *W. K. Lutz, P. U. Früh, W. Simon,* Helv. Chim. Acta *54*, 2767 (1971).

[27] *W. K. Lutz, H.-K. Wipf, W. Simon,* Helv. Chim. Acta *53*, 1741 (1970).

[28] Review: *M. R. Truter,* Struct. Bonding *16*, 71 (1973).

[29] *S. Lindenbaum, L. Sternson, S. Rippel,* J. Chem. Soc. Chem. Commun. *1977*, 268.

[30] Cf. [20b] and [20c]; [18a] and [18b]. Monensin and nigericin also have H bonded cyclic structures in solution [27].

[31] *M. Alleaume, B. Busetta, C. Farges, P. Gachon, A. Kergomard, T. Staron,* J. Chem. Soc. Chem. Commun. *1975*, 411.

[32] a) *C. Riche, C. Pascard-Billy,* J. Chem. Soc. Chem. Commun. *1975*, 951; b) recent examples of acyclic antibiotic ionophores: *M. Shiro, H. Nakai, K. Nagashima, N. Tsuji, ibid. 1978*, 682; *N. Otake, T. Ogita, H. Nakayama, S. Sato, Y. Saito, ibid. 1978*, 875.

[33] Cf. *G. D. J. Phillies, H. E. Stanley,* J. Am. Chem. Soc. *98*, 3892 (1976).

[34] *S. M. Johnson, J. Herrin, S. J. Liu, I. C. Paul,* Chem. Commun. *1970*, 72; *S. M. Johnson, J. Herrin, S. Jan Liu, I. C. Paul,* J. Am. Chem. Soc. *92*, 4428 (1970).

[35] Reviews referring to historic work: *S. E. Livingstone,* Q. Rev. Chem. Soc. *19*, 386 (1965); *M. Schmidt, G. G. Hoffmann,* Phosph. Sulf. *4*, 239 (1978).

[36] *N. V. Sidgwick, S. G. P. Plant,* J. Chem. Soc. *127*, 209 (1925); *N. V. Sidgwick, F. M. Brewer, ibid. 127*, 2379 (1925); *F. M. Brewer, ibid. 1931*, 361; cf. also *R. B. Heslop, P. L. Robinson:* Inorganic Chemistry. Elsevier, Amsterdam 1960; *Ph. J. Durrant, B. Durrant:* Introduction to Advanced Inorganic Chemistry. Longmans, London 1962; *T. P. Whaley* in *H. J. Emeléus, R. Nyholm, A. F. Trotman-Dickenson:* Comprehensive Inorganic Chemistry. Pergamon Press, Oxford 1973.

[37] We designate acyclic *acid* ligand molecules as *chelands* (complexes: chelates) and thus distinguish them from the likewise acyclic but *neutral* "podands" *(vide infra)*.

[38] *G. Schwarzenbach, H. Ackermann,* Helv. Chim. Acta *30*, 1798 (1947); E. Merck AG, Darmstadt: Komplexometrische Bestimmungsmethoden mit Titriplex; *F. Přibil:* Komplexometrie. Vol. I. 2nd Edit., VEB Deutscher Verlag für Grundstoffindustrie, Leipzig 1963; *H. A. Flaschka:* EDTA Titrations. 2nd Edit., Pergamon Press, Oxford 1964.

[39] *G. Schwarzenbach, E. Kampitsch, R. Steiner,* Helv. Chim. Acta *29*, 364 (1944); *H. Irving, J. J. R. F. DaSilva,* J. Chem. Soc. *1963*, 448.

[40] *H. Irving, J. J. R. F. DaSilva,* J. Chem. Soc. *1963*, 1144.

[41] *H. Irving, J. J. R. F. DaSilva,* J. Chem. Soc. *1963*, 945.

[42] *H. Stetter, W. Frank,* Angew. Chem. *88*, 760 (1976); Angew. Chem. Int. Ed. Engl. *15*, 686 (1976); cf. also *H. Häfliger, T. A. Kaden,* Helv. Chim. Acta *62*, 683 (1979).

[43] *G. Ferguson, A. J. McAlees, R. McCrindle, R. J. Restivo, P. J. Roberts,* J. Am. Chem. Soc. *99*, 3170 (1977).

[44] *M. Miyazaki, Y. Shimoishi, H. Miyata, K. Tôei,* J. Inorg. Nucl. Chem. *36*, 2033 (1974).

[45] *N. P. Marullo, R. A. Lloyd,* J. Am. Chem. Soc. *88*, 1076 (1966); cf. also *T. C. Shields,* Chem. Commun. *1968*, 832.

[46] *H. Plieninger, B. Kanellakopulos, K. Stumpf,* Angew. Chem. *79*, 155 (1967); Angew. Chem. Int. Ed. Engl. *6*, 184 (1967); we thank Prof. *Plieninger* for communication of unpublished results.

[47] *P. Piret, L. Rodrique, Y. Gobillon, A. van Meerssche,* Acta Crystallogr. *20*, 482 (1966); *A. R. Hands, A. J. Mercer,* J. Chem. Soc. *A 1968*, 449; see also functionalized diphenylphosphane podands: *M. E. Wilson, R. G. Nuzzo, G. M. Whitesides,* J. Am. Chem. Soc. *100*, 2269 (1978).

[48] *W. Hewertson, B. T. Kilbourn, R. H. B. Mais,* Chem. Commun. *1970*, 952, and references cited therein.

[49] *E.g. Y. M. G. Yasin, O. J. R. Hodder, H. M. Powell,* Chem. Commun. *1966*, 705.

[50] *G. H. W. Milburn, M. R. Truter, B. L. Vickery,* Chem. Commun. *1968*, 1188.

[51] *A. K. Banerjee, A. J. Layton, R. S. Nyholm, M. R. Truter,* Nature *217*, 1147 (1968); J. Chem. Soc. *A 1969*, 2536.

[52] *F. Wudl,* J. Chem. Soc. Chem. Commun. *1972*, 1229.

[53] Review: a) *R. M. Izatt, D. J. Eatough, J. J. Christensen,* Struct. Bonding *16*, 161 (1973); b) *H. K. Frensdorff,* J. Am. Chem. Soc. *93*, 600 (1971).

[54] Cf. *D. J. Cram, J. M. Cram,* Acc. Chem. Res. *11*, 8 (1978).

[55] *E. P. Kyba, R. C. Helgeson, K. Madan, G. W. Gokel, T. L. Tarnowski, S. S. Moore, D. J. Cram,* J. Am. Chem. Soc. *99*, 2564 (1977).

[56] *D. K. Cabbiness, D. W. Margerum,* J. Am. Chem. Soc. *91*, 6540 (1969); see also [4b].

[57] *M. Kodama,* J. Chem. Soc. Chem. Commun. *1975*, 891; *A. Auidini, L. Fabrizzi, P. Paoletti,* Inorg. Chim. Acta *24*, 41 (1977); *L. Fabrizzi, P. Paoletti, A. B. P. Lever,* Inorg. Chem. *15*, 1502 (1976).

[58] *T. E. Jones, L. L. Zimmer, L. L. Diaddario, D. B. Rorabacher, L. A. Ochrymowycz,* J. Am. Chem. Soc. *97*, 7163 (1975).

[59] *A. Dei, R. Gori,* Inorg. Chim. Acta *14*, 157 (1975); *G. F. Smith, D. W. Margerum,* J. Chem. Soc. Chem. Commun. *1975*, 807; *M. Kodama, E. Kimura,* J. Chem. Soc. Dalton Trans. *1976*, 116, 1720.

[60] *M. Kodama, E. Kimura,* Bull. Chem. Soc. Jpn. *49*, 2465 (1976).

[61] *G. Chaput, G. Jeminet, J. Juillard,* Can. J. Chem. *53*, 2240 (1975).

[62] For the ability of ethers to form complexes in general, see *S. Searles, Jr., M. Tamres* in *S. Patai:* The Chemistry of the Ether Linkage. Interscience, London 1967, p. 243.

[63] *U. Takaki, J. Smid,* J. Am. Chem. Soc. *96*, 2588 (1974).

[64] The number following the designation glyme shows—by analogy with crown ether nomenclature, according to a proposal by *J. Smid* [65]—the total number of O atoms in the glyme molecule. In the other conventional names such as di-, tri-, and tetraglyme the numbers refer to the sum of the CH_2CH_2O units.

[65] Reviews of ion pair structures and effects: a) *J. Smid,* Angew. Chem. *84*, 127 (1972); Angew. Chem. Int. Ed. Engl. *11*, 112 (1972); b) *M. Szwarc:* Ions and Ion Pairs in Organic Reactions. Vol. 1 and 2. Wiley, New York 1972 and 1974; c) *T. E. Hogen-Esch,* Adv. Phys. Org. Chem. *15*, 153 (1977).

[66] *R. J. H. Clark, A. J. McAlees,* J. Chem. Soc. Dalton Trans. *1972*, 640; *L. R. Nylander, S. F. Pavkovic,* Inorg. Chem. *9*, 1959 (1970); *G. W. A. Fowles, D. A. Rice, R. A. Walton,* J. Inorg. Nucl. Chem. *31*, 3119 (1969); *W. Ludwig, H. P. Schröer,* Z. Anorg. Allg. Chem. *357*, 74 (1968); *H. P. Schröer, B. Heyn,* Z. Chem. *7*, 238 (1967).

[67] a) *R. Iwamoto,* Bull. Chem. Soc. Jpn. *46*, 1114 (1973); b) *46*, 1118 (1973); c) *46*, 1123 (1973); d) *46*, 1127 (1973).

[68] *R. Iwamoto, H. Wakano,* J. Am. Chem. Soc. *98*, 3764 (1976).

[69] A $Mg^{2\oplus}$-monoglyme solvate can only be formed in the presence of the stabilizing anion $SbCl_6^{\ominus}$: *M. DenHeijer, W. L. Drieessen,* Inorg. Chim. Acta *26*, 277 (1977).

[70] Cf.: a) *H. Tadokoro, Y. Chatani, T. Yoshihara, S. Tahara, S. Murahashi,* Makromol. Chem. *73*, 109 (1964); b) *R. Iwamoto, Y. Saito, H. Ishihara, H. Tadokoro,* J. Polym. Sci. Part A-2, *6*, 1509 (1968); c) *M. Yokoyama, H. Ishihara, R. Iwamoto, H. Tadokoro,* Macromolecules *2*, 184 (1969).

[71] Reviews: *T.-L. Ho,* Chem. Rev. *75*, 1 (1975); Hard and Soft Acids and Bases Principle in Organic Chemistry. Academic Press, New York 1977.

[72] See *M. J. Taylor:* Metal-to-Metal Bonded States of the Main Group Elements. Academic Press, London 1975.

[73] *K. Broderson, R. Eder,* Chem. Ber. *110,* 2392 (1977).

[74] *K. Broderson, G. Jordan,* Chem. Ber. *111,* 1221 (1978).

[75] *J. S. Bradshaw, B. L. Haymore, R. M. Izatt, J. J. Christensen,* J. Org. Chem. *40,* 1510 (1975).

[76] *F. Arnaud-Neu, M. J. Schwing-Weill,* Inorg. Nucl. Chem. Lett. *11,* 655 (1975); cf. *ibid. 11,* 131 (1975).

[77] *S. Ahrland, J. Chatt, N. R. Davies,* Q. Rev. Chem. Soc. *12,* 265 (1958).

[78] Reviews: a) *D. St. C. Black, A. J. Hartshorn,* Coord. Chem. Rev. *9,* 219 (1972—1973); b) *L. F. Lindoy,* Q. Rev. Chem. Soc. *25,* 379 (1971).

[79] *C. D. Hurd, R. J. Sims,* J. Am. Chem. Soc. *71,* 2443 (1949); see also *D. E. Fenton,* J. Chem. Soc. Dalton Trans. *1973,* 1380.

[80] *S. E. V. Phillips, J. Trotter,* Can. J. Chem. *54,* 2723 (1976).

[81] *C. D. Hurd,* J. Org. Chem. *39,* 3144 (1974).

[82] Cf. *S. E. V. Phillips, M. R. Truter,* Chem. Soc. Exp. Synop. J. Mark II, *1975,* 14, 16; J. Chem. Soc. Dalton Trans. *1974,* 2517; *D. L. Hughes, S. E. V. Phillips, M. R. Truter, ibid. 1974,* 907.

[83] *J. C. Barnes, C. S. Duncan,* J. Chem. Soc. Dalton Trans. *1972,* 1732.

[84] *W. L. Driessen, P. L. A. Everstijn,* Z. Naturforsch. *B 32,* 1284 (1977).

[85] *E. A. Green, W. L. Duax, G. M. Smith, F. Wudl,* J. Am. Chem. Soc. *97,* 6689 (1975).

[86] *I. M. Kolthoff, E. B. Sandell, E. J. Meehan, S. Bruckenstein:* Quantitative Chemical Analysis. 4th Edit., MacMillan, New York 1969, pp. 264, 664 ff.

[87] *P. Pfeiffer, W. Christeleit,* Z. Anorg. Allg. Chem. *239,* 133 (1938); *P. Pfeiffer, B. Werdelmann, ibid. 261,* 197 (1950).

[88] a) *N. S. Poonia,* Inorg. Chim. Acta *23,* 5 (1977); *M. D. Grillone, M. A. Nocilla,* Inorg. Nucl. Chem. Lett. *14,* 49 (1978); see also *C. Chassapis, G. Pneumatikakis,* Inorg. Chim. Acta *27,* 67 (1978); b) *W. Rasshofer, W. M. Müller, F. Vögtle,* J. Isr. Chem. *1979,* in press; c) *G. Oepen, F. Vögtle,* Justus Liebigs Ann. Chem. *1979,* in press.

[89] *A. Naumann, J. Schroeder,* Ber. Dtsch. Chem. Ges. *37,* 4609 (1904).

[90] *L. Kahlenberg, F. C. Krauskopf,* J. Am. Chem. Soc. *30,* 1104 (1908).

[91] *F. Vögtle, H. Sieger,* Angew. Chem. *89,* 410 (1977); Angew. Chem. Int. Ed. Engl. *16,* 396 (1977); cf. also ref. [92].

[92] *E. Weber, F. Vögtle,* Tetrahedron Lett. *1975,* 2415.

[93] a) *U. Heimann, F. Vögtle,* Chem. Ber. *112,* 3034 (1979); b) cf. NO_2 function as donor terminal group [91]; see also *E. Weber, W. Wieder, F. Vögtle, ibid. 109,* 1002 (1976).

[94] *W. Rasshofer, W. M. Müller, G. Oepen, F. Vögtle,* J. Chem. Res. (S) *1978,* 72; (M) *1978,* 1001.

[95] a) *W. Rasshofer, G. Oepen, F. Vögtle,* Chem. Ber. *111,* 419 (1978); b) *W. Rasshofer, W. M. Müller, F. Vögtle, ibid. 112,* 2095 (1979).

[96] *N. S. Poonia,* J. Am. Chem. Soc. *96,* 1012 (1974).

[97] *E. Weber, F. Vögtle,* Chem. Ber. *109,* 1803 (1976), and further information given therein.

[98] Cf. *D. G. Parsons, M. R. Truter, J. N. Wingfield,* Inorg. Chim. Acta *14,* 45 (1975); *D. G. Parsons, J. N. Wingfield, ibid. 18,* 263 (1976); *M. E. Farago, ibid. 25,* 71 (1977), and [96].

[99] Regarding the discussion, see *N. S. Poonia, M. R. Truter,* J. Chem. Soc. Dalton Trans. *1973,* 2062; *A. Seminara, G. Siracusa, A. Cassol,* Inorg. Chim. Acta *20,* 105 (1976); *D. G. Parsons, J. N. Wingfield, ibid. 17,* L 25 (1976); *R. B. King, P. R. Heckley,* J. Am. Chem. Soc. *96,* 3118 (1974), and [96].

[100] See [1b], Fig. 5, p. 23. Cf. recent circular dichroism studies: *H. Klein,* Tetrahedron Lett. *1979,* 3835.

[101] *W. Saenger, H. Brand, F. Vögtle, E. Weber* in *B. Pullmann, N. Goldblum:* Metal-Ligand Interactions in Organic Chemistry and Biochemistry. Part 1. Reidel, Dordrecht 1977, p. 363; *W. Saenger, H. Brand,* Acta Crystallogr. *B 35,* 838 (1979).

[102] *D. Bright, M. R. Truter,* J. Chem. Soc. *B 1970,* 1544.

[103] *E. g. M. A. Bush, M. R. Truter,* Chem. Commun. *1970,* 1439 and [102].

[104] We thank Prof. *W. Saenger,* Max-Planck-Institut für Experimentelle Medizin, Göttingen, for this investigation and for communication of the results.

[105] a) *G. Weber, W. Saenger, F. Vögtle, H. Sieger,* Angew. Chem. *91,* 234 (1979); Angew. Chem. Int. Ed. Engl. *18,* 226 (1979); b) *G. Weber, W. Saenger, ibid. 91,* 237 (1979) and *18,* 227 (1969), respectively.

[106] Cf. *C. J. Pedersen* in [1c], p. 43.

[107] *A. H. Alberts, K. Timmer, J. G. Noltes, A. L. Spek,* J. Am. Chem. Soc. *101,* 3375 (1979).

[108] a) Cf. *D. Live, S. I. Chan,* J. Am. Chem. *98,* 3769 (1976); *B. Dietrich, J.-M. Lehn, J. P. Sauvage,* Tetrahedron *29,* 1647 (1973); b) *K. Sakamoto, M. Oki,* Bull. Chem. Soc. Jpn. *49,* 3159 (1976).

[109] See *E. de Boer, A. M. Grotens, J. Smid,* Chem. Commun. *1970,* 1035.

[110] *J. A. Dixon, P. A. Gwinner, D. C. Lini,* J. Am. Chem. Soc. *87,* 1379 (1965).

[111] *L. L. Chan, K. H. Wong, J. Smid,* J. Am. Chem. Soc. *92,* 1955 (1970); *K. H. Wong, G. Konizer, J. Smid, ibid. 92,* 666 (1970).

[112] *F. Vögtle, H. Sieger,* unpublished.

[113] *W. Rasshofer, G. Oepen, W. M. Müller, F. Vögtle,* Chem. Ber. *111,* 1108 (1978).

[114] a) *R. Büchi, E. Pretsch,* Helv. Chim. Acta *60,* 1141 (1977); b) *R. Büchi, E. Pretsch, W. Simon, ibid. 59,* 2327 (1976); c) Tetrahedron Lett. *1976,* 1709; d) *R. Büchi, E. Pretsch, W. E. Morf, W. Simon,* Helv. Chim. Acta *59,* 2407 (1976).

[115] Review: *P. Laszlo,* Angew. Chem. *90,* 271 (1978); Angew. Chem. Int. Ed. Engl. *17,* 254 (1978).

[116] Review: *Yu. A. Ovchinnikov, V. T. Ivanov, A. M. Shkrob,* BBA Libr. *12,* 1 (1974).

[117] *B. Tümmler, G. Maass, E. Weber, W. Wehner, F. Vögtle,* J. Am. Chem. Soc. *99,* 4683 (1977).

[118] *B. Tümmler, G. Maass, F. Vögtle, U. Heimann, H. Sieger, E. Weber,* J. Am. Chem. Soc. *101,* 2588 (1979).

[119] See *L. G. Silleu, A. E. Martell:* Stability Constants of Metal-Ion Complexes. Chemical Society, London 1964.

[120] See, however, *J. S. Bradshaw, L. D. Hansen, S. F. Nielson, M. D. Thompson, R. A. Reeder, R. M. Izatt, J. J. Christensen,* J. Chem. Soc. Chem. Commun. *1975,* 874; *N. S. Poonia, B. P. Yadav, V. W. Bhagwat, V. Naik, H. Manohar,* Inorg. Nucl. Chem. Lett. *13,* 119 (1977).

[121] *D. J. Cram* in *A. Weissberger:* Techniques of Chemistry. Vol. X/2. Wiley, New York 1976.

[122] Cf. *J. M. Larson, L. R. Sousa,* J. Am. Chem. Soc. *100,* 1943 (1978); *H. F. Beckford, R. M. King, J. F. Stoddart, R. F. Newton,* Tetrahedron Lett. *1978,* 171.

[123] See *E. Kauffmann, J.-M. Lehn, J. P. Sauvage,* Helv. Chim. Acta *59,* 1099 (1976); *G. Anderegg, ibid. 58,* 1218 (1975); cf. [1a, 1c, 53a].

[124] *J. Grandjean, P. Laszlo, F. Vögtle, H. Sieger,* Angew. Chem. *90,* 902 (1978); Angew. Chem. Int. Ed. Engl. *17,* 856 (1978).

[125] *M. Eigen, L. D. Maeyer* in *A. Weissberger:* Techniques of Organic Chemistry. Vol. III/2. Wiley, New York 1963, Chap. 18; *C. R. Rabl* in *H. J. Rehm:* Technische Biochemie. Dechema Monographien No. 71. Verlag Chemie, Weinheim 1973, p. 187.

[126] Cf. corresponding values measured for [2.2.2]cryptand complexes: *K. Henco, B. Tümmler, G. Maass,* Angew. Chem. *89,* 567 (1977); Angew. Chem. Int. Ed. Engl. *16,* 538 (1977).

[127] *R. Winkler,* Dissertation, Universität Wien 1969; *M. Eigen,* Ber. Bunsenges. Phys. Chem. *67,* 93 (1969).

[128] *M. Eigen, G. Maass,* Z. Phys. Chem. (Frankfurt) *49,* 193 (1966); *H. Diebler, M. Eigen, G. Ilgenfritz, G. Maass, R. Winkler,* Pure Appl. Chem. *20,* 93 (1969).

[129] *M. Eigen, R. Winkler,* Neurosci. Res. Program Bull. *9,* 330 (1971); *R. Winkler,* Struct. Bonding *10,* 1 (1972).

[130] *F. Vögtle, U. Heimann,* Chem. Ber. *111,* 2757 (1978).

[131] Cf. Naturwissenschaften *63,* 575 (1976); see also *W. Schoner,* Angew. Chem. *83,* 947 (1971); Angew. Chem. Int. Ed. Engl. *10,* 883 (1971).

[132] See *D. W. Urry,* Biochim. Biophys. Acta *265,* 115 (1972); cf. also *S. R. Byrn,* Biochemistry *13,* 5186 (1974); *H. A. Kolb, E. Bamberg,* Biochim. Biophys. Acta *464,* 127 (1977).

[133] See *R. J. Levins,* Anal. Chem. *43,* 1045 (1971) and [70a].

[134] *C. J. Pedersen,* J. Org. Chem. *36,* 1690 (1971).

[135] Cf. a) *F. Cramer:* Einschlussverbindungen. Springer, Heidelberg 1954; b) *W. Saenger,* Umschau *74,* 635 (1974); c) *J. E. D. Davies,* J. Chem. Educ. *54,* 536 (1977); d) *D. D. MacNicol, J. J. McKendrick, D. R. Wilson,* Chem. Soc. Rev. *7,* 65 (1978); e) *K. Pollmer,* Z. Chem. *19,* 81 (1979).

[136] a) *J. Goldberg,* Acta Crystallogr. *B 31,* 754 (1975); b) *G. W. Gokel, D. J. Cram, C. L. Liotta, H. P. Harris, F. L. Cook,* J. Org. Chem. *39,* 2445 (1974); c) *A. El Basyony, J. Klimes, A. Knöchel, J. Oehler, G. Rudolph,* Z. Naturforsch. *B 31,* 1192 (1976); *R. Kaufmann, A. Knöchel, J. Kopf, J. Oehler, G. Rudolph,* Chem. Ber. *110,* 2249 (1977); d) *F. Vögtle, W. M. Müller, E. Weber, ibid.* (1979), in press.

[137] a) *A. Knöchel, J. Kopf, J. Oehler, G. Rudolph,* J. Chem. Soc. Chem. Commun. *1978,* 595; b) *F. Vögtle, W. M. Müller,* Chem. Ber., in press.

[138] *W. Rasshofer, F. Vögtle,* Tetrahedron Lett. *1978,* 309.

[139] See *W. Schlenk Jr.* in *Houben-Weyl-Müller:* Methoden der Organischen Chemie. Vol. I/1, 4th Edit., Thieme, Stuttgart 1958, p. 391.

[140] *I. H. Suh, W. Saenger,* Angew. Chem. *90,* 565 (1978); Angew. Chem. Int. Ed. Engl. *17,* 534 (1978).

[141] Cf. *B. Wendt, W. Ried,* Angew. Chem. *63,* 218 (1951).

[142] *F. Vögtle, G. Oepen, W. Rasshofer,* Justus Liebigs Ann. Chem. *1979,* in press.

[143] Cf. "Circulare Wasserstoffbrückenbindungen", Nachr. Chem. Tech. Lab. *27,* 403 (1979).

[144] Review: *R. C. Hayward,* Nachr. Chem. Tech. Lab. *25,* 15 (1977).

[145] *E. g. J. F. Blount, R. H. Evans, Jr., C.-M. Liu, T. Hermann, J. W. Westley,* J. Chem. Soc. Chem. Commun. *1975,* 853, and references cited therein; *M. Alleaume, B. Busetta, C. Farges, P. Gachon, A. Kergomard, T. Staron, ibid. 1975,* 411.

[146] a) *D. L. Hughes, C. L. Mortimer, D. G. Parsons, M. R. Truter, J. N. Wingfield,* Inorg. Chim. Acta *21,* L23 (1977); *D. L. Hughes, C. L. Mortimer, M. R. Truter, ibid. 28,* 83 (1978); b) *D. L. Hughes, J. N. Wingfield,* J. Chem. Soc. Chem. Commun. *1978,* 1001.

[147] *N. Yamazaki, S. Nakahama, A. Hirao, S. Negi,* Tetrahedron Lett. *1978,* 2429.

[148] *W. Wierenga, B. R. Evans, J. A. Woltersom,* J. Am. Chem. Soc. *101*, 1334 (1979).
[149] *G. Oepen, J. P. Dix, F. Vögtle,* Justus Liebigs Ann. Chem. *1978*, 1592.
[150] *F. Vögtle, F. Ley,* unpublished.
[151] *U. Heimann, F. Vögtle,* Angew. Chem. *90*, 211 (1978); Angew. Chem. Int. Ed. Engl. *17*, 197 (1978).
[152] Cf. data in [92].
[153] *D. Ammann, E. Pretsch, W. Simon,* Helv. Chim. Acta *56*, 1780 (1973); we thank Prof. *Simon* for communication of unpublished work.
[154] *M. Güggi, E. Pretsch, W. Simon,* Anal. Chim. Acta *91*, 107 (1977).
[155] a) *D. Ammann, E. Pretsch, W. Simon,* Anal. Lett. *7*, 23 (1974); b) *M. Güggi, U. Fiedler, E. Pretsch, W. Simon, ibid. 8*, 857 (1975); c) *D. Ammann, M. Güggi, E. Pretsch, W. Simon, ibid. 8*, 709 (1975).
[156] *E. Pretsch, D. Ammann, W. Simon,* Res. Developm. *25*, 20 (1974), Copyright 1974 by Technical Publishing Company: *R. Bissig, E. Pretsch, W. E. Morf, W. Simon,* Helv. Chim. Acta *61*, 1520 (1978); DBE = dibenzyl ether.
[157] *D. Ammann, E. Pretsch, W. Simon,* Anal. Lett. *5*, 843 (1972); Tetrahedron Lett. *1972*, 2473.
[158] *N. N. L. Kirch, W. Simon,* Helv. Chim. Acta *59*, 357 (1976).
[159] *N. N. L. Kirch, R. J. J. Funck, E. Pretsch, W. Simon,* Helv. Chim. Acta *60*, 2326 (1977).
[160] See *W. E. Morf, W. Simon,* Helv. Chim. Acta *54*, 794 (1971).
[161] *M. Güggi, M. Oehme, E. Pretsch, W. Simon,* Helv. Chim. Acta *59*, 2417 (1976). *o*-NPOE = *o*-nitrophenyl *n*-octyl ether.
[162] *D. Ammann, R. Bissig, Z. Cimerman, U. Fiedler, M. Güggi, W. E. Morf, M. Oehme, H. Osswald, E. Pretsch, W. Simon* in *M. Kessler, L. C. Clark, Jr., D. W. Lübbers, I. A. Silver, W. Simon:* Ion and Enzyme Electrodes in Biology and Medicine. Urban und Schwarzenberg, München 1976.
[163] *A. P. Thoma, Z. Cimerman, U. Fiedler, D. Bedekovic, M. Güggi, P. Jordan, K. May, E. Pretsch, U. Prelog, W. Simon,* Chimia *29*, 344 (1975).
[164] *A. P. Thoma, W. Simon* in *B. Pullmann, N. Goldblum:* Metal-Ligand Interactions in Organic Chemistry and Biochemistry. Part 2. Reidel, Dordrecht 1977, p. 37.
[165] *W. E. Morf, P. Wuhrmann, W. Simon,* Anal. Chem. *48*, 1031 (1976); *D. Erne, W. E. Morf, S. Arvanitis, Z. Cimerman, D. Ammann, W. Simon,* Helv. Chim. Acta *62*, 994 (1979).
[166] *W. E. Morf, E. Lindner, W. Simon,* Anal. Chem. *47*, 1596 (1975); see also [127].
[167] Theoretical approaches to complexation of carbonyl groups in ligands, see *T.-K. Ha, U. P. Wild, R. O. Kühne, C. Loesch, T. Schaffhauser, J. Stachel, A. Wokaun,* Helv. Chim. Acta *61*, 1193 (1978), and further data therein.
[168] *K. Neupert-Laves, M. Dobler,* Helv. Chim. Acta *60*, 1861 (1977).
[169] *H. Sieger, F. Vögtle,* Angew. Chem. *90*, 212 (1978); Angew. Chem. Int. Ed. Engl. *17*, 198 (1978).
[170] Cf. nonylphenoxy*poly*ethylene glycol-Ba and Sr-tetraphenyl borate complexes as neutral carriers in ion-selective electrodes [133]. Stoichiometric alkali- and alkaline earth metal-tetraphenyl borate adducts of *poly*ethylene and *poly*propylene glycols: *P. G. Delduca, A. M. Y. Jaber, G. J. Moody, J. D. R. Thomas,* J. Inorg. Nucl. Chem. *40*, 187 (1978).
[171] Ethylene glycol as bridging ligand in dimeric benzoyl acetone-Na complex, see *M. R. Truter,* Chem. Br. *7*, 203 (1971), and further information given therein.
[172] *H. Sieger, F. Vögtle,* Tetrahedron Lett. *1978*, 2709.
[173] *H. Ohmoto, Y. Kai, N. Yasuoka, N. Kasai, S. Yanagida, M. Okahara,* Bull. Chem. Soc. Jpn. *52*, 1209 (1979).
[174] *F. Vögtle, E. Weber,* Angew. Chem. *86*, 896 (1974); Angew. Chem. Int. Ed. Engl. *13*, 814 (1974).
[175] a) In solid/liquid phase transfer reactions, the activity is clearly reduced; cf. *A. Knöchel, J. Oehler, G. Rudolph,* Tetrahedron Lett. *1975*, 3167; b) for a possible explanation, see *F. De Jong, D. N. Reinhoudt, C. J. Smit,* Tetrahedron Lett. *1976*, 1371, 1375.
[176] *J. A. Hyatt,* J. Org. Chem. *43*, 1808 (1978).
[177] See also *H. J. Backer,* Rec. Trav. Chim. Pays-Bas *54*, 745, 905 (1935).
[178] *D. D. MacNicol, D. R. Wilson,* J. Chem. Soc. Chem. Commun. *1976*, 494.
[179] *E. Weber, W. M. Müller, F. Vögtle,* Tetrahedron Lett. *1979*, 2335.
[180] *D. D. MacNicol, A. D. U. Hardy, D. R. Wilson,* Nature *266*, 611 (1977).
[181] Cf. X-ray structure analysis of hexakis(bromomethyl)benzene: *P. Marsau,* Acta Crystallogr. *18*, 851 (1965).
[182] A similarly structured water-soluble morpholine-containing bisquaternary dispiro system could be suitable for inclusion of organic solvents in hydrophilic phases; X-ray structure analysis see *A. D. U. Hardy, D. D. MacNicol, D. R. Wilson,* J. Chem. Soc. Chem. Commun. *1977*, 525.
[183] *D. D. MacNicol, D. R. Wilson,* Chem. Ind. (London) *1977*, 84.
[184] *R. Fornasier, F. Montanari, G. Podda, P. Tundo,* Tetrahedron Lett. *1976*, 1381.
[185] *E. Buhleier, W. Wehner, F. Vögtle,* Synthesis *1978*, 155.
[186] *A. W. Langer,* Adv. Chem. Ser. *130* (1974).
[187] Cf. *N*-substituted triethylenetetramine complexes for hydrolysis of acetyl phosphate: *H. Lau, C. D. Gutsche,* J. Am. Chem. Soc. *100*, 1857 (1978).
[188] *J. A. Rendleman, Jr.,* J. Org. Chem. *31*, 1839 (1966).
[189] ^{1}H-NMR studies: a) *S. J. Angyal,* Tetrahedron *30*, 1695 (1974); b) *S. J. Angyal, K. P. Davies,* Chem. Commun. *1971*, 500; c) ^{23}Na-NMR measurements on sugar adducts: *C. Detellier, J. Grandjean, P. Laszlo,* J. Am. Chem. Soc. *98*, 3375 (1976).
[190] *J. A. Mills,* Biochem. Biophys. Res. Commun. *6*, 418 (1961).
[191] Cf. also *H. Grasdalen, T. Anthonsen, O. Harbitz, B. Larsen, O. Smidsrod,* Acta Chem. Scand. *A 32*, 31 (1978).
[192] a) *C. E. Bugg, W. J. Cook,* J. Chem. Soc. Chem. Commun. *1972*, 727; b) *C. E. Bugg,* J. Am. Chem. Soc. *95*, 908 (1973); c) *W. J. Cook, C. E. Bugg,* Carbohydr. Res. *31*, 265 (1973).
[193] *P. Charley, P. Saltman,* Science *139*, 1205 (1963); *C. L. Moore,* Biochem. Biophys. Res. Commun. *42*, 298 (1971).
[194] *W. E. Pricer, Jr., G. Ashwell,* J. Biol. Chem. *246*, 4825 (1971).
[195] *U. Heimann, F. Vögtle,* unpublished; cf. also [1e].
[196] *F. P. Dwyer, N. S. Gill, E. C. Gyarfas, F. Lions,* J. Am. Chem. Soc. *79*, 1269 (1957).
[197] *G. Anderegg, F. Wenk,* Helv. Chim. Acta *50*, 2330 (1967). For thermodynamics of metal complexation: *G. Anderegg, E. Hubmann, N. G. Podder, F. Wenk, ibid. 60*, 123 (1977).
[198] *F. Vögtle, W. M. Müller, W. Wehner, E. Buhleier,* Angew. Chem. *89*, 564 (1977); Angew. Chem. Int. Ed. Engl. *16*, 548 (1977).
[199] *U. Heimann, M. Herzhoff, F. Vögtle,* Chem. Ber. *112*, 1392 (1979).
[200] *F. Vögtle, W. M. Müller, E. Buhleier, W. Wehner,* Chem. Ber. *112*, 899 (1979).
[201] *H. Sieger, W. M. Müller, F. Vögtle,* J. Chem. Res. *1978* (S) 398; (M) 4848; cf. also *C. G. Krespan,* J. Org. Chem. *40*, 1205 (1975).
[202] *W. P. Weber, G. W. Gokel:* Phase Transfer Catalysis in Organic Synthesis. Springer, Berlin 1977; *S. L. Regen,* Angew. Chem. *91*, 464 (1979); Angew. Chem. Int. Ed. Engl. *18*, 421 (1979).
[203] Reviews: *E. V. Dehmlov,* Angew. Chem. *86*, 187 (1974); *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *13*, 170 (1974); *16*, 507 (1977); *A. Brändström,* Adv. Phys. Org. Chem. *15* (1977).
[204] *M. Cinquini, F. Montanari, P. Tundo,* J. Chem. Soc. Chem. Commun. *1975*, 393; *D. Landini, F. Montanari, F. Rolla,* Synthesis *1978*, 223.
[205] *B. G. Zupancic, M. Scopcic,* Synthesis *1979*, 123.
[206] a) *R. A. Bartsch, N. F. Haddock, D. W. McCaun,* Tetrahedron Lett. *1977*, 3779; b) *R. A. Bartsch, P. N. Juri, ibid. 1979*, 407.
[207] Cf. "Polyglycole Hoechst", Eigenschaften und Anwendungsgebiete der Polyäthylenglycole. Hoechst AG 1976.
[208] Cf. auxiliary compounds for asymmetric synthesis from tartaric acid: *D. Seebach, H.-O. Kalinowski, B. Bastani, G. Crass, H. Daum, H. Dörr, N. P. DuPreez, V. Ehrig, W. Langer, C. Nüssler, H.-A. Oei, M. Schmidt,* Helv. Chim. Acta *60*, 301 (1977), and references cited therein. Crown ethers as chiral additives in electroreductions: *L. Horner, W. Brich,* Chem. Ber. *111*, 574 (1978); cf. also *A. I. Meyers, G. S. Poindexter, Z. Brich,* J. Org. Chem. *43*, 892 (1978).
[209] *D. Seebach* in: 25 Jahre Fonds der Chemischen Industrie. Verband der Chemischen Industrie, October 1975, p. 13.
[210] Reviews: *E. Weber, F. Vögtle,* Kontakte (Merck) *3/77*, 36; *G. W. Gokel, H. D. Durst,* Synthesis *1976*, 168; *A. C. Knipe,* J. Chem. Educ. *53*, 618 (1976).
[211] Review: *E. Weber, F. Vögtle,* Kontakte (Merck) *2/78*, 16.
[212] *A. J. Hopfinger:* Intermolecular Interactions and Bimolecular Organization. Wiley, New York 1976.
[213] Review: *F. Vögtle, E. Weber, U. Elben,* Kontakte (Merck) *3/78*, 32; *1/79*, 3.

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

1,1′-Trimethylenebis(η^5-3-*tert*-butylcyclopentadienyl)-titanium(IV) Dichloride, a Chiral *ansa*-Titanocene Derivative[**]

By *Horst Schnutenhaus* and *Hans H. Brintzinger*[*]

Chiral organometallic compounds are of interest as stereoselective catalysts, especially for asymmetric reactions with prochiral olefins. With titanocene derivatives, from which catalysts for various olefin reactions can be obtained, chirality can be introduced in principle by multiple substitution at the ring ligands[1]. However, in order to be used as stereospecific catalysts, *e.g.* for olefin hydrogenation, compounds of this type have to retain their configurational stability even upon exchange of both equatorial ligands, which invariably occurs in catalytic reaction sequences[2]. Titanocene derivatives with configurational stability vis-à-vis exchange of equatorial ligands and with a high degree of stereorigidity can be obtained by introduction of ring substituents into a metallocene framework, in which both cyclopentadienyl rings are covalently connected by a $(CH_2)_n$ bridge[3]. We wish to report the synthesis of such a chiral titanocene derivative, the title compound *(1)*, and its resolution by way of a diastereomeric (*S*)-binaphtholate.

Reaction of the anion of *tert*-butylcyclopentadiene[4] with one half equivalent of 1,3-dibromopropane in anhydrous tetrahydrofuran (THF) under an atmosphere of nitrogen at $-10\,^\circ C$ affords 1,3-bis(3-*tert*-butylcyclopentadienyl)propane, which is aromatized without isolation and allowed to react with one equivalent of titanium(III) chloride. Subsequently, oxidation to the Ti^{IV} derivative is achieved by addition of 6 N aqueous hydrochloric acid. The crude product can be purified, albeit with considerable loss of yield, by high-pressure liquid-chromatography on silica gel (Lichrosorb SL 100, E. Merck & Co.) with toluene as eluent. The red-brown compound *(1)* is obtained as the main fraction[5]. In the ^{1}H-NMR spectrum of *(1)* (in $CDCl_3$, rel. $\delta(CHCl_3)=7.25$) a sharp multiplet at $\delta=6.05$—6.40 is attributed to six cyclopentadienyl protons, a somewhat broadened multiplet at $\delta=2.15$—2.35 to six methylene protons of the $(CH_2)_3$ bridge and a sharp singlet at $\delta=1.40$ to 18 *tert*-butyl protons. The occurrence of only one *t*-Bu signal confirms the steric uniformity of the product obtained. Apparently, the formation of isomers with 1,2-disubstituted or *meso*-coordinated ring ligands is suppressed by the substantial steric requirements of the *tert*-butyl groups.

In order to resolve the racemic mixture of *(1)*, the crude product is allowed to react with (*S*)-(−)-1,1′-bi-2-naphthol[6] in the presence of sodium or sodium amide in toluene for 24 h at 60 °C. The reaction products are separated by high-pressure liquid-chromatography of the solution on a reversed-phase-adsorbent (Lichrosorb RP18, E. Merck & Co.) with methanol as eluent. Besides small amounts of unbridged $(t\text{-}BuC_5H_4)_2Ti(O_2C_{20}H_{12})$ and of doubly bridged $\{(CH_2)_3\}_2(t\text{-}BuC_5H_2)_2Ti(O_2C_{20}H_{12})$, one obtains as main fraction the desired compound $(CH_2)_3(t\text{-}BuC_5H_3)_2Ti(O_2C_{20}H_{12})$ *(2)*[7]. In the ^{1}H-NMR spectrum of *(2)*, the expected multiplets of the binaphtholate protons are observed at $\delta=7.87$—7.78 and 7.22—6.95, the multiplets of the cyclopentadienyl protons at $\delta=6.53$—6.12 and 5.17, and the signals of the methylene bridge at $\delta=1.26$ and 1.22 (1:2). The *tert*-butyl groups give rise to one singlet at $\delta=0.96$. The equivalence of both *tert*-butyl groups documents, also for the diastereomeric product *(2)*, a stereochemical uniformity, *i.e.* the absence of substitutional or configurational isomers and indicates that the molecule has, at least on the NMR timescale, the expected axially symmetric structure (see Fig. 1). The specific rotation of *(2)* is found to be $[\alpha]_{577}^{20}=+590^\circ$ ($c=0.8$ g/100 ml diethyl ether); this value remains unchanged after repeated chromatographic purification. The visible part of the CD spectrum of *(2)* shows positive maxima at 480 and 365 nm, a minimum at 445 nm, and a crossover to negative $\Delta\varepsilon$ values at 305 nm.

Interestingly, the high-pressure liquid-chromatographic separation of the reaction product of *(1)* with (*S*)-1,1′-bi-2-naphthol yields only one of the possible diastereomers of *(2)*. Probably, the formation of *(2)* is highly stereoselective. A molecular model (Fig. 1) shows that for the 1*R*,1′*R* enantiomer[8] as well as for the *meso*-form of *(1)*, the introduction

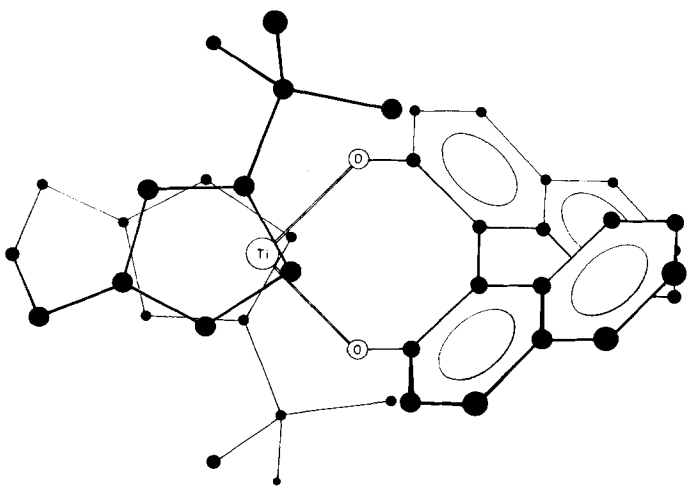


Fig. 1. Molecular model of 1*S*,1′*S*-trimethylenebis(3-*tert*-butylcyclopentadienyl)titanium(IV) (*S*)-1,1′-bi-2-naphtholate *(2)* (projected on TiO_2 plane, height of C atoms above and below this plane indicated by size of dark spheres) [8]

[*] Prof. Dr. H. H. Brintzinger, Dipl.-Chem. H. Schnutenhaus
Fakultät für Chemie der Universität
Postfach 733, D-7750 Konstanz (Germany)

[**] *ansa*-Metallocenes, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and by research funds of the University of Konstanz. We wish to thank Dipl.-Chem. *M. Böhme* for help with the chromatographic separations.—Part 1: *J. Smith, J. von Seyerl, G. Huttner, H. H. Brintzinger*, J. Organomet. Chem. *173*, 175 (1979).

of the (*S*)-binaphthol ligand is opposed by substantial steric repulsion between the *tert*-butyl groups of the titanocene framework and the H atoms in the 3-position of the naphthol ligand; only for the 1*S*,1′*S* enantiomer of *(1)* does the equidirectional helicity of the titanocene framework permit an uninhibited introduction of the (*S*)-binaphthol ligand.

On reaction with HCl in diethyl ether at 0 °C the diastereomer *(2)* is converted into (*S*)-binaphthol and one of the enantiomers of *(1)*, whose specific rotations are $[\alpha]_{435.8}^{20} = -127°$ and $[\alpha]_{365.4}^{20} = +253°$ ($c = 0.16$ g/100 ml diethyl ether). The CD spectrum, with positive maxima at 475 and 330 nm, a negative double maximum at 395 and 415 nm, and with a cross-over to negative $\Delta\varepsilon$ values at 305 nm corresponds—with a shift of one of the bands to shorter wavelengths—largely to the CD spectrum of the binaphtholate derivative *(2)*.

The correspondence of the CD spectra of *(2)* and *(1)* is in accord with our original expectation, *viz.* that an exchange of equatorial ligands would leave the configuration of the chiral *ansa*-titanocene framework unchanged. Based on this assumption, and on the structure of the diastereomer *(2)* represented in Fig. 1, we can assign to the finally obtained enantiomer of *(1)* a 1*S*,1′*S*-configuration.

Received: April 27, 1979 [Z 277 IE]
German version: Angew. Chem. *91*, 837 (1979)

CAS Registry numbers:
(1), 71316-79-5; *(2)*, 71316-80-8; 1,3-bis(3-*tert*-butylcyclopentadienyl)propane, $TiCl_3$, 7705-07-9

[1] *A. Dormond, J. Tirouflet, F. Le Moigne*, J. Organomet. Chem. *69*, C7 (1974); *J. Besançon, S. Top, J. Resançon, S. Top*, J. Organomet. Chem. *127*, 139 (1977); J. Organomet. Chem. *127*, 139, 153 (1977).

[2] For this reason, compounds of general type $(C_5H_4R^1)(C_5H_4R^2)TiXY$, in which the chirality center is situated on the titanium atom (*C. Moïse, J. C. Leblanc, J. Tirouflet*, J. Am. Chem. Soc. *97*, 6277 (1975)), are unsuitable candidates for such an asymmetric catalyst.

[3] Cf. the studies by *K. Schlögl et al.* [Fortschr. Chem. Forsch. *6*, 479 (1966); Top. Stereochem. *1*, 39 (1967)], on chiral, bridged ferrocene derivatives.

[4] *R. Riemschneider, R. Nehring*, Monatsh. Chem. *90*, 568 (1959).

[5] Mass spectrum with molecular ion $[(CH_2)_3(C_4H_9\ \ C_5H_3)_2TiCl_2]^+$ and fragment ions $[M-Cl]^+$ and $[M-2HCl]^+$.

[6] For the resolution of 1,1′-bi-2-naphthol, the procedure reported by *J. Jacques, C. Fouquey, R. Viterbo* (Tetrahedron Lett. *1971*, 4617) was modified by reacting 1,1′-bi-2-naphthol and $POCl_3$ in the presence of pyridine, and by a direct reduction of the unmethylated phosphoric acid ester of *(S)*-1,1′-bi-2-naphthol with $LiAlH_4$. A similar procedure has recently been reported by *E. P. Kyba, G. W. Gokel, F. de Jong, K. Koga, L. R. Sousa, M. G. Siegel, L. Kaplan, G. D. Y. Sogah, D. J. Cram*, J. Organic Chem. *42*, 4173 (1977).

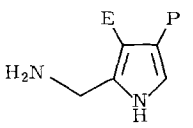
[7] Mass spectrum with molecular ion $[(CH_2)_3(C_4H_9\ \ C_5H_3)_2Ti(O_2C_{20}H_{12})]^+$ and fragment ion $[(CH_2)_3(C_4H_9\ \ C_5H_3)_2Ti-2H]^+$.

[8] For a stereochemical description of the substituted *ansa*-titanocene framework, we follow the extension of the Cahn-Ingold-Prelog notation to substituted metallocenes as proposed by *Schlögl*[3]. For the compounds under consideration here, the configuration of the complete ligand framework is unambiguously described by denoting the configuration of one of the ring atoms in each ring, in our case *e.g.* that of the bridgehead atoms 1 and 1′.

Enzymatic Formation of Uroporphyrinogen I and III from a Substituted Bilane[**]

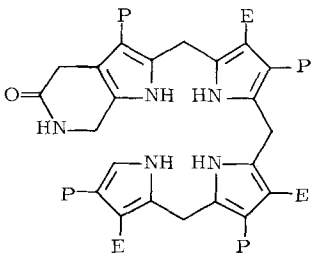
By *Peter Kammerer, Gertrud Wörner*, and *Gerhard Müller*[*]

All natural porphyrins, chlorins, isobacteriochlorins, and corrins are derived from uroporphyrinogen (uro'gen) III. This compound has an arrangement of side chains on ring D opposite to that of uro'gen I. Enzymatic transformation of four molecules of porphobilinogen *(1)* into uro'gen III is catalyzed by "porphobilinogenase"[1]. This enzyme system consists of two enzymes, *viz.* uroporphyrinogen I synthase (porphobilinogen deaminase) and the thermally labile uroporphyrinogen III cosynthase (isomerase). Only the deaminase catalyzes formation of uro'gen I. The uro'gen III:I ratio is determined on enzymatic uro'gen formation by means of the isomerase content of the porphobilinogenase preparation[1]. It was recently deduced from experiments on unlabeled[2] and ^{14}C-labeled[3] bilane *(3)* that the first steps of uro'gen I and uro'gen III synthesis are the same. Accordingly, uro'gen III is formed by isomerization on ring closure of the bilane *(3)* which arises by formal "head-to-tail" condensation of four molecules of *(1)*. NMR spectroscopic studies by *Battersby et al.*[3c] with ^{13}C-labeled bilanes revealed that *(3)* is transformed into uro'gen III by intramolecular rearrangement of the unit forming ring D. Other workers assumed, on the basis of extensive experiments with di- and tripyrrolylmethanes, that isomerization is the first step of enzymatic formation of uro'gen III and arises by "head-to-head" condensation of the first two units of *(1)*[1,4].—Our enzymatic studies have shown that the bilane *(3)* is converted into uro'gen III by "porphobilinogenase".

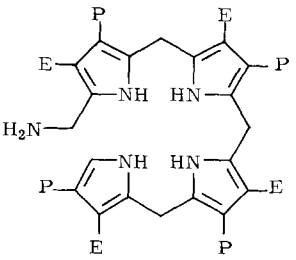


(1)

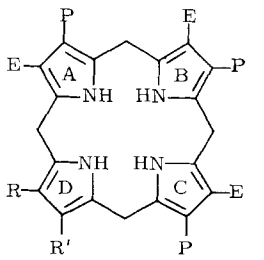
E = $-CH_2-COOH$
P = $-CH_2-CH_2-COOH$



(2)



(3)



Uro'gen I, R = P, R′ = E
Uro'gen III, R = E, R′ = P

Alkaline hydrolysis (1 M KOH, 48 h, 30 °C) of the lactam *(2)* (see [2] for synthesis) gives the bilane *(3)*[2], from which uro'gen I is obtained almost exclusively (contains <3% uro'gen III; overall yield *ca.* 70% after 16 h at 37 °C) by chemical cyclocondensation (phosphate buffer, pH = 7—8). The porphobilinogenase preparations from cell extracts of *Clostridium tetanomorphum* were enriched by ammonium sulfate fractionation (30–50% saturation) and on Sephadex DEAE A-25 and were free from porphyrinogen[5]. The uro'gens obtained chemically or enzymatically were dehydrogenated to the uroporphyrins and quantitatively determined according to *Cornford*[6]. For isomer analysis, the uroporphyrins were fixed to Sephadex DEAE A-25, esterified with CH_3OH/H_2SO_4, and isolated as octamethyl esters[5]. After decarboxylation, the resulting coproporphyrins (see [2]) were analyzed by TLC according to *Frydman et al.*[4a] and the coproporphyrin tetrapropyl esters (after esterification of the coproporphyrins with 1-propanol/H_2SO_4) by HPLC (Merck Hibar column; Li Chrosorb RP-18, 5 μm; acetoni-

[*] Dipl.-Chem. P. Kammerer, G. Wörner, Dr. G. Müller
Institut für Organische Chemie, Biochemie und Isotopenforschung der Universität
Pfaffenwaldring 55, 7000 Stuttgart 80 (Germany)

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

trile/water 83:17, v/v)[7]. Quantitative determination of the isomeric composition was by HPLC.

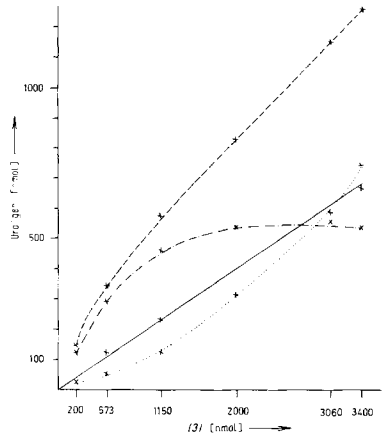


Fig. 1. Chemical and enzymatic formation of uroporphyrinogen as function of concentration of bilane *(3)*. The incubation mixtures contain 1600 mg of protein in 80 ml of 52 mM phosphate buffer, pH = 7.7, as well as the amounts of bilane given, based on unhydrolyzed lactam *(2)*; after hydrolysis of *(2)* the mixture is neutralized with NaH_2PO_4. Incubation: 1 h, 37 °C.—Chemically formed uro'gen I (contains <3% uro'gen III); bilane and protein were incubated separately for this purpose (each 80 ml, see above) and combined after uro'gen dehydrogenation. Enzymatically formed uro'gen: --- total amount, -·-·- uro'gen III, ····· uro'gen I.

The results of Figures 1 and 2 and Table 1 clearly demonstrate that bilane *(3)* is a substrate of "porphobilinogenase". Enzymatic cyclization of *(3)* gives far higher yields than chemical cyclization. Since the content of uro'gen III is proportional to the amount of cosynthase in the porphobilinogenase preparation[1], the highest uro'gen III contents (up to 90%) arise at low bilane concentrations; the total amount of uro'gen III reaches a limiting value at high bilane concentrations. More uro'gen I than III is formed in this region (Fig. 1). Expectedly, the uro'gen III:I ratio increases on incubation with substrate saturation when increasing amounts of "porphobilinogenase" are employed (Fig. 2). The results ob-

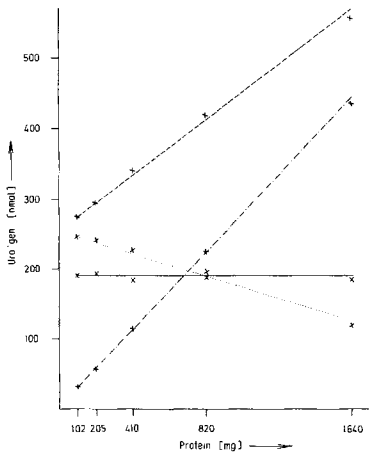


Fig. 2. Uroporphyrinogen formation as function of porphobilinogenase concentration. The incubation mixtures contained 925 nmol of bilane *(3)* (see Fig. 1) in 80 ml of 52 mM phosphate buffer, pH = 7.7, as well as the amounts of protein given. Incubation: 1 h, 37 °C. Enzymatically formed uro'gen: ----- total amount, -·-·- uro'gen III, ····· uro'gen I.——— Chemically formed uro'gen (98% type I) produced under same conditions (see Fig. 1).

tained with enzyme preparations heated for various lengths of time to denature the cosynthase (Table 1) also show conclusively that the "porphobilinogenase" catalyzes both isomerization and cyclization. The deaminase expectedly cata-

Table 1. Formation of uroporphyrinogen I and III from 450 nmol of bilane *(3)* (see Fig. 1) and porphobilinogenase preparations (500 mg of protein in 65 ml of 52 mM phosphate buffer pH = 7.7) which had previously been heated to 60 °C for time *t*. Incubation: 1 h, 37 °C.

Heating *t* [min]	Uro'gen isolated [nmol]	[%]	I : III
—	221	49.1	23 : 77
15	222	49.3	59 : 41
30	219	48.7	76 : 24
45	216	48.0	84 : 16
90	204	45.3	91 : 9
[a]	81	18.0	98 : 2

[a] Chemical formation of uroporphyrinogen (see Fig. 1).

lyzes formation of uro'gen I. Surprisingly, no reaction of bilane *(3)* was observed with deaminase-free preparations[8] of cosynthase. This shows that transformation of unisomerized bilane *(3)* into uro'gen III requires both the deaminase and the cosynthase[9].

Received: June 29, 1979 [Z 294 IE]
German version: Angew. Chem. *91*, 838 (1979)

CAS Registry numbers:
(2), 58860-69-8; *(3)*, 36459-84-4; uroporphyrogen I, 1867-62-5; uroporphyrogen III, 1976-85-8

[1] *A. M. Del, C. Battle, M. V. Rossetti,* Int. J. Biochem. *8*, 251 (1977), references cited.

[2] *H.-O. Dauner, G. Gunzer, I. Heger, G. Müller,* Hoppe-Seylers Z. Physiol. Chem. *357*, 147 (1976), and references cited therein; for other syntheses of *(3)* see *B. Franck, A. Rowold,* Angew. Chem. *87*, 418 (1975); Angew. Chem. Int. Ed. Engl. *14*, 423 (1975) and [3b].

[3] a) *A. R. Battersby, E. McDonald, D. C. Williams, H. K. W. Wurziger,* J. Chem. Soc. Chem. Commun. *1977*, 113; b) *A. R. Battersby, E. McDonald,* Acc. Chem. Res. *12*, 14 (1979), and references cited therein; c) *A. R. Battersby, C. J. R. Fookes, E. McDonald, M. J. Meegan,* J. Chem. Soc. Chem. Commun. *1978*, 185.

[4] a) *R. B. Frydman, E. S. Levy, A. Valasinas, B. Frydman,* Biochemistry *17*, 115 (1978), and references cited therein; b) *A. I. Scott, K. S. Ho, M. Kajiwara, T. Takahashi,* J. Am. Chem. Soc. *98*, 1589 (1976).

[5] *K. H. Bergmann, R. Deeg, K. D. Gneuss, H. P. Kriemler, G. Müller,* Hoppe Seylers Z. Physiol. Chem. *358*, 1315 (1977).

[6] *P. Cornford,* Biochem. J. *91*, 64 (1964).

[7] *P. Kammerer,* Dissertation, Universität Stuttgart 1979.

[8] Separation of deaminase and cosynthase (isomerase) can be accomplished on AH-Sepharose 4B with 0.06 M Tris/HCl buffer, pH = 7.2, + increasing amounts of NaCl; the deaminase is eluted by 0.2 M NaCl buffer solutions and the cosynthase by 0.3 M NaCl buffer solutions. *G. Gunzer,* Dissertation, Universität Stuttgart 1978.

[9] After conclusion of the present investigation *A. R. Battersby, C. J. R. Fookes, G. W. J. Matcham, E. McDonald, K. E. Gustafson-Potter,* J. Chem. Soc. Chem. Commun. *1979*, 316 as well as *G. Burton, P. E. Fagerness, S. Hosozawa, P. M. Jordan, A. I. Scott, ibid. 1979*, 202 reported ^{13}C-NMR-studies on enzymatic formation of uroporphyrinogen III. Despite differing interpretation of the results, both groups show that the final product of the deaminase reaction is a tetrapyrrole that is not identical with bilane *(3)*. Since *(3)* is a substrate of "porphobilinogenase" (deaminase + cosynthase) (see above), the deaminase must catalyze a further reaction of bilane *(3)* along the pathway *(3)*→uro'gen III.

Complexes with Chiral Alkylcyclopentadienyl Ligands for Homogeneous Catalytic Asymmetric Hydrogenation of 2-Phenyl-1-butene

By *E. Cesarotti, R. Ugo,* and *H. B. Kagan*[*]

Homogeneous asymmetric hydrogenation of double bonds by metal complexes with chiral ligands such as phosphanes,

[*] Dr. E. Cesarotti [+], Prof. Dr. R. Ugo
Istituto di Chimica Generale e Inorganica und Centro CNR
Via Venezian 21, I-20133 Milano (Italy)
Prof. Dr. H. B. Kagan
Laboratoire de Synthèse Asymetrique, Université de Paris-Sud
Centre d'Orsay
F-91405 Orsay (France)
[+] To whom correspondence should be addressed.

amines, and alcohols has been a subject of intense research whereas very little attention has been paid to the use of optically active hydrocarbon ligands.

We have focused our attention on the η^5-cyclopentadienyl ligand and its derivatives which not only form well characterized complexes with many metals but have also been used in catalysts for various organic reactions (hydrogenation[1a], hydroformylation[1b], polymerization[1c]) and for stoichiometric organic reactions such as those related to hydrozirconation[2]. Titanium(IV) complexes with the menthyl- and neomenthylcyclopentadienyl ligands[3] show appreciable catalytic activity for the hydrogenation of simple olefins, including 2-phenyl-1-butene *(1)*, in the presence of a reducing agent, such as "Red-Al" $[Li(H_2Al(OCH_2CH_2OCH_3)_2)]$ acting as a cocatalyst[4].

We have now found that on hydrogenation of the prochiral olefin *(1)* to 2-phenylbutane *(2)* in the presence of one of the catalysts *(3)—(6)*, the (*R*)- or (*S*)-enantiomer predominates in the product (Table 1).

$$\underset{(1)}{H_3C{-}CH_2{-}CPh{=}CH_2} \rightarrow \underset{(2)}{H_3C{-}CH_2{-}CHPh{-}CH_3}$$

Table 1. Asymmetric hydrogenation of *(1)* to *(2)* with the catalysts *(3)—(6)*. Pentane (5 ml, solvent), *(1)* (4 mmol), "Red-Al" as cocatalyst in toluene, and the catalyst in tetrahydrofuran (THF) are introduced in that order with a syringe into a thermostated reactor: *(1)*/Red-Al/catalyst = 75/6/1. $p = 1$ atm, $T = 20\,^\circ C$; 100% conversion [a].

	Catalyst [b]	Product *(2)*	$[\alpha]_D$ [°] [c]	e.e. [%] [d]
(3)	$(\eta^5\text{-MCp})_2TiCl_2$	(*S*)-(+)	$+3.2 \pm 0.3$	14.9
(4)	$(\eta^5\text{-NMCp})_2TiCl_2$	(*R*)-(−)	-1.6 ± 0.3	7.0
(5)	$(\eta^5\text{-MCp})(\eta^5\text{-Cp})TiCl_2$	(*S*)-(+)	$+1.9 \pm 0.3$	8.4
(6)	$(\eta^5\text{-NMCp})(\eta^5\text{-Cp})TiCl_2$	(*R*)-(−)	-2.3 ± 0.3	10.0

[a] The hydrogen uptake was measured with a gas burette and monitored by GLC of the reaction mixture; no isomerization products were detected. [b] MCp = (−)-menthylcyclopentadienyl; NMCp = (+)-neomenthylcyclopentadienyl. [c] After each introduction of air the reaction mixture was evaporated down and vacuum-distilled. The distilled samples were separated by preparative GLC (instrument: Carlo Erba GT 200 with one SS column (¼″ × 2.5 m); 20% Carbowax 1500 on Chromosorb W 60/80; helium; $T_i = 150\,^\circ C$; $T_0 = 100\,^\circ C$). *(2)* was collected in a liquid nitrogen trap. The $[\alpha]_D$ values ($c = 6$, EtOH) of a distilled sample and of one separated by GLC were in agreement (±0.3). [d] Enantiomeric excess: mean values from at least three determinations. $[\alpha]_D$ of (*S*)-(+)-*(2)* = +22.7° ($c = 1$, EtOH, 95%); *J. Cymerman Craig, W. E. Pereira, B. Halpern, J. W. Westley*, Tetrahedron *27*, 1173 (1971).

The catalysts *(3)* and *(5)* with (−)-menthylcyclopentadienyl lead to (*S*)-(+)-*(2)*, whereas the catalysts *(4)* and *(6)* with (+)-neomenthylcyclopentadienyl give (*R*)-(−)-*(2)*. Whether one or two chiral alkylpentadienyl groups are present has hardly any effect on the enantiomeric excess.

The enantiomeric excess obtained with catalyst *(3)* is comparable with that found for metal complexes of chiral phosphanes[5]. A higher asymmetric induction has also been observed with special complexes[6].

However, hydrogenation of *(1)* with the chiral complex *(7)* as catalyst did not lead to optically active *(2)*[7].

$$[\eta^5\text{-}C_6H_5CH(CH_3)C_5H_4](\eta^5\text{-}C_5H_5)Zr(CH_3)_2 \qquad (7)$$

Our titanium compounds *(3)—(6)* prove to be inactive towards olefins with donor groups such as CN, COR, COOR. Studies on other simple prochiral olefins should reveal the manner in which these relatively flat and rigid ligands effect preferential formation of one enantiomer.

Received: May 3, 1979 [Z 290 IE]
German version: Angew. Chem. *91*, 842 (1979)

CAS Registry numbers:
(1), 2039-93-2; *(S)*-(+)-*(2)*, 5787-28-0; *(R)*-(−)-*(2)*, 5787-29-1; *(3)*, 69108-09-4; *(4)*, 69175-90-2; *(5)*, 71301-36-5; *(6)*, 69108-11-8; *(7)*, 68193-57-7

[1] a) *J. H. Craddock, A. Hersham, F. E. Paulik, J. F. Roth*, Ind. Eng. Chem. Prod. Res. Dev. *1969*, 8; *A. Miyake, H. Kondo*, Angew. Chem. *80*, 663 (1968); Angew. Chem. Int. Ed. Engl. *7*, 631 (1968); *R. L. Funk, K. P. C. Vollhardt*, J. Am. Chem. Soc. *99*, 5483 (1977); *C. White, D. S. Gill, J. W. Kang, H. B. Lee, P. M. Maitlis*, Chem. Commun. *1971*, 734; *M. J. Russel, C. White, P. M. Maitlis*, J. Chem. Soc. Chem. Commun. *1977*, 427; b) *E. Cesarotti, A. Fusi, R. Ugo, G. M. Zanderighi*, J. Mol. Catal. *4*, 205 (1978); *L. Marko* in *R. Hugo:* Aspects of Homogeneous Catalysis. Vol. II. Reidel, Dordrecht 1974, p. 50; *J. Tsuji, Y. Mori*, Bull. Chem. Soc. Jpn. *42*, 527 (1969); c) *J. N. Hay, R. M. S. Obaid*, Eur. Polym. J. *14*, 965 (1968), and references therein.

[2] *J. Schwartz, J. A. Labinger*, Angew. Chem. *88*, 402 (1976); Angew. Chem. Int. Ed. Engl. *15*, 333 (1976); *A. Nakamura, S. Otsuda*, J. Am. Chem. Soc. *95*, 7262 (1973).

[3] *E. Cesarotti, H. B. Kagan, R. Goddard, C. Krüger*, J. Organomet. Chem. *162*, 297 (1978).

[4] *R. Stern, L. Sajus*, Tetrahedron Lett. *1968*, 6313; *R. Stern, G. Hillon, L. Sajus, ibid. 1969*, 156; *Y. Tayima, E. Kumioka*, J. Organomet. Chem. *33*, 1689 (1968).

[5] *L. Horner, H. Siegel, H. Büthe*, Angew. Chem. *80*, 1034 (1968); Angew. Chem. Int. Ed. Engl. *7*, 942 (1968); *J. Morrison et al.*, J. Am. Chem. Soc. *93*, 1301 (1971).

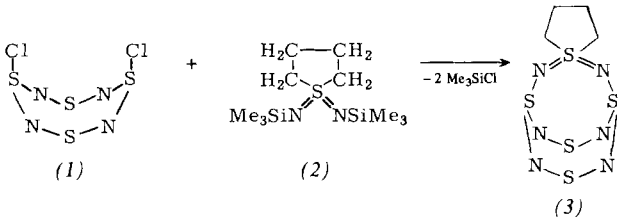
[6] *T. Hayashi, M. Tanaka, J. Ogata*, Tetrahedron Lett. *1977*, 295; *G. Consiglio, P. Pino*, Isr. J. Chem. *15*, 221 (1976/77); *G. Consiglio, W. Arber, P. Pino*, Chim. Ind. (Milano) *60*, 396 (1978).

[7] *S. Couturier, B. Gautheron*, J. Organomet. Chem. *157*, C 61 (1978).

$S_5N_6(CH_2)_4$—The First Spirocyclic $1'\lambda^6$-Thiacyclopentane Derivative of a Sulfur-Nitrogen Compound[**]

By *Herbert W. Roesky, Cornelia Graf, M. N. S. Rao, Bernt Krebs*, and *Gerald Henkel*[*]

The presence of sulfur atoms of coordination number 2 in the basket-like compound S_5N_6[1] should permit derivatization. Formal dialkyl substitution at the S atom of the "handle" in the molecular skeleton of S_5N_6 can be accomplished by reaction of $S_4N_4Cl_2$ *(1)* with thiacyclopentane *S,S*-bis(trimethylsilylimide) *(2)*[2]. Compound *(1)* is accessible by reaction of S_4N_4 with chlorine[3].



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

The spirocyclic product *(3)* was isolated as yellow crystals which are stable towards air and moisture. On heating to 150 °C a red coloration is observed, and explosive decomposition occurs at 151 °C (we detected only fragments of the new compound in the mass spectrum). It fails to dissolve without decomposition in all the usual solvents; hence no ^{1}H-NMR investigation has yet proved successful.

[*] Prof. Dr. H. W. Roesky, Dipl.-Chem. C. Graf, Dr. M. N. S. Rao [+]
Anorganisch-chemisches Institut der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. Dr. B. Krebs, Dr. G. Henkel
Anorganisch-chemisches Institut der Universität
Gievenbecker Weg 9, D-40 Münster (Germany)

[+] Alexander von Humboldt fellow.

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

X-ray structure analysis of *(3)* (monoclinic, space group $P2_1/c$, $a = 7.056(2)$, $b = 13.272(4)$, $c = 11.660(3)$ Å, $\beta = 101.57(3)°$, $Z = 4$; four-circle diffractometer data, $R = 3.4\%$) proves the spiro-linkage of the thiacyclopentane ring to S1 of the bicyclic SN skeleton (Fig. 1).

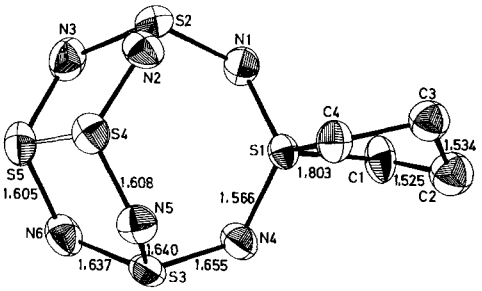


Fig. 1. Molecular structure of $S_5N_6(CH_2)_4$ in the crystal with bond lengths (σSN and σSC = 0.003, σCC = 0.010 Å) and vibrational ellipsoids (50% probability).

The eight-membered ring without S1, N1, and N4 has a conformation analogous to that of the S_4N_4 molecule; the other two rings (S1—N1—S2—N2—S4—N5—S3—N4 and S1—N1—S2—N3—S5—N6—S3—N4) have a crown shape comparable with that of the S_8 molecule. The distance of 2.454(1) Å between S4 and S5 corresponds to a transannular interaction. This contact is stronger than in S_4N_4 (2.58 Å) but weaker than in S_5N_6 (2.425(2) Å)[1] and in $S_5N_6(CH_3)_2$ (2.433(3) Å)[4]. Neglecting the $S(CH_2)_4$ five-membered ring, the molecule of *(3)* has C_s symmetry. The bond lengths averaged over both halves of the molecule are shown in Figure 1; bond angles S—N—S 121.1(2)—125.3(2), N—S(trivalent)—N 104.0(2)—111.0(2). N—S(divalent)—N 118.4(2)—119.2(2), N—S(tetravalent)—N 124.1(2)°.

Procedure

A solution of *(2)* (5 mmol) in CH_3CN (25 ml) is added dropwise to a cooled (−5 to −10 °C) and stirred solution of *(1)* (5 mmol) in CH_3CN (50 ml). A grayish-brown precipitate appears on slow warming of the reaction mixture to room temperature (12 h). The product is purified by dissolving samples of *ca.* 50 mg in a mixture of CH_2Cl_2 (30 ml) and CH_3CN (10 ml). After removing part of the CH_2Cl_2 (25 ml) the solution is allowed to stand in a refrigerator, whereupon yellow crystals of *(3)* precipitate. The yield is 40% (before recrystallization).

Received: June 5, 1979 [Z 295b IE]
German version: Angew. Chem. *91*, 846 (1979)

[1] *T. Chivers, J. Proctor*, J. Chem. Soc. Chem. Commun. *1978*, 642; *H. W. Roesky, M. N. S. Rao, T. Nakajima, W. S. Sheldrick*, Chem. Ber., in press.
[2] *H. W. Roesky, C. Graf*, unpublished.
[3] *L. Zborilova, P. Gebauer*, Z. Anorg. Allg. Chem. *448*, 5 (1979).
[4] *W. S. Sheldrick, M. N. S. Rao, H. W. Roesky*, Inorg. Chem., in press.

Chemistry of the $H_3B(CH_3)_2P$ Group[**]: Unusual Properties of Some Simple Reference Compounds

By *Hubert Schmidbaur* and *Erwin Weiss*[*]

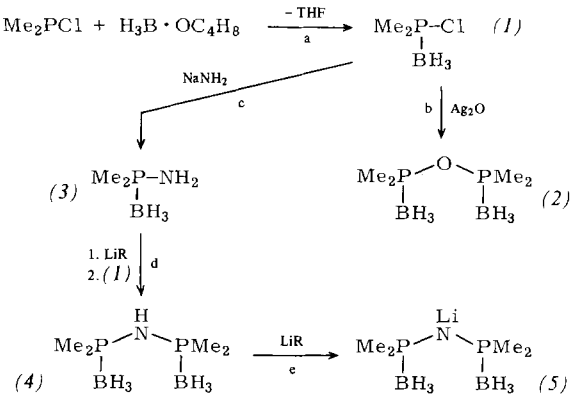
The trimethylsilyl group Me_3Si— confers synthetically, technically, and analytically valuable properties on a variety of compounds. Its advantages as a protecting and leaving group and as an inert and hydrophobic synthetic moiety having influence on the solubility, volatility and surface nature of substances were soon recognized and rapidly led to a wide spectrum of practical applications.



It appears inapposite at first sight to expect similar properties of the isoelectronic $Me_2(H_3B)P$-group, since the otherwise typical lability of the BH-function and the formal charges would suggest such substances to have a completely different character. We have found, however, that 1) all $Me_2(H_3B)P$ compounds analogous to the Me_3Si parent compounds can exist, that these 2) are surprisingly thermally and chemically stable and 3) open up access to a variety of derivatives by substitution reactions.

The chlorophosphaneborane *(1)* corresponding to chloro(trimethyl)silane is readily and quantitatively obtainable (route a) from inexpensive starting materials; the stable, distillable liquid is only slightly sensitive to moisture[1].

The compound *(2)* analogous to disiloxane can be prepared from *(1)* by controlled hydrolysis or—better—with Ag_2O (route b); its air- and water-stable crystals, m.p. 74 °C, are sublimable without decomposition.



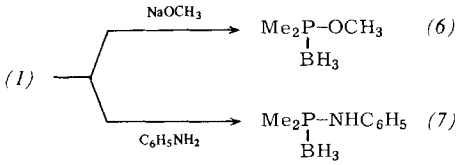
Ammonolysis of *(1)* with NH_3 in diethyl ether or the reaction with $NaNH_2$ (route c) leads quantitatively to the analog of (unstable![2]) amino(trimethyl)silane; the product *(3)* is a deliquescent crystalline substance at room temperature which loses neither NH_3 nor H_2 spontaneously and can be distilled without decomposition. After metalation with *n*-C_4H_9Li in pentane, the reaction (route d) with further *(1)* affords the compound *(4)* corresponding to disilazane; like *(2)* it is air- and water-stable, can be sublimed, and can be metalated once again at the NH group (route e), giving the important versatile reagent *(5)*[3].

Reaction of *(1)* with $NaOCH_3$ in diethyl ether/methanol quantitatively affords the methoxyphosphaneborane *(6)*, whose aromatic odor is reminiscent of that of the corresponding silyl ether. The CH_3O— moiety in *(6)* is readily replaceable by other RO groups. On reaction with aniline in diethyl ether, *(1)* is completely converted into *(7)* already at room temperature. Other amines give analogous products.

The structure and composition of all the named compounds was confirmed by complete elemental analyses and spectroscopic investigations [MS, IR, NMR, ^1H, ^{13}C, ^{31}P].

[*] Prof. Dr. H. Schmidbaur, Dipl.-Chem. E. Weiss
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Part 1.



The unusual properties of these prototypes deserve comment: it is a little-known fact that the BH_3 group in phosphaneboranes has, for much discussed but still unclear reasons[4], lost its hydride activity to such an extent that it is even stable towards acids and bases[5]. According to our findings the monofunctional derivatives behave similarly and thus the $H_3B(CH_3)_2P$ group proves to be a relatively inert and readily exchangeable substituent. It is apparent then that many of the known reactions of $(CH_3)_3Si$ compounds can be accomplished with the corresponding $H_3B(CH_3)_2P$ compounds, but the products have a characteristically higher polarity.

Experimental

(1): A 1 M THF solution of $BH_3 \cdot C_4H_8O$ (63 ml, 63 mmol) is added to 6.0 g (62.7 mmol) Me_2PCl at 0 °C. The solvent is removed at 20 mbar/20 °C and the residue distilled at 0.1 mbar/20 °C; colorless liquid[1].

(2): To a solution of *(1)* (0.46 g, 4.2 mmol) in THF (15 ml) is added Ag_2O (0.48 g, 2.1 mmol) and the mixture stirred in a sealed vessel for one week at 20 °C. All volatile components are removed at 0.1 mbar/20 °C, and the residue washed with pentane (5 ml) and sublimed at 60 °C/10^{-4} mbar. Yield 66%; m.p. 74 °C.

(3): *(1)* (2.96 g, 26.8 mmol) is added to a solution of $NaNH_2$ (1.10 g, 20.2 mmol) in THF (10 ml) at −78 °C. The mixture is warmed up and stirred for 1 h. Workup as in the case of *(2)* gives *(3)* in 68% yield.—The same product is obtained on passage of NH_3 into a solution of *(1)* (5.00 g, 45.3 mmol) in ether (75 ml) at 0 °C. After filtration from precipitated NH_4Cl and removal of solvent, *(3)* is obtained in 98% yield; m.p. 29 °C.

(4): One equivalent of *t*-BuLi in pentane is added to a suspension of *(3)* (2.33 g, 25.6 mmol) in pentane (20 ml) at 0 °C and the mixture stirred for 12 h at 20 °C. *(1)* (2.80 g, 25.6 mmol) is then added at 0 °C and stirring continued for a further 4 h at 20 °C. Removal of solvent, washing with 2 × 10 ml water, and crystallization from toluene affords *(4)* in 47% yield; m.p. 164 °C.

(6): To a solution of $CH_3ONa \cdot CH_3OH$ (0.93 g, 10.8 mmol) in ether (10 ml) is added 1.19 g (10.8 mmol) of *(1)* at 0 °C and the mixture is stirred for 1 h. Workup as for *(1)* affords *(6)* in 73.5% yield; colorless liquid.

NMR data of the new $H_3B(CH_3)_2P$ compounds; coupling constants in Hz.

Solvent / Compound		C_6D_6 *(2)*	C_6D_6 *(3)*	$CDCl_3$ *(4)*	$CDCl_3$ *(6)*	C_6D_6 *(7)*
^1H	δCH_3P	1.35, "d"	1.03, d	1.19, "d"	1.51, d	0.60
	$^2J(PH)$	9.0	10.5	9.5	9.2	10
	δBH_3	1.30, dq	1.05, dq	br	0.48	br
	$^1J(BH)$	98	97.5	[a]	96.5	[c]
	$^2J(PH)$	14	16.5		16 [b]	
^{31}P	δP	127, br	45.5, q	58.4, br	118.2, q	47.4, q
	$^1J(PB)$	—	73	—	70.1	70.1
^{13}C	δCH_3P	17.2, "d"	17.2, d	17.0, "d"	14.8, d	—
	$^1J(PC)$	39.1	41	42	41 [b]	—

[a] $\delta NH = 2.86$, broad. IR: $\nu(NH) = 3180$, $\nu(BH) = 2380\ cm^{-1}$.
[b] $\delta CH_3O = 3.63$, d, $^3J(PH) = 12$; $\delta CH_3O = 52.9$, d, $^2J(PC) = 3.9$.
[c] $\delta NH = 3.70$, d, $^2J(PH) = 13$; $\delta C_6H_5 = 5.83$–6.97, m.

(7): A solution of aniline (1.45 g, 15.6 mmol) in ether (5 ml) is added to a solution of *(1)* (0.86 g, 7.80 mmol) in ether (20 ml). A colorless precipitate is formed which is filtered off and washed with redistilled solvent. The filtrate is evaporated to dryness. Yield 88%; m.p. 57 °C.

Received: June 1, 1979 [Z 296a IE]
German version: Angew. Chem. *91*, 847 (1979)

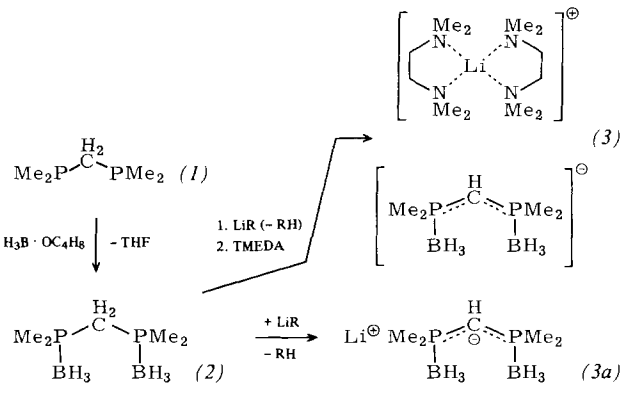
[1] Earlier data referring to a product prepared from Me_2PCl and B_2H_6 gas which was described as decomposable could not be confirmed; most of the spectroscopic findings, however, correspond to our findings for *(1)*: *J. D. Odom, S. Riethmiller, J. R. Durig*, J. Inorg. Nucl. Chem. *36*, 1713 (1974).
[2] *N. Wiberg, W. Uhlenbrock*, Chem. Ber. *104*, 2643 (1971).
[3] Cf. the reactivity of $LiN(SiMe_3)_2$: *U. Wannagat, H. Niederprüm*, Z. Anorg. Allg. Chem. *308*, 337 (1961).
[4] *A. B. Burg, R. J. Wagner*, J. Am. Chem. Soc. *75*, 3872 (1953); *F. Hewitt, A. K. Holliday*, J. Chem. Soc. *1953*, 530; *F. G. A. Stone*, Q. Rev. Chem. Soc. *9*, 174 (1955); *E. L. Muetterties:* Boron Hydride Chemistry. Academic Press, New York 1975.
[5] Gmelin Handbuch der Anorganischen Chemie, Supplement to the 8th edit., Vol. 19, Part 3. Springer-Verlag, Berlin 1975, p. 117ff.

Synthesis and Crystal Structure of a Salt Containing the Anion $[H_3B(CH_3)_2P{\cdots}CH{\cdots}P(CH_3)_2BH_3]^-$; Precursors and Related Compounds[**]

By *Hubert Schmidbaur, Erwin Weiss,* and *Beate Zimmer-Gasser*[*]

Phosphaneboranes R_3PBH_3 are relatively inert owing to the reduction in polarity of their HB and BP structural elements by specific bonding in the H_3BP group. CH_3 groups (R = Me) in such compounds, however, have distinct acidic character due to the stability of the corresponding ylide bases[1]. This effect ought to be much more pronounced in compounds of the type $[R_2(H_3B)P]_2CH_2$ and thus enable metalation at the central atom.

Starting from the bisphosphane *(1)*[2] and the borane adduct $H_3B \cdot OC_4H_8$, we have now synthesized *(2)*, which crystallizes in the form of stacked hexagonal scales (a crystal structure analysis could not be carried out because of the extreme thinness of the flakes). Conversion into a metalated derivative was accomplished by reaction with alkyllithium in an inert solvent, and a crystalline Li-complex salt *(3)* could be isolated by precipitation with tetramethylethylenediamine (TMEDA).



[*] Prof. Dr. H. Schmidbaur, Dipl.-Chem. E. Weiss, Dipl.-Chem. B. Zimmer-Gasser
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstr. 4, D-8046 Garching (Germany)

[**] Chemistry of the $H_3B(CH_3)_2P$ Group, Part 2.—Part 1: [4].

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1010-0782 $ 02.50/0

In order to confirm the proposed structure and to gain a closer insight into the characteristic geometries of $Me_2(H_3B)P$ compounds in general, an X-ray structure analysis was carried out on *(3)*[3]. As expected, independent ions are present in the crystal. In the anion (Fig. 1) both P atoms show a tetrahedral ligand arrangement PC_3B. The bond lengths in the angular (128.6°) PCP bridge are almost equal and distinctly shorter than the terminal PC bonds, thus proving the ylidic nature of the bridge. The lengths of the outer PC and PB bonds differ only slightly, so that the overall shape of the $H_3B(CH_3)_2P$ group does in fact closely resemble that of the isosteric $(CH_3)_3Si$ group[4]. Details can be correlated with the structure of $(Me_3Si)_2NH$.

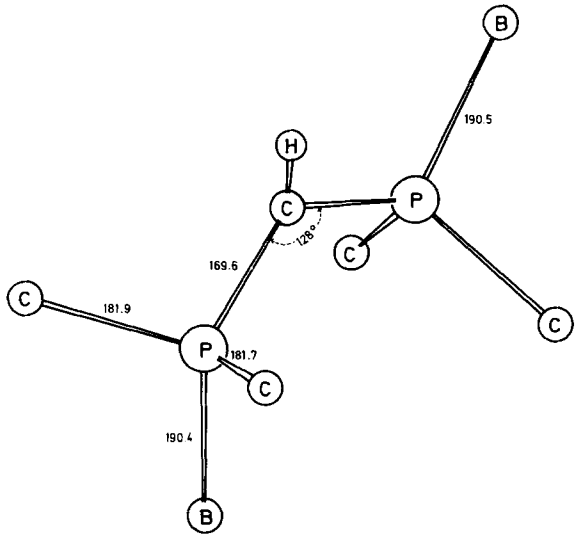
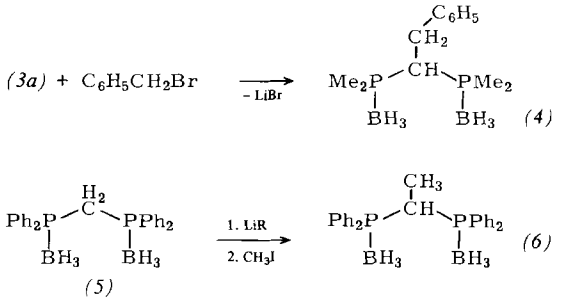
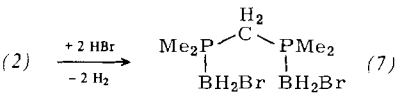


Fig. 1. Structure of the anion in the crystal of the complex salt *(3)*. Bond lengths in Å.

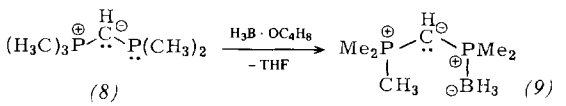
(3) is attacked by alkyl halides at the central C-atom, *e.g.* reaction with benzyl bromide leads to the crystalline product *(4)*. The already well-known[5] phenyl homolog of *(2)* can be alkylated in a similar way *via* the Li-salt [*(5)*→*(6)*].



In contrast to the metalation, the halogenation of *(2)* takes place at the B-atom. Thus, reaction with two equivalents of HBr affords the difunctional haloborane *(7)*, which readily undergoes further reaction.



The phosphino-substituted ylide *(8)*[6] leads to a molecule isosteric with the anion in *(3)* since it reacts with $H_3B \cdot OC_4H_8$ at the P-atom to give the phosphaneborane *(9)*. The formal



replacement of one B-atom in *(3)* by a C-atom determines the neutral character of *(9)*, which now has only four alternating charges.

The composition and structure of all the new compounds have been confirmed by elemental analysis and by IR, NMR, and mass spectrometry.

Experimental

(2): To a solution of *(1)* (2.73 g, 20.8 mmol) in THF (50 ml) is added two equivalents of $H_3B \cdot C_4H_8O$ (46.5 ml of a 0.9 M THF solution). After 30 minutes' stirring at 20 °C, filtration, removal of solvent and crystallization from THF affords 2.85 g (84%) of *(2)*; m.p. 145 °C.

NMR data of the new phosphaneboranes; coupling constants in Hz.

	Solvent Compound	CD_2Cl_2 *(2)*	Dioxane *(3a)*	C_6D_6 *(3)*	CD_2Cl_2 *(4)*	$CDCl_3$ *(6)*	CD_2Cl_2 *(7)*	C_6D_6 *(9)*
^1H	δCH_3	2.09, d	1.20, d	1.40, d [a]	2.14, dd	—	1.65, d	1.15, d; 1.29, d
	$^2J(PH)$	10.8	10.5	10.5	10.5	—	11.2	12.7; 11.0
	δCH_xP_2	2.54, t	−0.29, t	0.03, t	3.13, tt	3.87, qt	2.43, t	0.05, m
	$^2J(PH)$	12.0	3.5	5.3	6.0 [b]	7.0 [c]	13.1	—
	δBH_3	1.20, dq	br	br	br	br	br	1.50, dq
	$^1J(BH)$	99.8	—	—	—	—	—	95.4
	$^2J(PH)$	14.2	—	—	—	—	—	13.5
^{31}P	δP	1.23, m	7, m	−6.20, q	17.1, m	21.6, br	3.9, br	4.1, d; −8.5, d
	$^1J(PB)$	—	—	85.4	—	—	—	70.1
	$^1J(PP)$	—	—	—	—	—	—	51.8
^{13}C	δCH_3P	13.6, d	—	19.5, d [a]	—	—	—	18.4 [d]
	$^1J(PC)$	39	—	41.0	—	—	—	—
	δCHP_2	25.3, t	—	11.0, t	—	—	—	4.4 [d]
	$^1J(PC)$	24.4	—	38	—	—	—	—

[a] Cation: $\delta CH_3 = 2.20$, s; $\delta CH_2 = 2.20$, s; $\delta CH_3 = 46.0$, s; $\delta CH_2 = 57.4$, s.
[b] $^3J(HH) = 6.0$; $\delta CH_2 = 4.03$, dt, $^3J(PH) = 13.2$; $\delta C_6H_5 = 8.20$, s.
[c] $^3J(HH) = 7.0$; $\delta CH_3C = 1.23$, dt, $^3J(PH) = 15.0$; $\delta C_6H_5 = 7.33$—8.33, m.
[d] 4 lines, whose assignment is uncertain.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0783 $ 02.50/0*

(3): a) Metalation of *(2)* (1 g, 5.9 mol) in pentane (10 ml) with one equivalent of *t*-BuLi at 0 °C for 12 h furnishes a product, which, after removal of solvent, has the composition corresponding to *(3a)*; dec. pt. 90 °C, soluble in ether, THF, dioxane.—b) Addition of TMEDA and of pentane to an ethereal solution of *(3a)* leads on cooling to quantitative precipitation of the crystalline complex *(3)*; m.p. 70 °C.

(4): Reaction of *(3a)* with excess benzyl bromide in pentane at 20 °C for 12 h and separation of LiBr affords *(4)* in 74% yield; m.p. 123 °C (from THF).

(6): Metalation of *(5)*[5] with excess CH_3Li in ether at 0 °C, followed by reaction with excess CH_3I and hydrolytic workup, furnishes *(6)* in 95% yield; m.p. 197 °C (dec., from CH_2Cl_2).

(7): HBr gas is passed into a solution of *(2)* (2.61 g, 15.9 mmol) in benzene (100 ml) until evolution of H_2 ceases. Yield 75% after removal of benzene and crystallization from CH_2Cl_2 at −78 °C; m.p. 131 °C.

(9): A solution of *(8)*[6] (0.9 g, 6 mmol) in THF (10 ml) is allowed to react with one equivalent of $H_3B \cdot C_4H_8O$ for 1 h at 20 °C. Removal of solvent, dissolution of the residue in benzene, filtration, removal of benzene, and crystallization from pentane affords *(9)* in 80% yield; m.p. 46 °C.

Received: June 1, 1979 [Z 296b IE]
German version: Angew. Chem. *91*, 848 (1979)

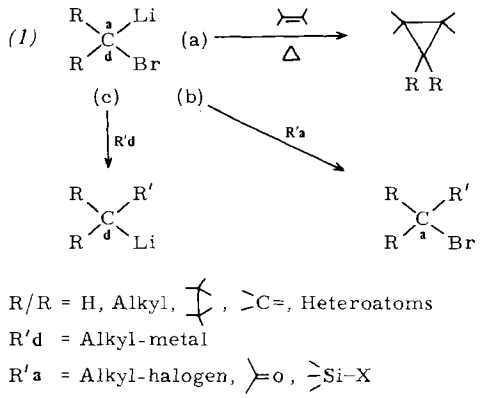
[1] *H. Schmidbaur, G. Müller, U. Schubert, O. Orama,* Angew. Chem. *90*, 126 (1978); Angew. Chem. Int. Ed. Engl. *17*, 126 (1978).
[2] *H. H. Karsch, H. Schmidbaur,* Z. Naturforsch. *B 32*, 762 (1977).
[3] Monoclinic, $P2_1/c$; $a = 9.30(1)$, $b = 20.07(3)$, $c = 16.31(2)$ Å, $\beta = 110.3(1)°$, $V = 2854(8)$ Å^3, $\rho_{calc} = 0.94$ g cm^{-3}. MoK$_\alpha$ radiation, Syntex four circle diffractometer, $R = 0.095$.
[4] *H. Schmidbaur, E. Weiss,* Angew. Chem. *91*, 847 (1979); Angew. Chem. Int. Ed. Engl. *18*, 781 (1979).
[5] *K. C. Nainan, G. E. Ryschkewitsch,* Inorg. Chem. *8*, 2671 (1969).
[6] *H. Schmidbaur, W. Tronich,* Chem. Ber. *101*, 3545 (1968).

Direct ^{13}C-NMR Spectroscopic Observation of Cyclopropylidene Bromolithiocarbenoids

By *Dieter Seebach, Herbert Siegel, Klaus Müllen,* and *Kurt Hiltbrunner*[*]

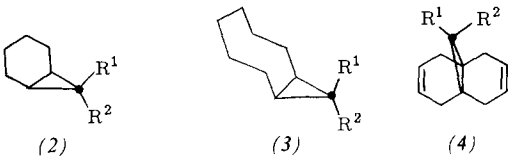
The first detection of a halolithiocarbenoid by *Köbrich* and *Trapp*[1a] was followed by initially extensive mechanistic studies[1b] while the preparative scope of this class of substances, which are stable only at very low temperatures, was not fully appreciated until the 1970's[2]. The geminal position of the positive (metal) and negative (halogen) leaving group, *i.e.* the joint acceptor and donor properties of the C atom of compounds such as *(1)*, leads to the versatile and surprisingly stereoselective[3] reaction behavior shown in Scheme 1. In spite of, or precisely because of, the plethora of chemical results available the nature of the bond in intermediates like *(1)* is still unclear; they have hitherto escaped direct observation in the temperature range[4] in which the reactions mentioned take place.

We have successfully examined by ^{13}C-NMR spectroscopy the carbenoids *(2b)—(4b)* generated in an NMR sample tube in tetrahydrofuran solution at −100 °C from the ^{13}C-labeled (●) dibromides[5] *(2a)—(4a)* and *n*-butyllithium (solution in hexane).



Scheme 1. Acceptor and donor reactivity of bromocarbenoids *(1)*.

For comparison we also determined the ^{13}C-(●)-NMR shifts of the corresponding Br/Br, Br/H, Li/H, and H/H compounds *(2a, c—e)—(4a, c—e)*. All the data are compiled in Table 1. The signals of the lithium derivatives are on average *ca.* 8 ppm wide at −100 °C and are without structure; they become sharper at higher temperature. Chemical proof of the identity of the organometallic species was provided by protonation (in the sample tube and on a preparative scale[7]) to the corresponding CH compounds *(2c, e)—(4c, e)* and their NMR analysis and isolation. In the case of *(3b)*, the rearrangement[8] to the 1,2-cyclononadiene ($\delta C^2 = 208$[9]) which occurs on warming could be monitored: the signal of *(3b)* became increasingly sharp at −80 and −70 °C, and reached normal line width (as for solvent signals) at −60 °C; at the same time it loses intensity in favor of the allene-C^2 signal.



(a): $R^1 = R^2 = Br$
(b): $R^1 = Li$, $R^2 = Br$
(c): $R^1 = H$, $R^2 = Br$
(d): $R^1 = H$, $R^2 = Li$
(e): $R^1 = R^2 = H$

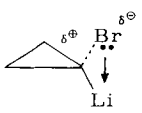
Table 1. ^{13}C-NMR shifts of the 90% ^{13}C-labeled (●) compounds *(2)—(4)* in δ values relative to TMS. Temperature −100 °C, solvent C_4H_8O/C_4D_8O (9:1); Varian XL-100 spectrometer, 25 MHz measuring frequency; FT recording technique up to 2500 pulses.

	Chemical shift or shift difference						
Compound	*(a)*	*(b)*	*(c)*	$\Delta\delta_{bc}$	*(d)*	*(e)*	$\Delta\delta_{de}$
(2)	40.1	87.0	24.5	62.5	10.0	9.6	0.4
(3)	37.9	80.7	24.9	55.8	10.8	10.3	0.5
(4) [6]	53.8	102.0	35.4	66.6	11.8	11.8	0.0

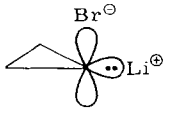
The *pronounced downfield shift* $\Delta\delta_{bc}$ of the Li/Br carbenoid C atoms (●) by values of up to 67 relative to the H/Br compounds is surprising (cf. Table 1): large shift differences are not normally found for the saturated (sp^3) C atom between CH and CLi derivatives[10,11], as is confirmed by the cyclopropanes *(2d, e)—(4d, e)* ($\Delta\delta_{de}$ in Table 1). The observed deshielding is also unexpectedly large in comparison

[*] Prof. Dr. D. Seebach, Dr. H. Siegel, Prof. Dr. K. Müllen [**], K. Hiltbrunner
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)
[**] Present address: Institut für Organische Chemie der Universität, Greinstrasse 4, D-5000 Köln 4 (Germany)

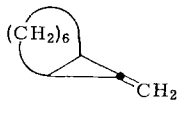
with sulfur- and phosphorus-substituted carbanionoid centers[13] ($\Delta\delta$ *ca.* -10 to $+10$). Replacement of H by Br leads in the Li derivatives *(2)—(4)* ($\Delta\delta_{bd}=70$—90) to a four- to five-fold greater downfield shift than that in the H compounds ($\Delta\delta_{ce}=14$—24). Thus it may be concluded that considerable weakening *(5a)* of the CBr bond[14] or even rehybridization *(5b)* have taken place in the cyclopropylidene carbenoids, cf. (●) shift in *(6)*[12] and *(7)*[15]. Further studies[12] (variation of halogen and metal, measurement of ^{13}C-^{13}C coupling constants, *etc.*) are necessary to obtain more precise information[16].



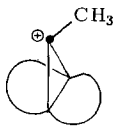
(5a)



(5b)



(6), δ = 142



(7), δ = 210

Received: June 21, 1979 [Z 297a IE]
German version: Angew. Chem. *91*, 844 (1979)

CAS Registry numbers:
(2a), 2415-79-4; *(2b)*, 57640-05-8; *(2c)*, 1121-39-7; *(2d)*, 61184-95-4; *(2e)*, 286-08-8; *(3a)*, 1196-95-8; *(3b)*, 58681-23-5; *(3c)*, 36616-95-2; *(3d)*, 71648-11-8; *(3e)*, 286-60-2; *(4a)*, 4578-96-5; *(4b)*, 71648-12-9; *(4c)*, 4622-37-1; *(4d)*, 71648-13-0; *(4e)*, 27714-83-6

[1] a) *G. Köbrich, H. Trapp*, Z. Naturforsch. *B 18*, 1125 (1963); b) *G. Köbrich*, Angew. Chem. *84*, 557 (1972); Angew. Chem. Int. Ed. Engl. *11*, 473 (1972); *P. J. Stang*, Chem. Rev. *78*, 383 (1978).

[2] *T. Hiyama, H. Saimoto, K. Nishio, M. Shinoda, H. Yamamoto, H. Nozaki*, Tetrahedron Lett. *1979*, 2043; *R. Dammann, D. Seebach*, Chem. Ber. *112*, 2167 (1979); *D. Masure, C. Chiut, R. Sauvêtre, J. F. Normant*, Synthesis *1978*, 458; *D. Seyferth, R. L. Lambert, M. Massol*, J. Organomet. Chem. *88*, 255 (1975) and earlier work cited therein.

[3] For (a) retention of olefin configuration; for (c) retention at the carbenoid C atom; for (b) stereoselectivity of hitherto unelucidated configuration [2].

[4] Matrix IR measurements on $M^+CCl_3^-$ at 15 K: *D. A. Hatzenbühler, L. Andrews, F. A. Carey*, J. Am. Chem. Soc. *97*, 187 (1975).

[5] *(2a)—(4a)* are obtained from $^{13}CHBr_3$ and the olefins by *Doering*'s method: *H. Siegel, D. Seebach*, J. Lab. Compd. *1979*, in press.

[6] We thank Prof. *E. Vogel*, Köln, for a sample of bicyclo[4.4.0]deca-1(6)3,8-triene, the precursor of *(4a)*.

[7] *M. Braun, R. Dammann, D. Seebach*, Chem. Ber. *108*, 2368 (1975).

[8] *L. Skattebøl*, Acta Chem. Scand. *17*, 1683 (1963).

[9] *C. Charrier, D. E. Dorman, J. D. Roberts*, J. Org. Chem. *38*, 2644 (1973).

[10] *J. P. C. van Dongen, H. W. D. van Dijkman, M. J. A. de Bie*, Rec. Trav. Chim. Pays-Bas *93*, 29 (1974).

[11] Ethenyl [10] (sp^2) and ethynyl [12] (sp) C atoms undergo a downfield shift on replacement of H by Li, probably due to polarization of the π system: *J. E. Williams, Jr., A. Streitwieser, Jr.*, J. Am. Chem. Soc. *97*, 2634 (1975). The $\Delta\delta_{de}$ values are therefore more compatible with the sp^3 model of cyclopropane (*Coulson-Moffit*, banana bonds) than with *Walsh*'s sp^2 model.

[12] *H. Siegel, K. Hiltbrunner, D. Seebach*, unpublished results.

[13] *G. Chassaing, A. Marquet*, Tetrahedron *34*, 1399 (1978); *T. Bottin-Strzalko, J. Seyden-Penne, M. J. Pouet, M. P. Simonnin*, J. Org. Chem. *43*, 4346 (1978).

[14] Formulations of this kind are already found in *Köbrich*'s publications [1b] and were deduced from purely chemical evidence.

[15] *G. A. Olah, G. Liang, D. B. Ledlie, M. G. Costopoulos*, J. Am. Chem. Soc. *99*, 4196 (1977).

[16] *(5b)* could be regarded as the LiBr complex of singlet cyclopropylidene whose carbene C is calculated to have a charge of -0.21 [*R. Gleiter, R. Hoffmann*, J. Am. Chem. Soc. *90*, 5457 (1968)]. The well-documented destabilization on going from pyramidal to planar-trigonal arrangement of atoms in the three-membered rings appears at first sight to disfavor formulation *(5b)* based on the geometry [*P. W. Dillan, G. R. Underwood*, J. Am. Chem. Soc. 99, 2435 (1977); *D. J. Pasto, M. Haley, D. M. Chipman, ibid. 100*, 5272 (1978)] of cyclopropylidene.

^{13}C-NMR Spectra of Tribromomethyllithium and 1,1-Dibromoethyllithium

By *Herbert Siegel, Kurt Hiltbrunner*, and *Dieter Seebach*[*]

After addition of *n*-butyllithium to a solution of ^{13}C-labeled tetrabromomethane[1] [*(1a)*, $\delta=-29.8$] in tetrahydrofuran, *i.e.* after bromine/lithium exchange to give *(1b)*, at $-100\,^\circ C$ in an NMR sample tube[2], the ^{13}C-NMR spectrum shown in Figure 1A is observed. Almost the entire intensity of the label appears in three stable (at least for several hours) low-field signals: a quartet (q_1, $J=43$ Hz) at $\delta=101.5$, a sharp singlet (s) at $\delta=144.1$, and a second quartet (q_2, $J=40$ Hz) at $\delta=152.2$. Addition of methanol immediately quenches all three resonances. On warming to $-80\,^\circ C$, q_1 disappears in favor of q_2, which concomitantly becomes less structured: at $-70\,^\circ C$ only s is still present; its intensity decreases on further warming but reaches zero only at $-40\,^\circ C$[3]. Addition of methanol at $-70\,^\circ C$ to the solution displaying only the singlet does not lead to tribromomethane [*(1c)*, $\delta_{^{13}C}=9.7$]; the hydrolysis product characteristic[4] of tribromomethyllithium *(1b)* is formed only so long as the two other signals are visible.

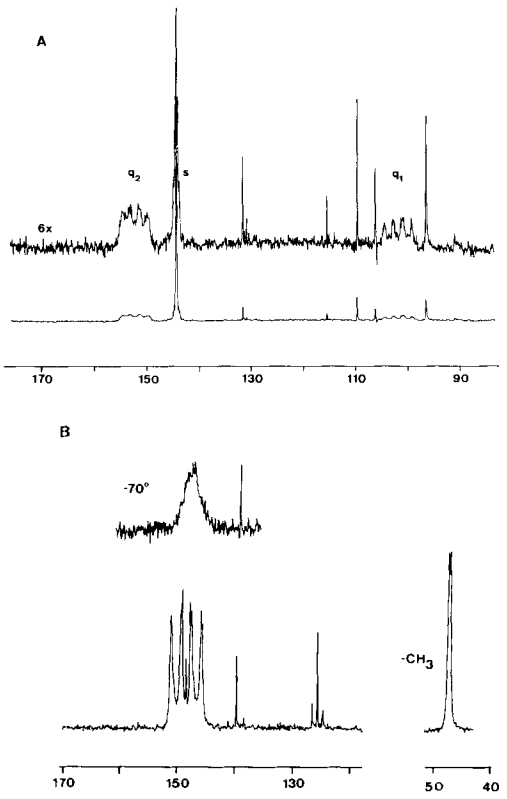


Fig. 1. ^{13}C-NMR spectra (H-decoupled) of solutions of *(1b)*, A, and *(2b)*, B, in THF/perdeuterio-THF (9:1) at $-100\,^\circ C$. As in the text, the shifts are given as δ values relative to TMS. Varian XL 100 spectrometer, FT mode.

Figure 1B shows the *sole* low-field signal obtained in the same way for 1,1,1-tribromoethane [*(2a)*, 90% $^{13}CBr_3$, 20% $^{13}CH_3$; produced from *(1b)* and labeled iodomethane]: it is a 45 Hz quartet having 8 Hz of fine structure ($J_{^{13}C^{13}C}$). As in the case of *(1b)*, warming to $-80\,^\circ C$ leads to a loss of structure; however, no singlet occurs even at high temperatures.

[*] Prof. Dr. D. Seebach, Dr. H. Siegel, K. Hiltbrunner
Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

The signal can still be observed—with reduced intensity—at $-40\,^{\circ}C$. On renewed cooling to $-100\,^{\circ}C$ it reassumes a quartet structure. *(2b)* reacts with methanol to give 1,1-dibromoethane *(2c)*.

Br_3CR CH_3-CBr_2R

(1) *(2)*

(a): R = Br, *(b)*: R = Li, *(c)*: R = H

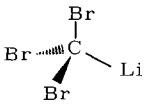
Table 1. Chemical shifts and coupling constants of *(2a)*—*(2c)*.

	δC^1	$J_{C,C}$ [Hz]	δC^2	$J_{C,H}$ [Hz]
(2a)	31.5	38	49.4	132
(2b)	147.0	8	45.4	127
(2c)	40.1	37	31.8	180 (C^1)
				131 (C^2)

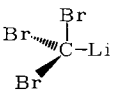
As with the cyclopropylidene derivatives[2], the ^{13}C-NMR signals of the bromolithiocarbenoids *(1b)* and *(2b)* presently being studied appear at *unexpectedly low field:* replacement of H by Li in tribromomethane and of Br by Li in tetrabromomethane causes a downfield shift (q_2) of $\Delta\delta = 142$ and 182 (Table 1 lists the data of the ethanes recorded in THF).

Three species are present in the solution of *(1b)*. As with *(2b)*, two of them show a 1:1:1:1 quartet coupling with one ^7Li atom (nuclear spin $^3/_2$). This is the first proof of non-ionized *organolithium compounds* which are *monomeric* on the NMR time scale. The coupling constants $J_{^7Li,^{13}C}$ of 40—45 Hz are *three to four times greater* than for RLi aggregates[5]; on the other hand, the C-C coupling constant falls from a value lying in the typical sp^3-sp^3 range (30—40 Hz) to about one fifth of that value (smallest $J_{^{13}C,^{13}C}$ ever measured in an ethane) on going from the haloalkane *(2a)* to the carbenoid *(2b)*[6].

Shifts and coupling constants indicate unusual bonding. It follows from the loss of quartet structure on warming (cf. also[2]) that the C–Li bond participates in faster and faster dynamic processes on the NMR time scale.



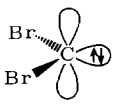
(3a)



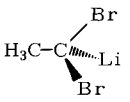
(3b)

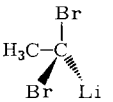


(3c)



(3d)





(4b)

The quartet signal q_1 of *(1b)* could be assigned to a normal tetrahedral structure *(3a)* with strongly polarized Br–C bonds; the greater downfield shift of the thermally more stable q_2 species could be explained in terms of structures such as *(3b)* or *(3c)*, in which stepwise[7] release of LiBr from the carbenoid C atom has led to a distortion towards sp^2 geometry, *(3b)*, or to a linear arrangement[8], *(3c)*, in which a bromide ion has migrated from the carbon to the lithium. *(3b)* and *(3c)* may be regarded as LiBr complexes of dibromocarbene *(3d)*, to which we assign the no longer Li-coupled s signal[9]. A much smaller shift is expected for free tribromomethyl anion or an O ylide[9a,10]. The loss of the s species by reaction between -70 and $-40\,^{\circ}C$ is compatible with the observation[4] of an exothermal reaction[11] in this temperature range.—Assuming the "normal" rules to apply, then the small C-C coupling constant of the ethane derivative *(2b)* indicates that the tetrahedral geometry *(4a)* is so distorted at the carbenoid center, see *(4b)*, that the C–C bond assumes considerably enhanced p character.

Received: August 2, 1979 [Z 297b IE]
German version: Angew. Chem. *91*, 845 (1979)

CAS Registry numbers:
(1a), 558-13-4; *(1b)*, 16644-71-6; *(1c)*, 75-25-2; *(2a)*, 2311-14-0; *(2b)*, 71648-14-1; *(2c)*, 557-91-5

[1] *H. Siegel, D. Seebach*, J. Lab. Compd. *1979*, in press.
[2] *D. Seebach, H. Siegel, K. Müllen, K. Hiltbrunner*, Angew. Chem. *91*, 844 (1979); Angew. Chem. Int. Ed. Engl. *18*, 784 (1979).
[3] The relative stability is therefore $q_1 < q_2 < s$ species; the fact that all three arise at a temperature ($-100\,^{\circ}C$) at which they do not interconvert is attributable to local brief warming on addition of butyllithium. Only q_1 and q_2 are observed if tribromomethyllithium is generated at $-110\,^{\circ}C$.
[4] *R. H. Fischer, G. Köbrich*, Chem. Ber. *101*, 3230 (1968).
[5] *L. D. McKeever, R. Waack, M. A. Doran, E. B. Baker*, J. Am. Chem. Soc. *90*, 3244 (1968); *S. Bywater, P. Lachance, D. J. Worsfold*, J. Phys. Chem. *79*, 2148 (1975); *J. Blenkers, H. K. Hofstee, J. Boersma, G. J. M. van der Kerk*, J. Organomet. Chem. *168*, 251 (1979).
[6] The changes in C-H coupling constant are much smaller in Li compounds: *J. P. C. van Dongen, H. W. D. van Dijkman, M. J. A. de Bie*, Rec. Trav. Chim. Pays-Bas *93*, 29 (1974); *G. Chassaing, A. Marquet*, Tetrahedron *34*, 1399 (1978).—In cyclopropanes the C-C coupling constant is *ca.* 15 Hz, and a coupling constant of 5 Hz was found for a bicyclobutane derivative: *M. Pomerantz, R. Fink, G. A. Gray*, J. Am. Chem. Soc. *98*, 291 (1976).—*i*-Propyl- and *t*-butyllithium have ^{13}C-^{13}C coupling constants of 22.9 and 28.4 Hz: *T. Spoormaker, M. J. A. de Bie*, Rec. Trav. Chim. Pays-Bas *98*, 380 (1979).
[7] *O. M. Nefedov* and *A. I. Dyachenko* deduce synchronous release of lithium chloride to be operative on decomposition of trichloromethyllithium [Angew. Chem. *84*, 527 (1972); Angew. Chem. Int. Ed. Engl. *11*, 507 (1972)].
[8] *D. A. Hatzenbühler, L. Andrews, F. A. Carey*, J. Am. Chem. Soc. *97*, 187 (1975).
[9] a) *(3c)* can also be regarded as dibromo(lithio)carbenium ion. Since the observed species are present in THF, structures such as $(CH_2)_4\overset{\oplus}{O}$ CBr_2Li [corresponding to *(3c)*] or $(CH_2)_4\overset{\oplus}{O}$ $\overset{\ominus}{C}Br_2$ and $[(CH_2)_4O]_2CBr_2$ [corresponding to *(3d)*] must also be considered. The fact that the q_2 species gives methanol with $CHBr_3$ is more compatible with *(3b)* than with *(3c)*.—b) Carbene ligands in transition metal complexes give δ values of 260—360: [*C. G. Kreiter, V. Formáček*, Angew. Chem. *84*, 155 (1972): Angew. Chem. Int. Ed. Engl. *11*, 142 (1972)]. The modest shift difference between s and q_2 suggests the q_2 species to closely resemble a carbene.—c) The presence of dibromocarbene is also supported by the isolation of 7,7-dibromonorcarane on decomposition of tribromomethyllithium in the presence of cyclohexene by *Fischer and Köbrich* [4].
[10] *T. Botton-Strzalko, J. Seyden-Penne, M. J. Pouet, M. P. Simonnin*, J. Org. Chem. *43*, 4346 (1978); *T. A. Albright, E. E. Schweizer, ibid. 41*, 1168 (1976).
[11] Besides insoluble carbon-like solids, we found the reaction products to contain the dimer of *(3d)*, tetrabromoethylene.

Detonation of Benzyl(triethyl)ammonium Permanganate

By *Horst Jäger, Johann Lütolf*, and *Max W. Meyer*[*]

When preparing benzyl(triethyl)ammonium permanganate *(1)* according to a recently published precedure[1] we witnessed a violent explosion on drying the crystalline compound at $80\,^{\circ}C/1$ torr.

The data given by *Schäfer et al.*[1] on the oxidation of hydrocarbons with *(1)* could be confirmed experimentally, but the data regarding the stability and shock resistance of this reagent are inconsistent with our observations.

[*] Dr. H. H. Jäger, J. Lütolf, Dr. M. W. Meyer
Ciba-Geigy AG, CH-4002 Basel (Switzerland)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1010-0786 $ 02.50/0

On warming at a rate of 4 °C/min in a sealed testing vessel (Mettler thermoanalyzer TA 2000) benzyl(triethyl)ammonium permanganate explodes violently at *ca.* 120 °C with liberation of about 350 kJ/mol heat. The compound also decomposes violently at lower temperatures, but only after expiration of a certain induction time dependent upon the temperature (autocatalytic decomposition)—*e.g.* 2g-amounts of *(1)* in an open vessel ignite spontaneously after 14 h at 60 °C, or after only 28 min at 90 °C. At 50 °C no measurable exothermic reaction could be observed within 92 h.

Benzyl(ethyl)ammonium permanganate is sensitive to impact (class 3; 49 Nm).

It is recommended that benzyl(triethyl)ammonium permanganate should not be kept in storage and that room temperature should not be exceeded on drying it *in vacuo*[2].

Received: June 12, 1979 [Z 298a IE]
German version: Angew. Chem. *91*, 852 (1979)

[1] *H.-J. Schmidt, H. J. Schäfer*, Angew. Chem. *91*, 77 (1979); Angew. Chem. Int. Ed. Engl. *18*, 68 (1979).
[2] Cf. also *H.-J. Schmidt, H. J. Schäfer*, Angew. Chem. *91*, 852 (1979); Angew. Chem. Int. Ed. Engl. *18*, 787 (1979).

Stability of Benzyl(triethyl)ammonium Permanganate

By *H.-Jürgen Schmidt* and *Hans J. Schäfer*[*]

We recently reported on the oxidation of hydrocarbons and ethers with benzyl(triethyl)ammonium permanganate *(1)*[1]. Crystalline *(1)* is less stable than we assumed on the basis of our previous observations—insensitive to hammer blows, stable on heating for 5 minutes to 100 °C[1]. We confirm the findings of *Jäger et al.*[2] regarding the thermal instability and sensitivity to shock and support their recommendations[2] for the handling of this reagent.

Benzyl(triethyl)ammonium permanganate decomposes violently after 7 min at 100 °C, and explodes after 25 min at 90 °C or 90 min at 80 °C. On thermal decomposition in a steel cylinder with a jet diameter of 2 mm (using the procedure for testing thermal sensitivity by heating sample in steel cylinders, as developed by the Materials Research Establishment of the Federal Republic of Germany)[3] the steel casing is shattered. The violet salt *(1)* is sensitive to heavy blows (30 Nm)[3].

300 g of benzyl(triethyl)ammonium permanganate, prepared from benzyl(triethyl)ammonium chloride[4] (m.p. 198—199 °C, from ethyl acetate/methanol) and commercially available potassium permanganate, has been dried over Sicapent (Merck) by us for 1 week at 40 °C.

Received: July 16, 1979 [Z 298b IE]
German version: Angew. Chem. *91*, 852 (1979)

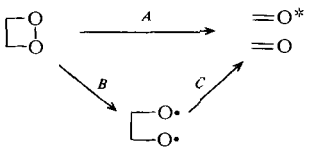
[*] Prof. Dr. H. J. Schäfer. Dipl.-Chem. H.-J. Schmidt
Organisch-chemisches Institut der Universität
Orleans-Ring 23, D-4400 Münster (Germany)

[1] *H.-J. Schmidt, H. J. Schäfer*, Angew. Chem. *91*, 77, 78 (1979); Angew. Chem. Int. Ed. Engl. *18*, 68, 69 (1979).
[2] *H. H. Jäger, J. Lütolf, M. W. Meyer*, Angew. Chem. *91*, 852 (1979); Angew. Chem. Int. Ed. Engl. *18*, 786 (1979).
[3] We thank Dr. *M. Klünsch*, Dynamit-Nobel AG, Leverkusen-Schlebusch, for carrying out the measurements.
[4] *S. D. Ross, M. Finkelstein*, J. Am. Chem. Soc. *79*, 6547 (1957).

Preparation and Chemiluminescence of *cis*-1,2-Cyclobutylene Dinitrite[**]

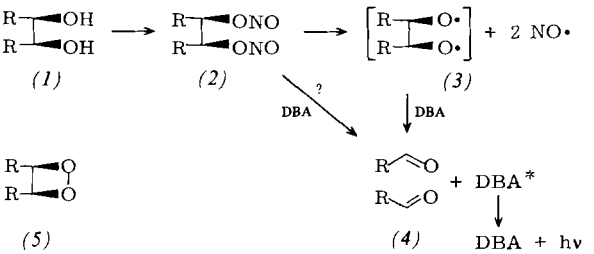
By *Nobutaka Suzuki*[*]

Two alternative mechanisms have been proposed for the chemiluminescence of simple 1,2-dioxetanes: the concerted (Route A) and the stepwise (radical) mechanism (Route B, C)[1].



Since organic nitrites react *via* radical intermediates[2] they should permit investigation of the chemiluminescence mechanism of 1,2-dioxetanes with 1,2-dinitrites. We have prepared the dinitrite *(2a)* (in spite of its extreme instability to hydrolysis) and the dinitrites *(2b)* and *(2c)* and tested their chemiluminescence in the presence of sensitizers. A solution of *(2)* (1.7×10^{-2} M) and 9,10-dibromo- or 9,10-diphenylanthracene (DBA or DPA: 1×10^{-4} to 2×10^{-2} M) in 2 ml DMSO (dried over CaH_2) under argon showed a weak light emission when heated to 140 °C; the maximum quantum yield of chemiluminescence was *ca.* 10^{-6} einstein/mol[2]. The identity of the aldehyde *(4)* formed on heating was confirmed by GLC, IR and ^{1}H-NMR spectroscopy on authentic samples.

The emission of light, though small, during thermal decomposition of *(2)* to *(4)* is an interesting phenomenon. Thus, *(2)* directly yields an electronically excited aldehyde *(4*)*, or it initially forms a diradical *(3)*, which then transforms into the electronically excited aldehyde *(4*)*[3]. These results suggest that most of the light emission from the 1,2-dioxetane *(5)* corresponding to the dinitrite *(2)* may be produced by the concerted mechanism, and not by the diradical mechanism.



(a), –R–R– = $-(CH_2)_2-$; *(b)*, –R–R– = $-(CH_2)_4-$; *(c)*, R = CH_3

Experimental

The dinitrites *(2)* are prepared under argon as follows: A solution of *(1)* (10.2 mmol) in saturated aqueous $NaNO_2$ (10 ml) is cooled in an ice/salt bath (−7 to −10 °C). Concentrated HCl (1.6 ml, 19.4 mmol; ρ = 1.187) is then added by means of an injector with a Teflon needle at such a rate that the temperature of the reaction mixture does not exceed

[*] Dr. N. Suzuki, Chemistry Department, Faculty of Engineering
Mie University, Tsu 514 (Japan)

[**] This work was performed at the Department of Chemistry of Johns Hopkins University, Baltimore, Maryland 21218 (USA) and supported by the U. S. Public Health Service (Grant GM 19488). I wish to thank Prof. *E. H. White* for helpful discussions and the Naito Foundation for providing a travel grant.

$-5\,^{\circ}C$. After 5 minutes' stirring at $-5\,^{\circ}C$, the solution is extracted with ether containing $NaHCO_3$, the extract washed with saturated $NaHCO_3$, and dried over Na_2SO_4 (containing $NaHCO_3$) at $0\,^{\circ}C$. After removal of solvent from the extracts (aspirator with a cold trap (CO_2/ether)) the residue is distilled *in vacuo* into a cold trap (CO_2/ether). *(2a)—(2c)* are yellow liquids, whose absorption spectra are almost identical; yield 35% (based on conc. HCl), 93% and 88%, respectively; b.p. $30\,^{\circ}C/1$ torr[4], $40\,^{\circ}C/2$ torr ($46\,^{\circ}C/4$ torr[5]), and $30\,^{\circ}C/2$ torr ($42\,^{\circ}C/50$ torr[5]), respectively.

Received: June 5, 1979 [Z 300 IE]
German version: Angew. Chem. *91*, 852 (1979)

CAS-Registry numbers:
(1a), 35358-33-9; *(1b)*, 1792-81-0; *(1c)*, 5341-95-7; *(2a)*, 71607-19-7; *(2b)*, 71607-20-0; *(2c)*, 71607-21-1

[1] a) Reviews: *W. Adam*, Adv. Heterocycl. Chem. *21*, 437 (1977); *K. A. Horn, J.-y. Koo, S. P. Schmidt, G. B. Schuster*, Mol. Photochem. *9*, 1 (1978/1979); b) *W. H. Richardson, F. C. Montgomery, P. Slusser, M. B. Yelvington*, J. Am. Chem. Soc. *97*, 2819 (1975); c) for 1,2-dioxetane containing N atom(s), the CIEEL (Chemically Initiated Electron Exchange Luminescence) mechanism was proposed: *F. McCapra*, J. Chem. Soc. Chem. Commun. *1977*, 946; *J.-y. Koo, G. B. Schuster*, J. Am. Chem. Soc. *99*, 6107 (1977).

[2] Compared with the chemiluminescence of luminol in aqueous solution: *J. Lee, H. H. Seliger*, Photochem. Photobiol. *4*, 1015 (1965); *15*, 227 (1972); *J. Lee, A. S. Wesley, J. F. Ferguson, H. H. Seliger* in *F. H. Johnson, Y. Haneda:* Bioluminescence in Progress. Princeton University Press, Princeton 1966, p. 35.

[3] Cf. *W. Adam, I. Erden*, Angew. Chem. *90*, 223 (1978); Angew. Chem. Int. Ed. Engl. *17*, 211 (1978).

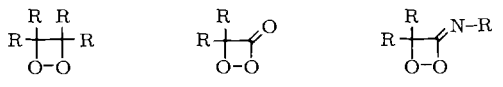
[4] In spite of its extreme sensitivity to hydrolysis *(2a)* has been characterized: λ_{max} (CCl_4) = 390 nm (sh) ($\log\varepsilon = 1.95$), 375 (2.20), 360 (2.24), 340 (2.18), 335 (2.08); $\tilde{\nu}_{max}$ (neat) = 2950 w, 1670 s, 1380 vs, 830 cm^{-1}; ^{1}H-NMR (CCl_4): $\delta = 2.44$ (m, 4H, CH_2), 6.03 (m, 2H, CHO).

[5] *L. P. Kuhn, L. DeAngelis*, J. Am. Chem. Soc. *76*, 328 (1954); *L. P. Kuhn, R. Wright, L. DeAngelis, ibid. 78*, 2719 (1956).

A 3-Imino-1,2-dioxetane *via* Singlet Oxygenation of a Ketenimine[**]

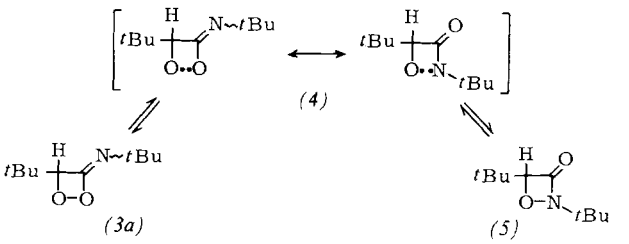
By *Waldemar Adam, Ottorino De Lucchi, Helmut Quast, Rautgundis Recktenwald*, and *Faris Yany*[*]

The synthesis of stable 1,2-dioxetanes *(1)* has been abundantly documented and extensively utilized for the mechanistic exploration of chemi-energized electronic excitation[1]. The considerably less stable α-peroxylactones *(2)*, which are



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

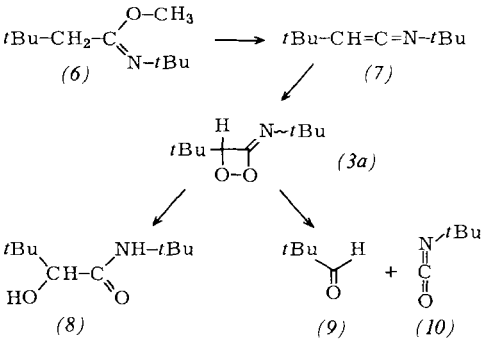
the postulated reaction intermediates in luciferin bioluminescence, produce electronic excitation through the novel electron exchange mechanism (CIEEL, *i.e.* chemically initiated electron exchange luminescence)[2]. They have also been isolated and characterized. We have now synthesized and characterized 4-*tert*-butyl-3-*tert*-butylimino-1,2-dioxetane *(3a)* as the first compound of type *(3)*. Besides assessing its thermal stability and chemi-energization efficiency, we thought that *(3a)* might isomerize to *(5)*; this reaction would proceed *via* the elusive 1,4-dioxyl radical *(4)*[3].



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

Heating of the *N*-*tert*-butyl imidate *(6)* together with an excess of methyllithium in ether or *tert*-butyllithium in hexane effected demethanolation, affording high yields of the ketenimine *(7)*[4]. Tetraphenylporphyrin-sensitized photo-oxygenation of *(7)* (0.02 M solution in $CFCl_3$, CH_2Cl_2, or xylene at $-78\,^{\circ}C$, 150-W sodium street lamp, continuous purging with a slow stream of dry oxygen) led to complete consumption of *(7)* within 50 min.

Subambient ^{1}H-NMR monitoring confirmed the presence of a thermally labile product, which exhibited proton resonances at $\delta = 1.22$ (9H, s), 1.60 (9H, s), and 5.59 (1H, s), consistent with structure *(3a)*. On warm-up to *ca.* $30\,^{\circ}C$, the sole products were 2,2-dimethylpropanal *(9)* and *tert*-butyl isocyanate *(10)*. So far we have no evidence for formation of the oxazetidinone *(5)*[5]. On flash distillation of a CH_2Cl_2 solution, the iminodioxetane *(3a)* codistilled with the solvent, showing that a monomeric material was on hand; however, extensive decomposition into aldehyde and isocyanate occurred. Isolation of *(3a)* in pure form was not attempted in view of its inherent explosive nature. Iodometric titration confirms that *(3a)* is formed in *ca.* 95% yield. Reaction with NaI in acetone/acetic acid gave the expected *N*-*tert*-butyl 2-hydroxy-3,3-dimethylbutyramide *(8)*[6].



(6) *(7)* *(3a)* *(8)* *(9)* *(10)*

These experimental facts clearly establish the proposed 3-imino-1,2-dioxetane structure *(3a)* for the singlet oxygenation product of the ketenimine *(7)*. Furthermore, although no direct chemiluminescence could be observed in the decomposition of *(3a)*, in the presence of fluorescers such as rubrene, pyrene, 9,10-diphenyl- or 9,10-dibromoanthracene, appreciably enhanced chemiluminescence was detected. In view of the thermal instability of *(3a)* (half-lives are of the order of a few seconds at $0\,^{\circ}C$), it was difficult to quantitatively estimate the singlet and triplet excitation yields[8]. However, our qualitative observations reveal that the excitation yields are much lower (*ca.* 1000-fold) than those ob-

[*] Prof. Dr. W. Adam (NIH Career Awardee, 1975—1980), Dr. O. De Lucchi, Dr. F. Yany
Department of Chemistry, University of Puerto Rico
Rio Piedras, Puerto Rico 00931 (USA)
Prof. Dr. H. Quast, Dipl.-Chem. R. Recktenwald
Institut für Organische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

[**] Acknowledgments are made to the Donors of the Petroleum Research Fund (11022-AC1), administered by the American Chemical Society, the National Science Foundation (CHE-78-12621), the National Institutes of Health (GM-00141-05 and RR-8102-07), and the Deutsche Forschungsgemeinschaft (Qu 25/6) for financial support.

served for the α-peroxylactones *(2)* and that the electron exchange mechanism does not operate[2].

On the basis of our preliminary results, we conclude that the 3-imino-1,2-dioxetanes *(3)* are thermally much less stable than the α-peroxylactones and are inefficient sources for chemi-energizing electronically excited products. In this context, it is of interest that the 3-imino-1,2-dioxetanes *(3)* derived from *N*-phenyl- and *N*-*p*-tolyl-diphenylketenimines and *N*-*p*-tolyl-*tert*-butylketenimine *via* singlet oxygenation were too unstable for ^{1}H-NMR observation even at −60 °C; only the carbonyl compound and isocyanate produced by fragmentation could be detected.

Received: August 17, 1979 [Z 301 IE]
German version: Angew. Chem. *91*, 855 (1979)

CAS Registry numbers:
(3a), 71607-22-2; *(5)*, 71607-23-3; *(6)*, 71607-24-4; *(7)*, 71607-25-5; *(8)*, 5510-45-2; *(9)*, 630-19-3; *(10)*, 1609-86-5

[1] a) *W. Adam*, Adv. Heterocycl. Chem. *21*, 437 (1977); b) *K. A. Horn, J.-Y. Koo, S. P. Schmidt, G. B. Schuster*, Mol. Photochem. *9*, 1 (1978/1979).

[2] a) *S. P. Schmidt, G. B. Schuster*, J. Am. Chem. Soc. *100*, 1966 (1978); b) *W. Adam, O. Cueto, F. Yany*, J. Am. Chem. Soc. *100*, 2587 (1978).

[3] *W. H. Richardson, J. H. Burns, M. E. Price, R. Crawford, M. Foster, P. Slusser, J. H. Anderegg*, J. Am. Chem. Soc. *100*, 7596 (1978).

[4] *(7)*, b.p. 40—45 °C/20 torr; ^{1}H-NMR (CCl_4), δ = 1.07 (*t*-Bu), 1.20 (*N*-*t*-Bu), 3.52 (C H); IR (CCl_4) $\tilde{\nu}$ = 2960—2860 (aliphatic C H), 2010 (C= C=N), 1395 and 1370 cm^{-1} (*t*-Bu). Also direct dehydration of *N*-*tert*-butyl 3,3-dimethylbutyramide by successive treatment with *n*-butyllithium, benzenesulfonyl chloride, and again *n*-butyllithium affords the ketenimine in moderate yields. *(7)* also results from the reaction between 1,3-di-*tert*-butylaziridinone and triphenylphosphane: *G. R. Krow*, Angew. Chem. *83*, 455 (1971); Angew. Chem. Int. Ed. Engl. *10*, 435 (1971).

[5] We would expect a carbonyl band at *ca.* 1780—1800 cm^{-1} for *(5)*; see *G. Kresze, A. Trede*, Tetrahedron *19*, 133 (1963).

[6] *(8)*, 52% yield; m.p. 91—92 °C (92 °C [7]). The ^{1}H-NMR and IR spectra were identical with those of an authentic sample.

[7] *D. Giraud-Clénet, J. Anatol*, C. R. Acad. Sci. Ser. C *262*, 224 (1966).

[8] *N. J. Turro, P. Lechtken, G. B. Schuster, J. Orell, H.-C. Steinmetzer, W. Adam*, J. Am. Chem. Soc. *96*, 1627 (1974).

1,4-Di-*tert*-butylsilabenzene: Generation and Trapping Reactions

By *Gottfried Märkl* and *Peter Hofmeister*[*]

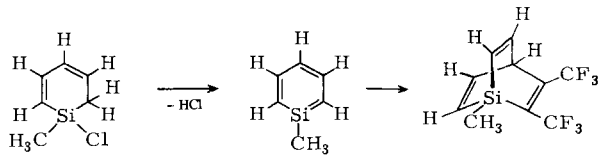
Now that the heteroatom homologues of pyridine have proved to be stable aromatic compounds, increasing attention is being turned to the question whether the higher homologues of benzene, *i. e.* silabenzene and germabenzene, are capable of existence.

Theoretical calculations on silabenzene have been performed by *Dewar et al.* (MINDO/3)[1], by *Schlegel et al.* (*ab initio*, GAUSSIAN 70 and FORCE program, STO 3G basis set)[2], and by *Blustin* (*ab initio*, Frost's Floating Spherical Gaussian Orbital (FSGO) Model)[3]. These studies give values of bond lengths and angles showing some degree of divergence; calculations by *Dewar et al.* and *Schlegel et al.* show silabenzene to have a singlet ground state and an aromatic stabilization energy of an order comparable with that of benzene.

According to the *ab initio* calculations, silabenzene exhibits strong polarization with a low electron density on silicon and an enhanced electron density in positions 2, 4, and 6—as expected from the electronegativities $\chi_C = 2.50$ (2.55) and $\chi_{Si} = 1.74$ (1.90).

The problems encountered in the silabenzene system are therefore due mainly to its pronounced electrophilic reactivity, arising from the δ^+ character of silicon. The silabenzene ring must be synthesized under conditions avoiding the presence and/or formation of nucleophiles capable of addition to the Si=C bond.

Barton et al.[4] have presented evidence supporting the formation of 1-methyl-1-silabenzene *(2)*, on elimination of HCl from *(1)* with the sterically hindered base $LiN(Si(CH_3)_3)_2$, by trapping of *(2)* with hexafluoro-2-butyne to give the 1-silabarrelene derivative *(3)*.

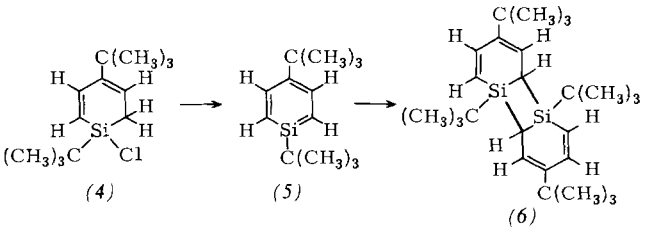


(1) *(2)* *(3)*

Simultaneous formation of 1-[*N*,*N*-bis(trimethylsilyl)amino]-1-methyl-1-sila-2,4-cyclohexadiene suggests that the elimination is accompanied by substitution at the silicon atom.

Starting from 1,1-di-*n*-butyl-4-*tert*-butyl-4-methoxy-1,4-dihydrostannin, we have prepared 1,4-di-*tert*-butyl-1-chloro-1-sila-2,4-cyclohexadiene *(4)* by a method resembling one which we recently described[5].

The sole product of reaction, apart from LiCl, of *(4)* with lithium diisopropylamide in *n*-pentane at 0 °C is a colorless crystalline compound, m.p. 204 °C, shown by analytical and spectroscopic data (Tables 1 and 2) to be the dimeric silabenzene *(6)*, having a 1,3-disilacyclobutane structure, which was predicted by *Dewar et al.*[1].



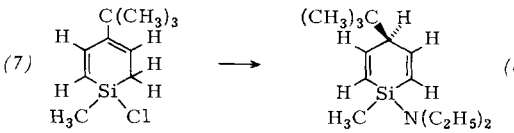
(4) *(5)* *(6)*

Is 1,4-di-*tert*-butylsilabenzene *(5)* an intermediate of dimer formation?

No diisopropylamine substitution product is formed on hydrogen chloride elimination; in contrast to the case with *(1)*, the steric effect of the *tert*-butyl group attached to silicon prevents both substitution of *(4)* by $LiN(iPr)_2$ and the conceivable addition of $LiN(iPr)_2$ or $HN(iPr)_2$ to the Si=C double bond of *(5)*.

This result rules out formation of *(6)* by a pathway other than dimerization of intermediate silabenzene *(5)*. The Si—C double bond of *(5)* thus behaves in an entirely analogous manner to silaethenes, which likewise dimerize to 1,3-disilacyclobutanes[6].

Support for elimination of HCl from *(4)* to give *(5)* is also provided by the reaction of 4-*tert*-butyl-1-chloro-1-methylsila-2,4-cyclohexadiene *(7)* with lithium diethylamide which, in contrast to *(4)*, gives almost exclusively the substitution product, which then isomerizes to the 2,5-diene *(8)*.



(7) *(8)*

Formation of *(5)* from *(4)* is proved just as unequivocally by the reaction of *(4)* with $LiN(iPr)_2$ in *n*-pentane in the presence of 1,3-dienes (1,3-butadiene, isoprene, 2,3-dimethyl-1,3-

[*] Prof. Dr. G. Märkl, P. Hofmeister
Institut für Chemie, Fakultät für Chemie und Pharmazie der Universität Universitätsstrasse 31, D-8400 Regensburg (Germany)

Table 1. Some physical data of *(4)*, *(6)*, and *(9)*.

Cpd.	Yield [%]	B.p. [°C] 10^{-2} torr [a]	Si CMe_3	C CMe_3	^{1}H-NMR, δ-values, *J* [Hz] [b] H^2	H^3 ($J(H^2,H^3)$)	H^5 ($J(H^3,H^5)$)	H^6 ($J(H^5,H^6)$).	—$CH_2CR{=}CR'CH_2$—
(4)	—	75—90	0.98 (s)	1.03 (s)	5.99 (d)	7.11 (dd) (15.0)	5.86 (td) (≈2.0)	1.75 (d) (5.5)	
(6)	29	m.p. 204 °C	0.93 (s)	1.03 (s)	5.59 (d)	7.02 (dd) (15.0)	5.72 (dd) (≈1.5)	1.92 (d) (9.5)	
(9a)	56	80—90	0.88 (s)	1.06 (s)	5.53 (d)	7.00 (dd) (14.0)	5.87 (dd) (≈1.5)	Band complex 0.96—2.63	
(9b)	68	90—100	0.86 (s)	1.04 (s)	5.81 (d)	6.94 (dd) (14.6)	5.73 (m) (1.66)	Band complex 0.84—2.51	CH ≈5.40—5.57 (m)
(9c)	53	100—110	0.86 (s)	1.04 (s)	5.76 (dd)	6.92 (dd) (14.6) [c]	5.68 (ddd) (1.58)	Band complex 0.83—2.50	

[a] Microdistillation in rotating *Kugelrohr*. [b] Solvent $CDCl_3$. [c] $J(H^2,H^5)=1.05$ Hz (90 MHz).

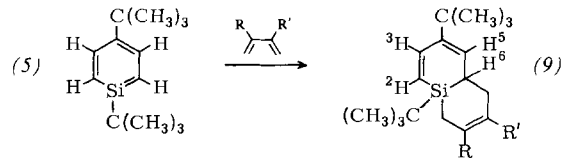
Table 2. Mass spectra of compounds *(9)* and *(6)* (Varian MAT 5, 70 eV).

Cpd.	M^+ *m/e*	*(5)*$^+$ *m/e*	$[(5)^+ - {}^\bullet CH_3]^+$ *m/e*	$[(5)^+ - {}^\bullet C_4H_9]^+$ *m/e*
(9a)	260 (15.5%)	206 (100%)	191 (45%)	149 (58%)
		*m** 163.2	*m** 177.1	*m** 107.8
(9b)	274 (20%)	206 (100%)	191 (49.5%)	149 (52%)
		*m** 154.9	*m** 177.1	*m** 107.8
(9c)	288 (28%)	206 (100%)	191 (11.5%)	149 (57%)
		*m** 147.3	*m** 177.1	*m** 107.8
(6) [a]	412 (45.5%)	206 (44%)	191 (54%)	149 (100%)

[a] Further fragments: $[M-{}^\bullet C_4H_9]^+$, 355 (28%); *m** 305.9; $[(5)^+ + {}^\bullet CH_3]^+$, 221 (93%).

butadiene) at 0 to −20 °C. Given a large excess of diene (diene/*n*-pentane = 1:1 v/v), the [4+2]cycloadducts *(9)* are obtained; dimerization of *(5)* to *(6)* can be completely suppressed under these conditions.

The Diels-Alder adducts *(9)* are identified by analytical and spectroscopic data (Table 1). On electron impact induced retro-Diels-Alder reaction, the adducts form the silabenzene derivative *(5)* with high intensity (Table 2).



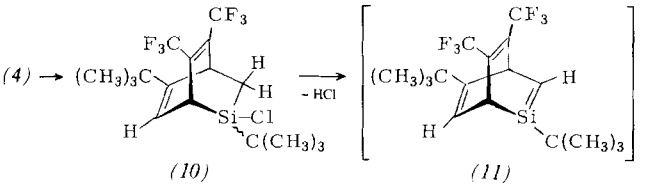
(9a), R = R' = H; *(9b)*, R = H, R' = CH_3; *(9c)*, R = R' = CH_3

The silabenzene *(5)* reacts as a dienophile towards 1,3-dienes and therefore resembles silaethenes in its chemical behavior; trapping reactions with 2,3-dimethyl-1,3-butadiene have been described for the latter[7].

Attempts to trap 1,4-di-*tert*-butylsilabenzene *(5)* as a diene (with inclusion of the Si=C bond) by reaction with dienophiles—by analogy with formation of 1-silabarrelene *(3)*[4]—have so far been unsuccessful.

In the presence of *(4)* the dienophile hexafluorobutyne reacts immediately, even at −100 °C, with $LiN(iPr)_2$ [or $LiN(Si(CH_3)_3)_2$] to give brown insoluble products, and the starting material *(4)* is recovered. Reactions of *(4)* with lithium amides in the presence of diethyl acetylenedicarboxylate, azodicarboxylic esters, and 2-butyne follow a similar course.

Steric hindrance could be responsible for the complete failure of attempts to trap *(5)* with alkyne dienophiles, which



(10) *(11)*

contrasts with the results of *Barton et al.*[4]; however, *(4)* does react smoothly at 60—100 °C with hexafluorobutyne to give the 2,3-dihydro-2-silabarrelene derivative *(10)* which can be dehydrochlorinated with $Li(iPr)_2$ to the spontaneously dimerizing 2-silabarrelene derivative *(11)*.

Received: June 27, 1979 [Z 302 IE]
German version: Angew. Chem. *91*, 863 (1979)

CAS Registry numbers:
(4), 71606-84-3; *(5)*, 71606-85-4; *(6)*, 71606-86-5; *(7)*, 71606-87-6; *(8)*, 71606-88-7; *(9a)*, 71606-89-8; *(9b)*, 71606-90-1; *(9c)*, 71606-91-2; *(10)*, 71606-92-3; *(11)*, 71606-93-4

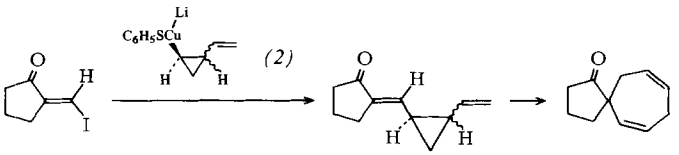
[1] *M. J. S. Dewar, D. H. Lo, Ch. A. Ramsden*, J. Am. Chem. Soc. *97*, 1311 (1975).
[2] *H. B. Schlegel, B. Coleman, M. Jones, Jr.*, J. Am. Chem. Soc. *100*, 6499 (1978).
[3] *P. H. Blustin*, J. Organomet. Chem. *166*, 21 (1979).
[4] *Th. J. Barton, D. S. Banasiak*, J. Am. Chem. Soc. *99*, 5199 (1977); see also *Th. J. Barton, G. T. Burns, ibid. 100*, 5246 (1978).
[5] *G. Märkl, P. Hofmeister*, Tetrahedron Lett. *1976*, 3419; *G. Märkl, H. Baier, P. Hofmeister, F. Kees, C. Soper*, J. Organomet. Chem. *173*, 125 (1979).
[6] *P. R. Jones, T. F. O. Lim*, J. Am. Chem. Soc. *99*, 2013 (1977); *O. L. Chapman, C. C. Chang, J. Kole, M. E. Jung, J. A. Lowe, Th. J. Barton, M. L. Tumey, ibid. 98*, 7844 (1976); *M. R. Chedekel, M. Skoglund, R. L. Kreeger, H. Shechter, ibid. 98*, 7846 (1976); see also [7b].
[7] a) *N. S. Nametkin, L. E. Gusel'nikov, R. L. Ushakova, V. M. Vdovin*, Dokl. Akad. Nauk SSSR *201*, 1365 (1971); *W. J. Bailey, M. S. Kaufmann*, 157th Nat. Meeting of the ACS, Minneapolis, Minn., April 1969; Abstract ORGN-55; *L. E. Gusel'nikov, N. S. Nametkin, V. M. Vdovin*, Acc. Chem. Res. *8*, 18 (1975); *C. M. Golini, R. D. Bush, L. H. Sommer*, J. Am. Chem. Soc. *97*, 7371 (1975); b) *N. Wiberg, G. Preiner*, Angew. Chem. *89*, 343 (1977); Angew. Chem. Int.. Ed. Engl. *16*, 328 (1977).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1010-0790 $ 02.50/0

Synthesis of *cis*-2-Vinylcyclopropyl Ketones; a New Synthesis of 4-Cycloheptenones[**]

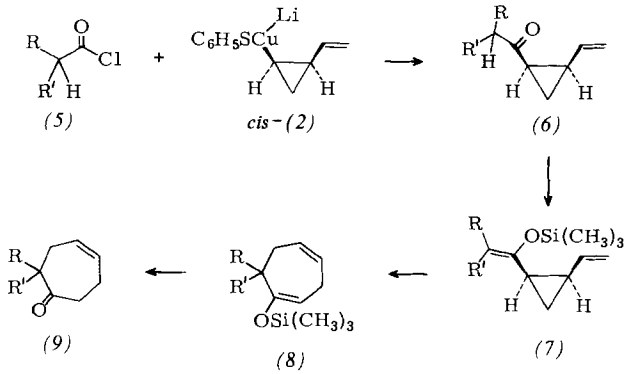
By *Edward Piers* and *Hans-Ulrich Reissig*[*]

Although the thermal (Cope) rearrangement of 1,2-divinylcyclopropane systems has been studied quite extensively from a mechanistic point of view[1], it is only recently that this type of transformation has been investigated with synthetic methodology in mind[2]. Our previous work in this area involved the development of new seven-membered ring annelation processes, in which the key steps entailed thermal rearrangement of α,β-unsaturated β-(2-vinylcyclopropyl) ketones[2b-d]. The latter compounds were prepared by reaction of β-iodoenones with lithium phenylthio(2-vinylcyclopropyl)cuprate reagents. For example, treatment of *(1)* with the cuprate *(2)* (mixture of epimers), followed by thermal rearrangement of the initially formed products *(3)*, yielded spiro[4,6]-undeca-6,9-dien-1-one *(4)* (84%)[2b].



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

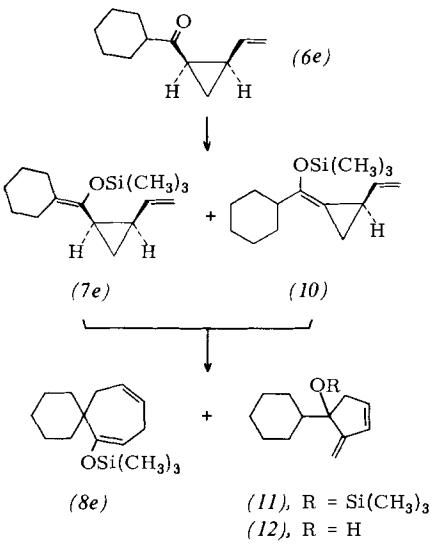
We report here on a potentially important extension of this type of methodology, involving (a) the reaction of acyl chlorides *(5)*[3] with *cis-(2)* to produce the ketones *(6)*, (b) the conversion of *(6)* into silyl enol ethers *(7)*, and (c) the thermal rearrangement of *(7)* into the cycloheptadiene derivatives *(8)*. The silyl enol ether moiety in the rearrangement products *(8)* can be removed by hydrolysis [to give the cycloheptenones *(9)*]; it should be noted however that this functionality is itself synthetically very versatile[4] (see experimental procedure).



(5) *cis-(2)* *(6)* *(7)* *(8)* *(9)*

(a), R R′ = $-(CH_2)_3-$; *(b)*, R—R′ = $-(CH_2)_4-$; *(c)*, R,R′ = H, n-C_4H_9; *(d)*, R,R′ = H, C_6H_5; *(e)*, R R′ = $(CH_2)_5$

Although conversion of *(5e)* into *(6e)* can also be carried out smoothly and efficiently (87% yield), subjection of *(6e)* to the lithium diisopropylamide/trimethylsilyl chloride sequence produces, in addition to the expected product *(7e)*, the isomer *(10)* (*ca.* 1:1)[8]. Thermolysis (150 °C, 30 min) of the mixture leads to *(8e)* + *(11)*[9], and hydrolysis to *(9e)* + *(12)* (*ca.* 4:3).



(6e) *(7e)* *(10)* *(8e)* *(11)*, R = $Si(CH_3)_3$ *(12)*, R = H

Experimental

Reduction of 1,1-dibromo-2-vinylcyclopropane[5] with zinc in ether/acetic acid affords a mixture (47%) of *cis*- and *trans*-1-bromo-2-vinylcyclopropane (ratio 5:1, respectively), from which the pure *cis* isomer[2e,6] can be isolated by column chromatography (silica gel). Treatment of the *cis* isomer with 1.1—1.2 equivalents of *tert*-butyllithium in ether (−78 °C, 2 h), followed by successive addition of tetrahydrofuran (THF) and copper benzenethiolate[7] (1 equivalent) affords a reddish-brown solution of *cis-(2)*. When the latter is allowed to react with 0.66 equivalents of *(5a)* (−78 °C, 5 min; −20 °C, 1 h; 20 °C, 1 h), the ketone *(6a)* is obtained in 93% yield. Conversion of *(6a)* into *(7a)* ($LiN(iPr)_2$, THF, −78 °C; $(CH_3)_3SiCl$, $(C_2H_5)_3N$, −78 °C to +20 °C), followed by thermal rearrangement (neat, 100—110 °C, 30 min) of *(7a)*, affords 5-(trimethylsiloxy)spiro[3.6]deca-5,8-diene *(8a)* (87%). Hydrolysis (1 N HCl in methanol, 20 °C, 1 h) of this material gives the corresponding ketone *(9a)* (91%) in 74% overall yield. *(5b)*—*(5d)* react in a very similar fashion; the overall yields are 70, 74 and 29%, respectively.

Received: April 17, 1979 [Z 303 IE]
German version: Angew. Chem. *91*, 857 (1979)

CAS-Registry numbers:
cis-(2), 71647-04-6; *(5a)*, 5006-22-4; *(5b)*, 4524-93-0; *(5c)*, 2528-61-2; *(5d)*, 103-80-0; *(5e)*, 98-88-4; *(6a)*, 71647-61-5; *(6b)*, 71647-62-6; *(6c)*, 71647-63-7; *(6d)*, 71647-64-8; *(6e)*, 28465-20-5; *(7a)*, 71647-65-9; *(7b)*, 71647-66-0; *(7c)*, 71647-67-1; *(7d)*, 71647-68-2; *(7e)*, 71647-69-3; *(8a)*, 71647-70-6; *(8b)*, 71647-71-7; *(8c)*, 71647-72-8; *(8d)*, 71647-73-9; *(8e)*, 71647-74-0; *(9a)*, 71647-75-1; *(9b)*, 71647-76-2; *(9c)*, 71647-77-3; *(9d)*, 71647-78-4; *(9e)*, 71647-79-5; *(10)*, 71647-80-8; *(11)*, 71647-81-9; *(12)*, 71647-82-0

[*] Prof. Dr. E. Piers, Dr. H.-U. Reissig
Department of Chemistry, University of British Columbia
2075 Wesbrook Mall Vancouver, B. C. (Canada) V6T 1W5

[**] Financial support from the National Sciences and Engineering Research Council Canada is gratefully acknowledged. One of us (H.-U. R.) is grateful to the Deutscher Akademischer Austauschdienst for a NATO Postdoctoral Fellowship.

[1] *S. J. Rhoads, N. R. Raulins*, Org. React. *22*, 54 (1971); *J. E. Baldwin, K. E. Gilbert*, J. Am. Chem. Soc. *98*, 8283 (1976); *M. P. Schneider, B. Csacsko*, J. Chem. Soc. Chem. Commun. *1977*, 330.

[2] a) *J. P. Marino, T. Kaneko*, Tetrahedron Lett. *1973*, 3975; J. Org. Chem. *39*, 3175 (1974); *J. P. Marino, L. J. Browne*, Tetrahedron Lett. *1976*, 3245; b) *E. Piers, I. Nagakura, ibid.* *1976*, 3237; c) *E. Piers, I. Nagakura, H. E. Morton*, J. Org. Chem. *43*, 3630 (1978); d) *E. Piers, E. Ruediger*, J. Chem. Soc. Chem. Commun. *1979*, in press; e) *P. A. Wender, M. P. Filosa*, J. Org. Chem. *41*, 3490 (1976).

[3] Other functional derivatives of carboxylic acids (*e.g.* thiol esters, selenol esters) also serve as suitable substrates for this reaction. Acyl imidazolides were found to be less satisfactory.

[4] *T. Mukaiyama*, Angew. Chem. *89*, 858 (1977); Angew. Chem. Int. Ed. Engl. *16*, 817 (1977); *E. W. Colvin*, Chem. Soc. Rev. *7*, 15 (1978).

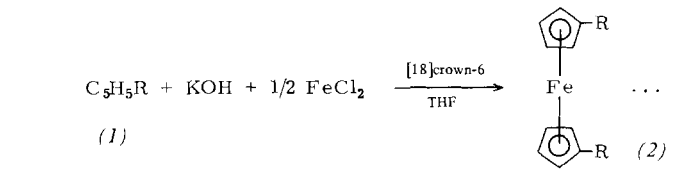
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0791 $ 02.50/0*

[5] *R. C. Woodworth, P. S. Skell,* J. Am. Chem. Soc. 79, 2542 (1957).
[6] All compounds reported herein gave spectral data in full accord with the assigned structures. New compounds which were sufficiently stable to allow for full characterization gave satisfactory elemental analyses and/or molecular weight measurements (high resolution mass spectrometry).
[7] *G. H. Posner, D. J. Brunelle, L. Sinoway,* Synthesis *1974*, 662.
[8] In the case of [*(6a)—(6d)*], silyl enol ether formation was highly regioselective [exclusive or nearly exclusive formation of *(7a)—(7d)*].—When lithium 2,2,6,6-tetramethylpiperidide was used as a base in the place of lithium diisopropylamide, *(10)* was formed as the major product.
[9] For studies related to the thermal rearrangement of methylene(vinyl)cyclopropane systems, see also *W. E. Billups, B. A. Baker, W. Y. Chow, K. H. Leavell, E. S. Lewis,* J. Org. Chem. *40*, 1702 (1975), and references cited therein.

Phase Transfer Catalyzed Synthesis of Ferrocene Derivatives[**]

By *MartaAlišová* and *Howard Alper*[*]

Phase transfer catalysis[1] is a valuable synthetic technique in transition metal organometallic chemistry, both for stoichiometric[2] and catalytic[3] reactions. This communication describes the first synthesis of metallocenes by phase transfer catalysis. This reaction proceeds rapidly, and occurs under very gentle conditions; it is also exceedingly simple, both in execution and work-up. Furthermore, the use of metallic sodium or potassium normally required to generate the cyclopentadiene anion is unnecessary, and rigorously dry conditions are not necessary either.



(a), R = H; *(b)*, R = CH_3; *(c)*, R = $C_6H_5CH_2$; *(d)*, R = n-C_3H_7; *(e)*, R = c-C_6H_{11}

Treatment of a tetrahydrofuran solution of cyclopentadiene *(1a)* with potassium hydroxide, ferrous chloride, and [18]crown-6 as the phase transfer catalyst (room temperature, one hour) affords ferrocene *(2a)*; the yield is 60%. Similar reaction of the substituted cyclopentadienes *(1b)—(1e)* gave the corresponding 1,1′-disubstituted ferrocenes *(2b)—(2e)* (in 45, 55, 40, and 65% yields, respectively). The physical data (m.p. or b.p., IR, NMR, and mass spectra) are in excellent accord with those given in the literature[4]. Other crown ethers (*e.g.* dibenzo[18]crown-6) may also be used, but work-up of the reaction is not as simple as with [18]crown-6. Less than 12% ferrocene was formed when the reaction of cyclopentadiene with ferrous chloride and potassium hydroxide was effected in the absence of the crown ether catalyst. The yields of ferrocenes obtained by the solid/liquid phase transfer reaction described above are much higher than the yields realized using liquid/liquid phase transfer catalysis [*(1)*, aqueous NaOH, $FeCl_2$, benzene, $PhCH_2N(C_2H_5)_3^+Cl^-$].

Procedure

To a tetrahydrofuran solution (60 ml) of *(1a)* (30 mmol) was added [18]crown-6 (15 mmol) followed by potassium hydroxide (2.5 g). After stirring the solution for 15 minutes, ferrous chloride (15 mmol) was added portionwise (over 5 minutes) and the resulting mixture was stirred vigorously for 25—40 min. The solution was transferred to a separatory funnel containing water and benzene. The benzene layer was washed with water, dried ($MgSO_4$), and concentrated to give the crude metallocene *(2a)*. Pure metallocene was then obtained by crystallization or by chromatography (Al_2O_3, hexane/benzene 5:1).

Received: June 15, 1979 [Z 304 IE]
German version: Angew. Chem. *91*, 858 (1979)

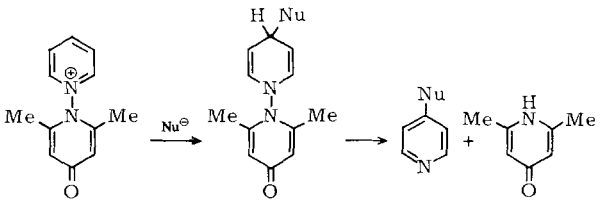
CAS Registry numbers:
(1a), 542-92-7; *(1b)*, 26519-91-5; *(1c)*, 27288-04-6; *(1d)*, 27288-07-9; *(1e)*, 52274-31-4; *(2a)*, 102-54-5; *(2b)*, 1291-47-0; *(2c)*, 12114-61-3; *(2d)*, 1274-04-0; *(2e)*, 71597-16-5

[1] *E. V. Dehmlow,* Angew. Chem. *89*, 521 (1977); Angew. Chem. Int. Ed. Engl. *16*, 493 (1977).
[2] *H. Alper, H. N. Paik,* J. Am. Chem. Soc. *100*, 508 (1978), and references cited therein.
[3] *H. Alper, J. K. Currie,* Tetrahedron Lett. *1979*, 2665; *H. Alper, J. K. Currie, H. des Abbayes,* J. Chem. Soc. Chem. Commun. *1978*, 311, and references cited therein.
[4] *M. Rosenblum:* Chemistry of the Iron Group Metallocenes, Part I. Wiley, New York, 1965; *W. L. Jolly,* Inorg. Syn. *11*, 120 (1968) describes a preparation of the parent compound in a dipolar aprotic solvent

Regiospecific Nucleophilic Attack at the γ-Position of 1-(2,6-Dimethyl-4-oxo-1,4-dihydro-1-pyridyl)pyridinium Compounds; Novel Synthesis of 4-Substituted Pyridines[**]

By *Alan R. Katritzky, Hector Beltrami, James G. Keay, David N. Rogers, Michael P. Sammes, Christopher W. F. Leung,* and *Cheuk Man Lee*[*]

We designed the substituent 2,6-dimethyl-4-oxo-1,4-dihydro-1-pyridyl [see *(1)*] which (i) could be attached to a pyridine nitrogen in two high-yield stages[1a], (ii) sterically shields the α-positions while activating the γ-position to nucleophilic attack [*(1)*→*(2)*], and (iii) then acts as a leaving group to rearomatize the 4-substituted dihydropyridine ring [*(2)*→*(3)*]. The success of this strategy was illustrated by the preparation of a series of 4-arylpyridines using Grignard reagents as the attacking nucleophile[1b]. We have now considerably extended this work and here illustrate the scope of application of the method to carbon, sulfur and nitrogen nucleophiles by reference to the novel preparations of five classes of compounds [*(3a)—(3e)*].



(a), Nu = Alkyl; *(b)*, Nu = CRR′COAlkyl; *(c)*, Nu = CRR′NO_2; *(d)*, Nu = SAlkyl or SAryl; *(e)*, Nu = 1-benzimidazolyl or 1-benzotriazolyl

[*] Prof. Dr. H. Alper, Dr. M.Ališová
Department of Chemistry, University of Ottawa
Ottawa, Ontario (Canada) K1N 9B4

[**] We are indebted to Imperial Oil Limited, and to the Natural Sciences and Engineering Research Council, for support of this work.

[*] Prof. Dr. A. R. Katritzky, H. Beltrami, J. G. Keay, and Dr. D. N. Rogers
School of Chemical Sciences, University of East Anglia
Norwich NR4 7TJ (England)
Dr. M. P. Sammes, C. W. F. Leung, C. M. Lee
Department of Chemistry, University of Hong Kong
Pokfulam Road (Hong Kong)

[**] Synthetic Applications of N ·N Linked Heterocycles, Part 6.—Part 5: see Ref. [1b].

a) 4-Alkylpyridines (3a): The cation *(1)* reacts with ethyl-, *n*-propyl-, isopropyl-, and *n*-butylmagnesium bromide directly [without isolation of the intermediate *(2a)*] to give the corresponding 4-alkylpyridines *(3a)* (average yield 82%). Other methods for the synthesis of *(3a), e.g.* by alkylation of 4-picoline[2], from 4-cyanopyridine *via* ketones[3] or according to *Arens'* procedure[4] are less generally applicable, tedious, and/or give poorer yields.

b) α-(4-Pyridyl)alkyl ketones (3b): Addition of the salt *(1)* to the lithium enolates of ketones in tetrahydrofuran gives the corresponding dihydro-intermediates *(2b)* which can be isolated by chromatography on Al_2O_3[5]. On boiling under reflux in CCl_4 in the presence of azobis(isobutyronitrile), the intermediates *(2b)* are decomposed in high yield into a readily separable mixture of *(3b)* and *(4)*. In this way *inter alia* diethyl ketone, methyl isobutyl ketone, pinacolone, benzyl methyl ketone, cyclohexanone, 2-methylcyclohexanone, cycloheptanone, acetophenone, and propiophenone were converted into *(2b)* and *(3b)*: average yields 81% and 85%, respectively. Previously the only practical route to *(3b)* has been the acylation of 4-alkylpyridines[6]; this restricts considerably the type of compound that can be prepared.

c) 4-(α-Nitroalkyl)pyridines (3c): Sodium derivatives of nitroethane, 2-nitropropane and 2-nitro-1-phenylpropane react with *(1)* in ethanol to give the intermediates *(2c)* (average yield 85%). Photolysis of *(2c)* in $CHCl_3$ in the presence of benzoyl peroxide gives *(3c)* (average yield 52%). Previous methods for the synthesis of *(3c)* involved nitration of alkylpyridines under acidic[7a] or basic conditions[7b]. The yields are usually 50—70%; a prerequisite, however, is that the corresponding 4-alkylpyridine must be available.

d) 4-Alkylthio- and 4-arylthio-pyridines (3d): The anions benzyl-, ethoxycarbonylmethyl-, furfuryl-, and *p*-chlorophenyl-thiolate in aqueous solution react with *(1)* to give the intermediates *(2d)* (average yield 72%). Decomposition of these adducts in refluxing carbon tetrachloride, with or without the addition of a free radical initiator gives *(3d)* (average yield 90%).

e) 4-(1-Benzimidazolyl)- and 4-(1-benzotriazolyl)pyridines (3e): The anions of benzimidazole and benzotriazole add in acetonitrile to *(1)* to give *(2e)* (average yield 74%). Photolytic decomposition in $CHCl_3$ in the presence of benzoyl peroxide and subsequent chromatography (Al_2O_3-$CHCl_3$) give *(3e)* (average yield 65%). Compounds of this type have been previously prepared by diverse methods which suffer from the number of stages involved, lack of generality, and/or poor yields, and all require 4-substituted pyridines as starting materials[8].

The method described here is of considerable potential for the synthesis of a wide variety of 4-substituted pyridines. Compounds of the type *(3a)*[9], *(3b)* and *(3c)*, bearing a 2- and/or 3-methyl group in the pyridinium ring, have already been obtained. In none of the reactions presently reported was any 2-substitution detected. Harder nucleophiles, however, attack at the α-position[10].

Received: June 26, 1979 [Z 305 IE]
German version: Angew. Chem. *91*, 856 (1979)

[1] a) *M. P. Sammes, Ho King Wah, A. R. Katritzky*, J. Chem. Soc. Perkin Trans. I *1977*, 327; b) *A. R. Katritzky, H. Beltrami, M. P. Sammes*, J. Chem. Soc. Chem. Commun. *1979*, 137.

[2] *C. Osuch, R. Levine*, J. Am. Chem. Soc. *78*, 1723 (1956).

[3] *K. B. Prasad, H. N. Al-Jallo, K. S. Al-Dulaimi*, J. Chem. Soc. *C 1969*, 2134.

[4] *J. F. Arens, J. P. Wibaut*, Rec. Trav. Chim. Pays-Bas *61*, 59 (1942).

[5] Satisfactory analytical data were obtained for all new 4-substituted pyridines reported in this paper.

[6] See *e.g., C. Osuch, R. Levine*, J. Org. Chem. *22*, 939 (1957); *R. Levine, D. A. Dimmig, W. M. Kadunce, ibid. 39*, 3834 (1974).

[7] a) *H. Feuer, J. Doty, J. P. Lawrence*, J. Org. Chem. *38*, 417 (1973); b) *H. Feuer, J. P. Lawrence, ibid. 37*, 3662 (1972).

[8] a) *N. Sawa*, Nippon Kagaku Zasshi *89*, 868 (1968); Chem. Abstr. *70*, 28867g (1969); b) *I. I. Grandberg, N. F. Krokhina, M. N. Kondrat'ev*, Khim.-Farm. Zh. *2*, 24 (1968); Chem. Abstr. *70*, 11624c (1969); c) *M. A. Khan, J. B. Polya*, J. Chem. Soc. *C 1970*, 85; d) *R. Robinson, S. Thornley*, J. Chem. Soc. *1924*, 2169.

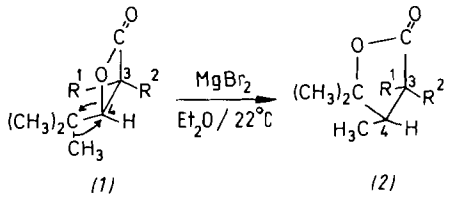
[9] In collaboration with *S. Cook*, and *A. J. Cozens*.

[10] *A. R. Katritzky et al.*, unpublished.

Stereospecific Synthesis of γ-Lactones by Dyotropic Wagner-Meerwein Rearrangement

By *Johann Mulzer* and *Gisela Brüntrup*[*]

The enormous relief of strain on going from a four- to a five-membered ring (*ca.* 22 kcal mol^{-1})[1] and the resulting driving force for ring expansion has so far been exploited only for the synthesis of carbocyclic compounds[2]. We report the ring expansion of 2-oxetanones (β-lactones) like *(1)* and *(3)* to 2-oxolanones (γ-lactones) like *(2)* and *(4)*—*(6)*. This isomerization, which is initiated by ethereal $MgBr_2$ and proceeds in a manner formally resembling a Wagner-Meerwein rearrangement[3], is of preparative interest because (i) it is quantitative, stereospecific, and can be run under extremely mild conditions; (ii) the required β-lactones are readily prepared in sterically pure form, *via* the 3-hydroxycarboxylic acids, from aldehydes and carboxylic acids[4]; and (iii) γ-lactones are of great importance in synthetic, analytical, and natural products chemistry.



(1) *(2)*

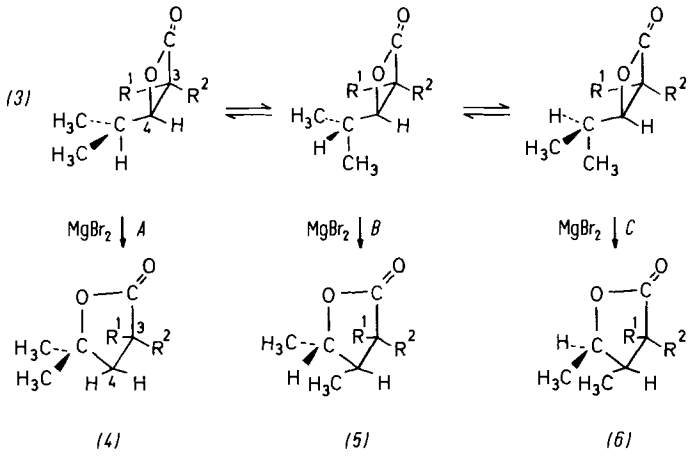
Scheme 1. R^1, R^2, see Table 1.

The steric course of the rearrangement of 4-*tert*-butyl-β-lactones *(1)* is shown in Scheme 1. The migrating CH_3 group and the C–O bond to be broken are in *anti* position, as is often observed in Wagner-Meerwein rearrangements[3]; as a result the configuration at the 3,4 bond is retained. The same stereospecificity is observed in the case of the 4-isopropyl-β-lactones *(3a)* and *(3b)* (Scheme 2). However, two additional problems are encountered: (i) CH_3- or H shift and (ii) control over the new chiral center at C-5. The three reaction pathways conceivable for *(3a)* and *(3b)*, *i.e. A* (H shift), *B* and *C* (CH_3 shift), are shown in Scheme 2. The relative contribution of *A, B,* and *C* is highly dependent upon the configuration of *(3)*. In the *trans* derivative *(3a)* the isopropyl group has almost unrestricted conformational mobility, and H shift predominates in this case (78% *A*). In the *cis*-lactone *(3b)*, however, steric hindrance occurs between the 3-phenyl and an isopropyl methyl group in the case of pathways *A* and *B*. Thus route *C* is adopted to an extent of >98% (TLC analysis), and *(6b)* is formed exclusively. Hence in this rearrangement all three stereocenters of the resulting γ-lactone are under complete control.

The stereospecificity of the ring expansion with respect to the C^3–C^4 axis is incompatible with a classical Wagner-

[*] Dr. J. Mulzer, G. Brüntrup
Institut für Organische Chemie der Universität
Karlstrasse 23, D-8000 München 2 (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0793 $ 02.50/0*



Scheme 2. *(a)*, $R^1=H$, $R^2=C_6H_5$; *(4a)*:*(5a)*:*(6a)* = 78:7:15. *(b)*, $R^1=C_6H_5$, $R^2=H$; >98% *(6b)* (see Table 1).

Table 1. γ-Lactones of types *(2)*, *(4)*, *(5)*, and *(6)* [a] prepared.

Cpd.	R^1	R^2	M.p. [°C] B.p. [°C/torr]	$\tilde{\nu}_{(C=O)}$ [cm^{-1}]
(2a)	H	C_6H_5	92—92	1765
(2b)	C_6H_5	H	84—85	1770
(2c)	H	$C(CH_3)_3$	100—110/0.1	1765
(2d)	H	SC_6H_5	150—160/0.1	1765
(2e)	H	OC_6H_5	74—75	1765
(4a) [b]	H	C_6H_5	50—51	1765
(5a) [b]	H	C_6H_5	90—100/0.1	1770
(6a) [b]	H	C_6H_5	90—100/0.1	1770
(6b)	C_6H_5	H	90—100/0.1	1770

[a] Yield 94—98%; all compounds gave correct CH analyses. The configurational assignment of the γ-lactones was based on ^{1}H-NMR spectra; thus we found that in *cis-trans* isomeric γ-lactones always $J_{3,4\text{-}cis} < J_{3,4\text{-}trans}$ and $\tau(cis\text{-}4\text{-}CH_3) > \tau(trans\text{-}4\text{-}CH_3)$. Cf. also *D. Sawostianoff, M. Pfau,* Bull. Soc. Chim. Fr. *1967*, 4162.

[b] Yield *(4a)* + *(5a)* + *(6a)* = 97%.

Meerwein carbenium-ion mechanism because such a process should involve at least partial rotation about the C^3—C^4 bond in the case of the *cis*-lactones *(1b)* and *(3b)*. We therefore assume that ring opening and migration of CH_3 or H are part of a concerted dyotropic rearrangement[5]. This assumption is further supported by two experimental results: (i) the reaction of *(1a)* with isopropylmagnesium bromide gives not only the Grignard adduct at the carbonyl group (5-hydroxy-2,6,6-trimethyl-4-phenyl-3-heptanone) but also considerable amounts of *(2a)*. The $MgBr_2$ generated in the Schlenck equilibrium[6] initiates the ring expansion of *(1a)*; if a carbenium ion were an intermediate it should be trapped by the organometallic species. (ii) In the reaction of 1 equiv. of $MgBr_2$ with *cis*-3-methyl-4-phenyl-2-oxetanone ring expansion cannot occur; instead, decarboxylation gives a quantitative yield of *trans*-1-phenylpropene. The carbenium ion apparently formed in this case decomposes *via* rotation and CO_2 elimination, *i.e.* reactions which are not observed with ring-expanding β-lactones.

Procedure

3.2 M $MgBr_2$-ether (1.55 ml, 4.9 mmol) is added to a water-cooled stirred solution of *(1a)* (1.00 g, 4.90 mmol) in anhydrous ether (10 ml). After 5 min, water (10 ml) is added and crystalline *(2a)* (98%) is isolated from the dried ether phase.

Received: June 29, 1979 [Z 306 IE]
German version: Angew. Chem. *91*, 840 (1979)

CAS Registry numbers:
(1a), 71647-83-1; *(1b)*, 71647-84-2; *(2a)*, 71647-85-3; *(2b)*, 71647-86-4; *(2c)*, 71647-87-5; *(2d)*, 71647-88-6; *(2e)*, 71647-89-7; *(3a)*, 70982-88-6; *(3b)*, 71647-90-0; *(4a)*, 20215-56-9; *(5a)*, 71647-91-1; *(6a)*, 71647-92-2; *(6b)*, 71647-93-3

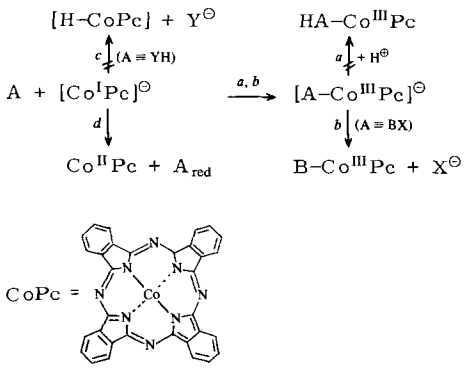
[1] *S. W. Benson:* Thermochemical Kinetics. Wiley, New York 1968.
[2] *D. Seebach* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Thieme, Stuttgart 1971, Vol. IV/4, pp. 430 ff. Concerning the oxetane→tetrahydrofuran rearrangement, see *H. A. Carless, H. S. Trivedi,* J. Chem. Soc. Chem. Commun. *1979*, 382. An H^+-catalyzed β-lactone→γ-lactone rearrangement is described by *R. H. Hasek, E. U. Elam,* US-Pat. 3004989 (1961), Eastman Kodak.
[3] Review: *Y. Pocker* in *P. de Mayo:* Molecular Rearrangements. Interscience, New York 1963, Vol. 1, pp. 1 ff.
[4] *J. Mulzer, A. Pointner, A. Chucholowski, G. Brüntrup,* J. Chem. Soc. Chem. Commun. *1979*, 52.
[5] Dyotropic Wagner-Meerwein reactions were previously unknown. For a review of dyotropic rearrangements, see *M. T. Reetz,* Adv. Organomet. Chem. *16*, 33 (1977).
[6] *E. C. Ashby, J. Laemmle, H. M. Neumann,* J. Am. Chem. Soc. *94*, 5412 (1972).

Cobalt(I)-phthalocyanine Anion as Vitamin B_{12s} Model: Selectivity in Reactions with Electrophiles

By *Heiner Eckert* and *Annette Schier*[*]

In order to understand vitamin B_{12}-catalyzed reactions[1,2] and to ascertain the scope of the cobalt(I)-phthalocyanine anion $[Co^IPc]^-$ as a stable reagent in synthetic chemistry (protecting group technique for syntheses of peptides[3a] and β-lactam antibiotics[3b], intermediate in the production of blue dyes[3c]), it is important to know the selectivity of this anion towards functional groups. Owing to the extremely high reactivity of cobal(I)amine[4] and its model compounds cobal(I)oxime[4] and $[Co^IPc]^-$[5] towards alkyl halides they are designated as "supernucleophiles".

We have now found that the cobalt(I)-phthalocyanine anion (as lithium salt $Li[Co^IPc]$) behaves as a supernucleophile in nucleophilic substitution of acyl compounds *(2a)* and *(2b)* (reaction *b*), while no nucleophilic additions (reaction *a*) were observed with carbonyl compounds *(1)*, including those with cumulated double bonds. Vinyl and aryl halides such as *(2c)* and *(2d)* do not undergo nucleophilic substitution (see Scheme 1 and Table 1).



Scheme 1. Reactions of compounds A with the cobalt(I)-phthalocyanine anion. See text for details.

[*] Dr. H. Eckert, A. Schier
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1010-0794 $ 02.50/0

Table 1. Reaction of Li[Co^{I}Pc] with compounds A in methanol or acetonitrile at 20 °C. Only compounds *(2a)*, *(2b)*, *(4a)*, and *(4b)* react with [Co^{I}Pc]$^{-}$.

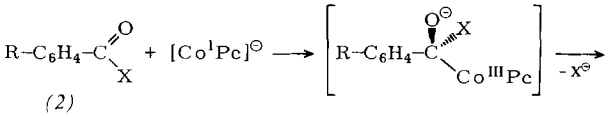
Compounds A No.	Type		Reaction	Solvent	Reaction time	Stirring time [h]	Oxid. of Co^{I} +/−	Yield [%] of isolated material: Reactants A	Reactants [Co^{I}Pc]	Products: CoPc complexes	Products: X or A_{red}
(1a)		n-C_3H_7CHO	*a*	MeOH	[b]	144	−	68 [c]	99	0	—
(1b)		C_6H_5CHO	*a*	MeOH	[b]	48	−	99 [d]	99	0	—
(1c)		$CH_2{=}CH\ COOC_2H_5$	*a*	MeOH	[b]	48	−	[e]	100	0	—
(1d)		$C_6H_5\ N{=}C{=}O$	*a*	MeCN	[b]	48	−	(91) [f]	99	0	—
(1e)		$O{=}C{=}O$	*a*	MeCN	[b]	960	−	—	93	0	—
(2a)	BX	p-$CH_3\ C_6H_4\ COCl$	*b*	MeCN	<1 min	2	+	0	0	100 B Co^{III}Pc	97 X [g]
(2b)	BX	$(C_6H_5CO)_2O$	*b*	MeCN	3 h	3—96	+	5—8 [h]	0	99 B Co^{III}Pc	69—85 X [i]
(2c)	BX	$C_6H_5COOCH_2CBr{=}CH_2$	*b*	MeOH	[b]	144	−	92	100	0	0
(2d)	BX	C_6H_5Cl	*b*	MeOH	[b]	288	−	87	96	0	0
(3a)	YH	C_6H_5OH	*c*	MeCN	[b]	4	−	100	100	—	0
(3b)	YH	$(C_2H_5OCO)_2CH_2$	*c*	MeCN	[b]	120	−	71	100	—	0
(4a)		$C_6H_5\ NO_2$	*d*	MeOH	2 min	1.5	+	0	0	102 Co^{II}Pc	(A_{red}) [j]
(4b)		p-Cl C_6H_4 NO	*d*	MeOH	20 h	72	+	0	0	98 Co^{II}Pc	[k]
(4c)		$CH_3\ C{\equiv}N$	*d*	MeCN	[b]	720	−	[l]	98	0	0
		Alkyl halides [5b]	*(b)*	MeOH	<1 min to 60 min	[5b]	+	0	0	[5b]	[5b]

[a] Gravimetrically as Co^{II}Pc after air-oxidation. [b] See text. [c] Gravimetrically as n-butyraldehyde 2,4-dinitrophenylhydrazone together with 17% of 2-ethyl-2-hexenal 2,4-dinitrophenylhydrazone. [d] Gravimetrically as benzaldehyde 2,4-dinitrophenylhydrazone. [e] Neither A nor products thereof were detected. [f] 91% of triphenyl isocyanurate. [g] Volumetrically according to *Mohr*. [h] 8% of *(2b)* were isolated after 3 h, and 5% after 96 h. [i] Gravimetrically as benzoic acid. [j] Product mixture, principal component $C_6H_5\ NO$ (from IR). [k] Reduction products not yet elucidated. [l] MeCN as reactant and solvent.

(1a), *(1b)*, and *(1c)* do not react with [Co^{I}Pc]$^{-}$ according to path *a*, neither under standard conditions for aldol condensations and Michael additions nor on 48 h refluxing in methanol. The aldehydes can be recovered as 2,4-dinitrophenylhydrazones; *(1a)* forms 17% of the aldol condensation product within 144 h. Nor does a Cannizzaro reaction occur under these conditions—thus indicating the low basicity of the supernucleophile [Co^{I}Pc]$^{-}$. Only on reaction of benzaldehyde *(1b)* with [Co^{I}Pc]$^{-}$ in 1,4-butanediol (150—170 °C, 72 h) can 30% of benzyl alcohol be isolated.

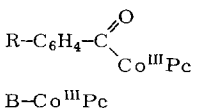
Likewise, no addition (reaction *a*) to the cumulated double bonds of phenyl isocyanate *(1d)* and carbon dioxide *(1e)* took place; *(1d)* undergoes quantitative trimerization to triphenyl isocyanurate.

In contrast, [Co^{I}Pc]$^{-}$ reacts very fast with p-toluoyl chloride *(2a)* and benzoic anhydride *(2b)*, reaction with *(2a)* being at least 10^3 times faster than with *(2b)*. This behavior accords with the basicity of the leaving groups chloride and benzoate in an addition-elimination reaction. The acylated complexes p-toluoyl- and benzoyl-cobalt(III)phthalocyanine



(2)

(a), R = p-CH_3, X = Cl
(b), R = H, X = $OCOC_6H_5$



B–Co^{III}Pc

(type B–Co^{III}–Pc) have been characterized by elemental analysis and IR spectra (ν(C=O) = 1740 cm^{-1}). The complexes, LiCl, and Li-benzoate can be isolated in quantitative yield.

2-Bromoallyl benzoate *(2c)* and chlorobenzene *(2d)* are completely inert toward nucleophilic attack by [Co^{I}Pc]$^{-}$ and are recovered quantitatively. The fact that no substitution occurs at the sp^2 carbon is a further criterion for the S_N2 character of the nucleophilic substitution reactions of [Co^{I}Pc]$^{-}$ with alkyl halides[5b].

The acidic compounds phenol *(3a)* and diethyl malonate *(3b)* do not react according to path *c*, but can be recovered quantitatively.

Nitrobenzene *(4a)* is reduced very fast, according to reaction *d*, to nitrosobenzene, which itself, like 1-chloro-4-nitrosobenzene, can be slowly reduced further by [Co^{I}Pc]$^{-}$. The nitrile group in acetonitrile is not attacked by [Co^{I}Pc]$^{-}$.

The CoPc complexes were obtained in quantitative yields as organo-Co^{III}Pc (reaction *b*), or Co^{II}Pc (reaction *d*), or, after air-oxidation of the unchanged [Co^{I}Pc]$^{-}$, as Co^{II}Pc (non-occurrence of reactions *a* and *c*) in quantitative yield.

These results show that the cobalt(I)-phthalocyanine anion [Co^{I}Pc]$^{-}$ differs from cobal(I)amine[2,6] and other strong nucleophiles by not undergoing nucleophilic additions; instead, as far as has been determined, it reacts only *via* nucleophilic substitution, with the exception of the reduction of nitro- and nitroso compounds. Thus [Co^{I}Pc]$^{-}$ resembles nucleophiles such as I^{-} in its selective behavior, but is considerably more reactive (relative logarithmic nucleophilic character of I^{-}: $n = 7.42$[7]; that of [Co^{I}Pc]$^{-}$ is $n = 10.8$[5a]). [Co^{I}Pc]$^{-}$ is thus to be regarded as a very strong soft[7] nucleophile (high polarizability of the $3d_{z^2}$ orbital of Co^{I}) with low basicity.

The selectivity for substitution reactions together with the strong nucleophilicity, the low reduction potential (−0.37 V[8]), and the extremely high stability recommend use of cobalt(I)-phthalocyanine anion, in spite of its high molecular weight (571), as a reagent for removal of β-halogenated alkyl protecting groups from sensitive systems[3b,9] such as penicillin and cephalosporin derivatives[3b].

Received: June 8, 1979 [Z 307 IE]
German version: Angew. Chem. *91*, 841 (1979)

CAS-Registry numbers:
(1a), 123-72-8; *(1b)*, 100-52-7; *(1c)*, 140-88-5; *(1d)*, 103-71-9; *(1e)*, 124-38-9; *(2a)*, 874-60-2; *(2b)*, 93-97-0; *(2c)*, 71616-09-6; *(2d)*, 108-90-7; *(3a)*, 108-95-2; *(3b)*, 105-53-3; *(4a)*, 98-95-3; *(4b)*, 932-98-9; *(4c)*, 75-05-8; [Co^{I}Pc]$^{-}$, 18974-06-6; p-$CH_3\ C_6H_4\ CO\ Co^{III}$ Pc, 71616-28-9; $C_6H_5CO\ Co^{III}$Pc, 71616-29-0; Co^{III}Pc, 3317-67-7

[1] *R. H. Abeles, D. Dolphin*, Acc. Chem. Res. *9*, 114 (1976); *G. N. Schrauzer*, Angew. Chem. *88*, 465 (1976); Angew. Chem. Int. Ed. Engl. *15*, 417 (1976).
[2] *A. Fischli*, Helv. Chim. Acta *62*, 882 (1979).
[3] a) *H. Eckert, I. Ugi*, Justus Liebigs Ann. Chem. *1979*, 278; b) *H. Eckert, I. Ugi, H.-J. Kabbe*, DOS 2619247 (1977), Bayer; Chem. Abstr. *88*, 61674

(1978); *H. Eckert, I. Ugi*, DAS 2747724 (1977), Bayer; c) *H. Seidler, K. Wunderlich, H. Eckert*, DOS 2555243 (1977), Bayer; Chem. Abstr. *87*, 153424 (1977).
[4] *G. N. Schrauzer, E. Deutsch*, J. Am. Chem. Soc. *91*, 3341 (1969).
[5] a) *H. Eckert, I. Ugi*, Angew. Chem. *87*, 847 (1975); Angew. Chem. Int. Ed. Engl. *14*, 825 (1975); b) *H. Eckert, I. Lagerlund, I. Ugi*, Tetrahedron *30*, 2243 (1977).
[6] *A. W. Johnson, L. Merwyn, N. Shaw, E. L. Smith*, J. Chem. Soc. *1963*, 4146.
[7] *R. G. Pearson, J. Songstad*, J. Am. Chem. Soc. *89*, 1827 (1967).
[8] *D. W. Clack, N. S. Hush, J. S. Woolsey*, Inorg. Chim. Acta *19*, 129 (1976).
[9] *S. Sommer, H. Eckert*, to be published.

Isopropyl Carboxylates—A New Class of Insect Pheromones

By *Wittko Francke, A. R. Levinson, T.-L. Jen*, and *H. Z. Levinson*[*]

The hide beetle *Dermestes maculatus* (Deg.), which feeds on animal tissues and animal products both as larva and as imago, causes considerable damage to stored products[1]. We have identified the pheromone bouquet of this beetle as a basis for biotechnological pest control (see Table 1).

In an exocrine abdominal gland absent in females, sexually mature males produce a series of sex-specific volatile compounds showing high biological activity[2]. GC-MS studies on pentane extracts[3] of prepared glands were initially concerned with a group of four closely related substances. The most volatile component of this group ($M_r = 242$) has a molecular weight two units higher than that of the other three compounds, which are transformed into the first-mentioned one on catalytic hydrogenation.

The ions observed at $m/z = 102$ (14%) and 115 (11.5%) in the mass spectrum of this substance are typical products of a McLafferty rearrangement and, in conjunction with intense fragments at $M^+ - 41$ (22%) and $M^+ - 42$ (28.5%), indicate the propyl ester of a carboxylic acid with 12 carbon atoms[4]. In fact, isopropyl laurate showed the same gas chromatographic retention time as the natural product and an identical mass spectrum.

Thus it had also been established that the other three components must be unbranched isopropyl dodecenoates. The principal component was isolated by preparative gas chromatography[5] and afforded heptanal as the major product on micro-ozonolysis; synthetic isopropyl *Z*-5-dodecenoate proved to be identical with the natural product. Identification of the other two compounds of mass 240 as isopropyl *Z*-7- and *Z*-9-dodecenoate was accomplished by comparison of their gas chromatographic retention times and mass spectra[6] with those of authentic compounds prepared from the corresponding alkenols[7] by oxidation and esterification (see Table 1).

Table 1. Quantitative composition of the isopropyl ester pheromone bouquet of male hide beetle *Dermestes maculatus* (Deg.). The weights refer to an individual insect (total *ca.* 0.9 μg).

Carboxylic acid	Type	Weight [ng]
Lauric acid	C_{12}	*ca.* 2.5
Z-5-Dodecenoic acid	*Z*-5-C_{12}	300
Z-7-Dodecenoic acid	*Z*-7-C_{12}	1
Lauroleic acid	*Z*-9-C_{12}	*ca.* 0.1
Myristic acid	C_{14}	25
Z-5-Tetradecenoic acid	*Z*-5-C_{14}	50
Z-7-Tetradecenoic acid	*Z*-7-C_{14}	100
Myristoleic acid	*Z*-9-C_{14}	150
Palmitic acid	C_{16}	25
Palmitoleic acid	*Z*-9-C_{16}	200
Oleic acid	*Z*-9-C_{18}	50

[*] Dr. W. Francke [+]
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)
Dr. A. R. Levinson, Dr. T.-L. Jen, Prof. Dr. H. Z. Levinson
Max-Planck-Institut für Verhaltensphysiologie, D-8131 Seewiesen (Germany)
[+] To whom correspondence should be addressed.

The Kováts indices $I_{WG11,\,150\,°C}$[8] of the isopropyl esters of all straight-chain dodecenoic acids are listed in Table 2: index differences of one unit can be distinguished on co-injection at comparable concentration; the working temperature must be reduced for smaller differences. It is seen that, on steady shift of the double bond from position 2 to 11, the initially more rapidly eluting *Z* compounds are "overtaken" by the *E* isomers. Isopropyl *Z*-6- and *E*-6-dodecenoate appear simultaneously; the ester of *Z*-5-dodecenoic acid is eluted faster than all other isopropyl dodecenoates.

Table 2. Kováts indices (*I*) of unbranched isopropyl dodecenoates on WG 11 at 150 °C [8].

Subst.	*I*	Subst.	*I*	Subst.	*I*	Subst.	*I*
Sat.	1841	*E*-5	1867	*E*-8	1876.5	11	1893
Z-5	1859	*Z*-6	1872	*Z*-3	1877	*Z*-9	1894
Z-4	1862	*E*-6	1872	*E*-9	1884.5	*E*-10	1906
Z-2	1864	*E*-7	1874	*Z*-8	1885	*Z*-10	1926
E-4	1866	*Z*-7	1876	*E*-3	1885.5	*E*-2	1970

Four other sex-specific substances found in the glands of male hide beetles contained two CH_2 groups more than the compounds previously identified. Gas chromatographic retention times and mass spectra[6] were in agreement with synthetic samples of methyl myristate and isopropyl *Z*-5-, *Z*-7-, and *Z*-9-tetradecenoate.

In the same way the isopropyl esters of palmitic, palmitoleic, and oleic acids were also detected as male-specific components of the gland extract.

Table 1 shows a quantitative composition of this pheromone bouquet, which is the most extensive yet identified in beetles. A mixture of synthetic substances in the same ratio exhibited similar electro- and behavioral-physiological activities as did pentane extract of the abdominal glands of male hide beetles. The isopropyl carboxylates now found for the first time in insects thus constitute a new class of pheromones.

Received: July 13, 1979 [Z 308 IE]
German version: Angew. Chem. *91*, 843 (1979)

CAS Registry numbers:
(1), 10233-13-3; *(2)*, 71597-90-5; *(3)*, 71597-91-6; *(4)*, 68862-21-5; *(5)*, 110-27-0; *(6)*, 71597-92-7; *(7)*, 71597-93-8; *(8)*, 68862-22-6; *(9)*, 142-91-6; *(10)*, 68862-23-7; *(11)*, 112-11-8; isopropyl *(Z)*-4-dodecenoate, 71597-94-9; isopropyl *(Z)*-2-dodecenoate, 71597-95-0; isopropyl *(E)*-4-dodecenoate, 71597-96-1; isopropyl *(E)*-5-dodecenoate, 71597-97-2; isopropyl *(Z)*-6-dodecenoate, 71597-98-3; isopropyl *(E)*-6-dodecenoate, 71597-99-4; isopropyl *(E)*-7-dodecenoate, 71598-00-0; isopropyl *(E)*-8-dodecenoate, 71598-01-1; isopropyl *(Z)*-3-dodecenoate, 71598-02-2; isopropyl *(E)*-9-dodecenoate, 71598-03-3; isopropyl *(Z)*-8-dodecenoate, 71598-04-4; isopropyl *(E)*-3-dodecenoate, 71598-05-5; isopropyl *(Z)*-9-dodecenoate, 68862-21-5; isopropyl *(E)*-10-dodecenoate, 71598-06-6;, isopropyl *(Z)*-10-dodecenoate, 71598-07-7; isopropyl *(E)*-2-dodecenoate, 71598-08-8

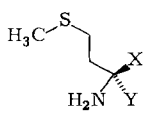
[1] *H. Z. Levinson, A. R. Levinson*, Entomol. Exp. Appl. *24*, 505 (1978).
[2] *H. Z. Levinson, A. R. Levinson, T.-L. Jen, J. L. D. Williams, G. Kahn, W. Francke*, Naturwissenschaften *65*, 543 (1978).
[3] 50-m glass capillary with WG 11 at 150 °C coupled directly to a Varian MAT 311 A mass spectrometer.
[4] *R. Ryhage, E. Stenhagen*, Ark. Kemi *14*, 483 (1959).

[5] 8-m, 10-mm i.d. steel column with 10% silicone oil DC 550X on Chromosorb W-AW-DMCS 60—80 mesh/Carlo Erba 2400.
[6] In contrast to methyl esters (*B. Hallgren, R. Ryhage, E. Stenhagen,* Acta Chem. Scand. *13*, 845 (1959)) the isopropyl esters of long-chain unsaturated carboxylic acids can be distinguished, with certain reservations, by mass spectrometry. *W. Francke et al.*, to be published.
[7] *M. Schwarz, R. M. Waters,* Synthesis *1972*, 567.
[8] *E. Kováts,* Helv. Chim. Acta *41*, 1915 (1958).

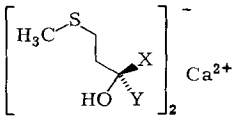
Enantioselective Synthesis of the Hydroxy-Analogues of D- and L-Methionine

By *Axel Kleemann, Bernd Lehmann,* and *Jürgen Martens*[*]

The calcium salt D,L-*(2)* of D,L-2-hydroxy-4-(methylthio)butyric acid ("hydroxy-analogue of methionine") is used, like D,L-methione D,L-*(1)*, for supplementing mixed feeds and for special diets. While the nutritional equivalence of D-*(1)* and L-*(1)* has been established experimentally[1], corresponding studies on D-*(2)* and L-*(2)* have yet to be performed.

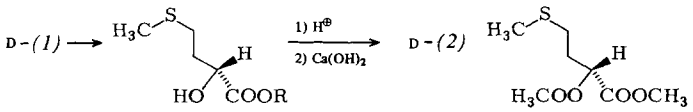


D-*(1)*, X = H, Y = COOH
L-*(1)*, X = COOH, Y = H



D-*(2)*, X = H, Y = COO
L-*(2)*, X = COO, Y = H

We have now prepared these enantiomers for the first time. Diazotization of D-methionine D-*(1)* (by analogy with ref. [2]) gave D-2-hydroxy-4-(methylthio)butyric acid D-*(3)* which was purified *via* the dicyclohexylammonium salt D-*(4)* ($[\alpha]_D^{25} = +22.2°$ ($c = 1$, ethanol, m.p. 127—129 °C) and transformed into the salt D-*(2)* with aqueous calcium hydroxide (no racemization) ($[\alpha]_D^{25} = +24.3$ ($c = 1$, H_2O)). L-*(2)* was obtained analogously from L-*(1)*. Apart from the rotations ((L-*(2)*: $[\alpha]_D^{25} = -25.3°$ ($c = 1$, H_2O); L-*(4)*: $[\alpha]_D^{25} = -22.5°$ ($c = 1$, ethanol)) all the physical data of L-*(2)*, L-*(3)*, and L-*(4)* agree with those of the D-series.



D-*(3)*, R = H
D-*(4)*, R = $(c\text{-}C_6H_{11})_2NH_2$

D-*(5)*

The enantiomeric purity of D-*(3)* was examined (i) by comparison with D-*(3)* obtained by a biochemical route and (ii) by NMR spectroscopy of the derivative D-*(5)*.

(i) The acid D-*(3)* produced by microorganisms[3] affords a salt D-*(4)* having $[\alpha]_D^{25} = +22.2°$ ($c = 1$, ethanol) and m.p. 128—129 °C. The mixed melting point recorded with chemically synthesized D-*(4)* showed no depression.

(ii) The methyl D,L- and D-2-acetoxy-4-(methylthio)butyrates D,L-*(5)* and D-*(5)*, respectively, produced from D,L-*(3)* and D-*(3)* were examined by ^{1}H-NMR spectroscopy[4]. The signals of the methine protons of D,L-*(5)* at 60 and 80 MHz can be separated by addition of the optically active shift reagent Eu(opt)$_3$. On irradiation at the resonance frequency of the neighboring methylene protons ("homo-decoupling"), the methine protons of the enantiomers each appear as singlets at $\delta = 6.48$ and 6.37 (1:1).—In the case of D-*(5)*, the methine proton was found to give a triplet at $\delta = 6.53$ and a singlet at $\delta = 6.53$ with Eu(opt)$_3$, without and with decoupling, respectively. Thus no L enantiomer can be detected in D-*(5)*. On mixing of D-*(5)* with D,L-*(5)* (1:1) and with Eu(opt)$_3$, the decoupled spectrum expectedly shows two signals for the methine proton at 6.50 and 6.37 (3:1).

Procedure

D-*(1)* (596.9 g, 4 mol) is dissolved in 10% sulfuric acid (3430 g) and treated at 0—5 °C with an ice-cooled solution of sodium nitrite (345 g, 5 mol) in water (500 ml). The mixture is allowed to warm overnight to 20—25 °C and then extracted four times with ether (600 ml). The ethereal phase is dried over sodium sulfate and the solvent stripped off; residue, 96.3 g (14.4%) crude D-*(3)* as oil. D-*(4)* crystallizes on addition of dicyclohexylamine to the ethereal solution of D-*(3)*. Repeated recrystallization from ethyl acetate/light petroleum gives 100.2 g (52.4%) of analytically pure[5] D-*(4)*. Hydrolysis of D-*(4)* with dilute sulfuric acid and work-up as above leads to pure D-*(3)*. This residue is taken up in water (100 ml) and treated with calcium hydroxide (9.9 g) in water (100 ml). After treatment with activated charcoal, the solution is evaporated to dryness in a water-pump vacuum; yield 45.4 g (88% of D-*(2)*).

Received: July 12, 1979 [Z 309 IE]
German version: Angew. Chem. *91*, 858 (1979)

CAS Registry numbers:
D-*(1)*, 348-67-4; L-*(1)*, 63-68-3; D-*(2)*, 71597-86-9; L-*(2)*, 71597-87-0; D-*(3)*, 39638-34-1; L-*(3)*, 48042-96-2; DL-*(3)*, 120-91-2; D-*(4)*, 71597-88-1; L-*(4)*, 42588-21-6; D-*(5)*, 71597-89-2; DL-*(5)*, 71629-35-1

[1] *Y. Izumi, I. Chibata, T. Itoh,* Angew. Chem. *90*, 187 (1978); Angew. Chem. Int. Ed. Engl. *17*, 176 (1978); *R. S. Katz, D. H. Baker,* J. Anim. Sci. *41*, 1355 (1975).
[2] *H. Sugano,* Bull. Chem. Soc. Jpn. *46*, 2168 (1973).
[3] We are indebted to Prof. *H. Simon,* München, for providing a solution of D-*(3)* obtained on bioreduction of 4-(methylthio)-2-oxybutyric acid. Analogous enzymatic hydrogenation of five other α-oxocarboxylic acids gave optically pure D-hydroxy carboxylic acids. *H. Simon,* unpublished; *E. Krezdorn,* Dissertation, Technische Universität München 1977.
[4] We thank *R. Benn,* Mülheim/Ruhr, for carrying out and evaluating the measurements.
[5] D-*(2)*, L-*(2)*, D-*(4)*, and L-*(4)* gave correct analyses. The purity of D-*(2)* (100.0%) and L-*(2)* (99.9%) was also determined by gas chromatography.

[*] Dr. A. Kleemann, Dr. B. Lehmann, Dr. J. Martens
Degussa, Fachbereich Forschung Chemie
Postfach 602, D-6450 Hanau (Germany)

Synthesis and Crystal Structure of a Chiral Complex Containing a Non-linear Heterotrimetal Chain: $PtMn_2(\mu_2\text{-}PPh_2)_2(CO)_9$[1]

By *Pierre Braunstein, Dominique Matt, Odile Bars,* and *Daniel Grandjean*[*]

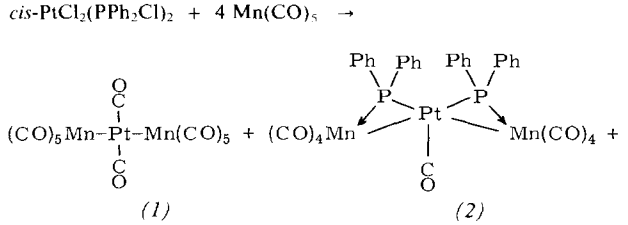
The course of reaction between metal carbonyl anions and square planar substrates of the type ML_2Cl_2 (M = Pd, Pt) depends markedly on the nature of L[2]. Thus *cis*-PtL_2Cl_2, where L = pyridine, reacts with $Mn(CO)_5^-$[3] to give a trimetallic complex containing the linear arrangement

[*] Dr. P. Braunstein [+], D. Matt
Laboratoire de Chimie de Coordination, Associé au C.N.R.S.
Université Louis Pasteur
4 rue Blaise Pascal, F-67070 Strasbourg (France)
Dr. O. Bars, Prof. Dr. D. Grandjean
Laboratoire de Cristallochimie, Associé au C.N.R.S.
Université de Rennes, F-35042 Rennes (France)
[+] Author to whom correspondence should be addressed.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0797 $ 02.50/0*

[Mn–Pt(py)$_2$–Mn], whereas when L = PEt_3 or PPh_3 the homopentametallic clusters $Pt_5(CO)(\mu_2\text{-}CO)_5L_4$[4] are formed.

We have now found that when L = PPh_2Cl, the complexes *(1)* and *(2)* with two new heterotrimetallic [Mn–Pt–Mn] chains can be generated[5] (see Experimental procedure).



(1) *(2)*

The mass spectrum of *(1)* shows the molecular ion at *m/e* = 641 (based on ^{195}Pt). According to dipole moment measurements the three metal atoms are linearly arranged. The ^{31}P-NMR spectrum of *(2)* contains a singlet with two ^{195}Pt-satellites ($\delta = 161$ rel. to H_3PO_4 ext., $^1J(P\text{-}Pt) = 2265$ Hz, in CD_2Cl_2), indicating that the phosphorus atoms are attached to the Pt atom[6]. Although the mass spectrum contains the molecular peak (*m/e* = 927), the molecular structure of *(2)* cannot be unequivocally derived from these data since, according to the 16–18 electron rule, either a closed or an open structure could be envisaged.

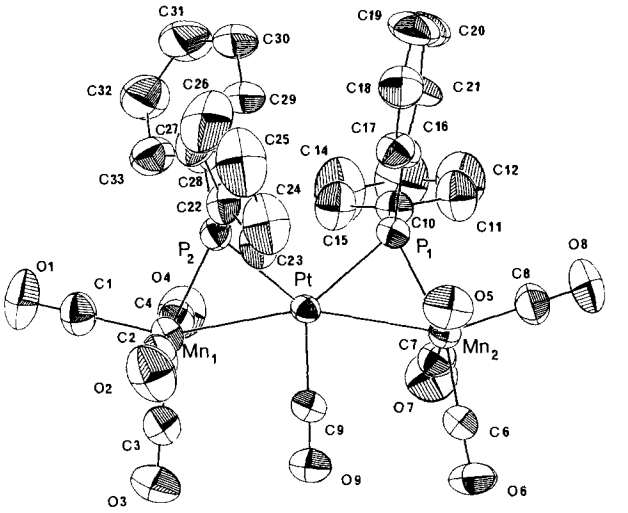


Fig. 1. Structure of *(2)*. Important bond lengths [pm] and angles [°]: Pt–Mn(1): 274.1(1); Pt–Mn(2): 274.7(1); P(2)–Mn(2): 223.7(2); P(1)–Mn(2): 224.1(3); P(1)–Pt: 230.5(2); P(2)–Pt: 231.9(3).
P(1)–Pt–P(2): 101.08(11); Mn(1)–Pt–P(2): 51.65(8); Mn(2)–Pt–P(1): 51.77(8); Mn(1)–Pt–Mn(2): 159.56(4).

As was shown by a single crystal X-ray structure analysis (Fig. 1)[7], each Mn atom is bonded to four terminal CO groups, to the Pt atom, and to a P atom bridging the Pt–Mn bond. (The use of PR_2Cl ligands to form PR_2-bridged metal-metal bonds is already known [8].) The Mn(1)–Pt–Mn(2) angle is 159.56°(4). The CO group which is bonded to the Pt atom is nearly in the plane of the metal atoms[9]. P(1) and P(2) are located on opposite sides of this plane (+0.59 Å (P1) and −0.36 Å (P2)).

The molecule *(2)* has no element of symmetry and thus is chiral. This chirality is inherent in the Mn(1)P(2)PtP(1)Mn(2) framework. Complexes like *(2)*, with a heterotrimetallic *bent* chain containing a Pt atom, were previously unknown. To our knowledge *(2)* is the first *neutral* complex with a nonlinear heterotrimetallic chain and chiral framework; the only other formally comparable species $Rh[Fe(PPh_2)(CO)_2(\pi\text{-}CH_3C_5H_4)]_2^+$[10] has a bent Fe–Rh–Fe chain and a chiral framework, but it is not neutral.

Experimental

All reactions and operations must be carried out under nitrogen. The solvents are dried and distilled under nitrogen before use. A tetrahydrofuran solution (40 ml) of $NaMn(CO)_5$ [prepared from $Mn_2(CO)_{10}$ (1.60 g, 4 mmol)] is filtered and added to a suspension of *cis*-$Pt(PPh_2Cl)_2Cl_2$ (1.41 g, 2 mmol) in THF (50 ml) at 0 °C. The dark-red mixture is then stirred for 2 h at room temperature. The residue obtained after filtration and evaporation under reduced pressure is chromatographed on a silica gel column (Kieselgel 60, Merck). Elution with pentane gives a red solution of *(1)*, affording analytically pure claret-colored needles on crystallization at −78 °C; yield 0.04 g (3% based on Pt), m.p. 60 °C (decomp.), ν(CO) in KBr: 2066 s, 2046 s, 2022 s, 1994 sh, 1984 vs, 1967 vs cm^{-1}. Further elution with pentane gives a more concentrated red solution from which orange-red analytically pure crystals of *(2)* can be obtained at −10 °C; yield: 0.20 g (11%), m.p. 171–172 °C, ν(CO) in KBr: 2069 s, 2050 s, 2000 sh, 1990 vs, 1970 vs, 1945 vs cm^{-1}. Elution with toluene/pentane mixtures gives products which have not yet been characterized.

Received: May 21, 1979 [Z 310 IE]
German version: Angew. Chem. *91*, 859 (1979)

CAS Registry numbers:
(1), 71597-14-3; *(2)*, 71597-15-4; $NaMn(CO)_5$, 13859-41-1; *cis*-$Pt(PPh_2Cl)_2Cl_2$, 61586-84-3

[1] Organometallic Complexes with Metal-Metal Bonds, Part 14. This work was supported by the Centre National de la Recherche Scientifique.—Part 13: *R. Bender, P. Braunstein, Y. Dusausoy, J. Protas*, J. Organomet. Chem. *172*, C 51 (1979).
[2] *R. Bender, P. Braunstein, Y. Dusausoy, J. Protas*, Angew. Chem. *90*, 637 1978); Angew. Chem. Int. Ed. Engl. *17*, 596 (1978); *J. P. Barbier, P. Braunstein, J. Fischer, L. Ricard*, Inorg. Chim. Acta *31*, L 361 (1978); *J. P. Barbier, P. Braunstein*, J. Chem. Res. (S) *1978*, 412; (M) *1978*, 5029.
[3] *P. Braunstein, J. Dehand*, J. Organomet. Chem. *81*, 123 (1974).
[4] *J. P. Barbier, R. Bender, P. Braunstein, J. Fischer, L. Ricard*, J. Chem. Res. (S) *1978*, 230; (M) *1979*, 2913.
[5] Both compounds were characterized by elemental analysis (C, H) and IR and mass spectrometry.
[6] A large downfield shift is not unusual for three-membered PM^1M^2 rings; see *e.g. C. W. Bushnell, K. R. Dixon, P. M. Moroney, A. D. Rattray, C. Wan*, J. Chem. Soc. Chem. Commun. *1977*, 709; *E. Keller, H. Vahrenkamp*, J. Organomet. Chem. *155*, C 41 (1978).
[7] *(2)*, triclinic crystals, space group $P\bar{1}$, $Z = 2$, $a = 10.240(5)$, $b = 10.812(4)$, $c = 17.483(8)$ Å, $\alpha = 94.89(3)$, $\beta = 101.41(5)$, $\gamma = 112.14(3)°$, $V = 1730$ Å^3. 4861 reflections ($1° < \theta < 30°$, $Mo_{K\alpha}$, graphite monochromated radiation). All reflections were used in structure solution and refinement; $R = 0.043$.
[8] *H. Vahrenkamp*, Angew. Chem. *90*, 403 (1978); Angew. Chem. Int. Ed. Engl. *17*, 379 (1978).
[9] The distance between C(9) and the Mn(1)–Pt–Mn(2) plane is +0.12 Å.
[10] *R. Mason, J. A. Zubieta*, J. Organomet. Chem. *66*, 279 (1974); *A. Agapiou, S. E. Pedersen, L. A. Zyzyck, J. R. Norton*, J. Chem. Soc. Chem. Commun. *1977*, 393.

The Morpholino Group as Stereoindicator in Aminobicyclo[4.1.0]heptanes[**]

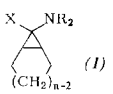
By *Elmar Vilsmaier* and *Wolfgang Tröger*[*]

The *exo-endo* assignment of aminobicyclo[*n*.1.0]alkanes *(1)*, especially those with two bridge substituents, is difficult if they are prepared from haloenamines ($n = 3$[2,4]; $n = 4$[4,6]) and nucleophiles. Among the compounds *(1)* synthesized in this way, the stereochemistry has been established by X-ray structure analysis [*(1a)*[5]] or from the ^1H-NMR coupling

[*] Prof. Dr. E. Vilsmaier, Dipl.-Chem. W. Tröger
Fachbereich Chemie der Universität
Paul-Ehrlich-Strasse, D-6750 Kaiserslautern (Germany)

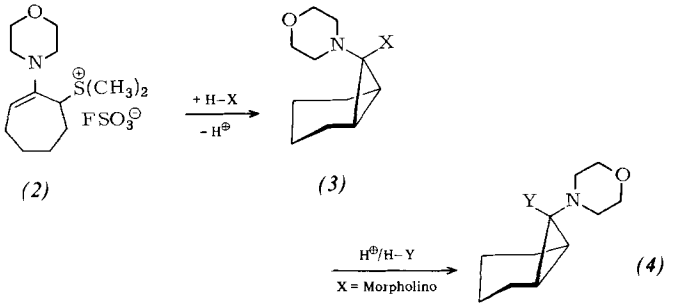
[**] Enaminosulfonium Salts, Part 3.—Part 2: [1].

constant for X=H [*(1b)*[5], *(1c)*[2b], *(1d)*[3]]. Aminobicyclo[*n*.1.0]alkanes *(1)* are of preparative and theoretical interest, *e.g.* as substrates for studies on the substitution of cyclopropane rings.



(1)

	n	X	NR_2
a	4	*endo*-OH	*exo*-Pyrrolidino
b	4	*exo*-H	*endo*-Pyrrolidino
c	3	*exo*-H	*endo*-Piperidino
d	3	*exo*-H	*endo*-$N(CH_3)_2$
e	4	Pyrrolidino	Pyrrolidino
f	4	OCH_3	Pyrrolidino



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

We have found the reaction of *S,S*-dimethyl(2-morpholino-2-cycloheptenyl)sulfonium fluorosulfonate *(2)*[1] with nucleophiles H–X and a base to provide a new entry to bicyclo[4.1.0]heptanes *(1)*, NR_2 = morpholino, $n=4$. Moreover, it was also found that the morpholino group in *(1)* permits facile ^{1}H-NMR spectroscopic assignment of *(1)* [see *(3)* and *(4)*].

Reaction of the sulfonium salt *(2)* and morpholine gives 7,7-dimorpholinobicyclo[4.1.0]heptane *(3g)*. A dimorpholinocycloheptene constitution can be ruled out on the basis of the IR (no C=C bond) and the ^{13}C-NMR spectrum (no signals with $\delta>90$ ppm). The ^{1}H-NMR spectrum (Table 1) shows an AA'XX' system for the protons of one morpholine ring and an ABXY system for the other. On heating ([D_5]nitrobenzene) the ABXY system coalesces at 125 °C ($\Delta G^{\neq}=80.9$ kJ/mol); at 210 °C these morpholine protons also show an AA'XX' system. The AA'XX' system of the protons belonging to the other morpholine ring recorded at room temperature does not coalesce on cooling to −40 °C (CD_2Cl_2).

In the case of morpholines bearing an achiral *N*-substituent, the ring protons appear as an AA'XX' system owing to fast rotation and inversion[7]. However, an ABXY system is to be expected if rotation[7,8] or inversion[7,8] are hindered. The ABXY pattern of *(3g)* resembles the low-temperature spectrum of *N*-methylmorpholine[7] (−40 °C, slow ring inversion) in shape and coupling constants. Owing to the steric situation in *(3g)*, the AA'XX' signal system must accordingly be assigned to the *exo*-morpholino and the ABXY system to the *endo*-morpholino group[9].

The dipyrrolidine compound analogous to *(3g)*, *i.e.* *(1e)*, affords *(1a)*[5] on treatment with aqueous hydrochloric acid and *(1f)* [no structure reported][6] with methanol. By analogy we obtained *(4h)* from *(3g)* and aqueous hydrochloric acid and *(4i)* with methanol/H^+. Both compounds exhibit an AA'XX' pattern (Fig. 1a) for the morpholine protons. We

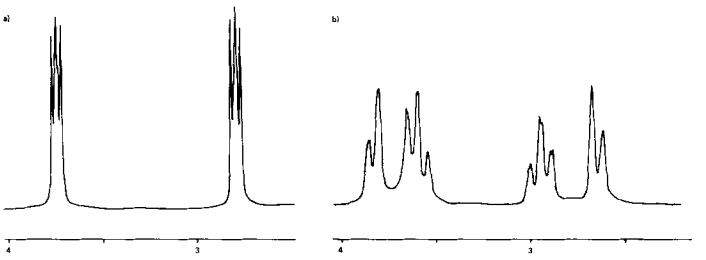


Fig. 1. ^{1}H-NMR morpholine signals of 7-morpholinobicyclo[4.1.0]heptan-7-ols. a) *(4h)* and b) *(3h)*; 200 MHz, $CDCl_3$, δ values.

obtained isomers of *(4h)* and *(4i)* by reaction of *(2)* with $OH^{\ominus}$ and $CH_3O^{\ominus}$. These isomers each give only an ABXY system for the morpholine protons (Fig. 1b). Thus it is possible to assign the *endo*-morpholine configuration to *(3h)* and *(3i)* and the *exo*-morpholine configuration to *(4h)* and *(4i)*.

We attribute the formation of *(3h)* and *(3i)* from *(2)* to steric effects of substitution. The isomerization of *(3h)* and *(3i)* to *(4h)* and *(4i)* even by traces of acid in chloroform can readily be followed by ^{1}H-NMR spectroscopy. Thus, the unexpected formation of *(1a)* from *(1e)* and of *(4h)* and *(4i)* from *(3g)* with acid is probably the result of thermodynamically controlled isomerization.

Hence introduction of the morpholino group in place of the previously used dimethylamino, pyrrolidino, and piperidino groups in 7-aminobicyclo[4.1.0]heptanes permits facile *exo-endo* assignment of the bridge substituents by ^{1}H-NMR spectroscopy.

Procedure

Synthesis of *(3g)*: Compound *(2)*[1] (34.1 g, 0.1 mol) is refluxed with morpholine (17.4 g, 0.2 mol) in anhydrous acetonitrile (80 ml) for 1.5 h. After removal of solvent *in vacuo*, the residue is extracted twice with ether (2 × 100 ml) and the ethereal phase is vacuum distilled; yield: 19.2 g (72%) of *(3g)*, b.p. 80—86 °C/0.02 torr.

Synthesis of *(3h)*: A solution of *(2)* (3.4 g, 10 mmol) and sodium carbonate (1.0 g, 10 mmol) in water (50 ml) is cov-

Table 1. Spectroscopic data of 7-morpholinobicyclo[4.1.0]heptanes of type *(3)* and *(4)*. δ values, solvent $CDCl_3$.

	Yield [%]	M.p. [°C]	^{1}H-NMR (200 MHz, 10 °C) Signal system	NCH_2 δ_A	NCH_2 δ_B	OCH_2 δ_X	OCH_2 δ_Y	^{13}C-NMR [a] NCH_2	OCH_2	quat. C atom
(3g), X = Morpholino	72	75	ABXY [b]	2.50	2.95	3.55	3.75	51.7	67.7	67.5
			AA'XX' [c]	2.55 (mc)		3.60 (mc)		50.0	67.6	
			AA'XX' [c, e]	2.60 (mc)		3.60 (mc)			—	
			AA'XX' [c, e]	2.75 (mc)		3.55 (mc)			—	
(3h), X = OH	61	75	ABXY [b, d]	2.45	2.95	3.60	3.85	48.2	67.4	75.9
(3i), X = OCH_3	72	49	ABXY [b, d]	2.80	3.10	3.55	3.80	49.9	67.9	82.3
(4h), Y = OH	69	128	AA'XX' [c]	2.75 (mc)		3.65 (mc)		47.5	67.3	77.0
(4i), Y = OCH_3	74	— [f]	AA'XX' [c]	2.85 (mc)		3.50 (mc)		49.1	67.8	82.0

[a] 3 further signals for ring C atoms. [b] *J* [Hz]: $J_{AB}=11.5$—11.6; $J_{XY}=10.4$—11.2; $J_{AX}\approx 2.0$; $J_{BX}\approx 11.5$; $J_{AY}<1.5$; $J_{BY}\approx 3.0$. [c] Typical morpholine AA'XX' system. [d] Addition of 5% pyridine to avoid isomerization. [e] At 210 °C. [f] B.p. 53–57 °C/0.02 torr.

ered with ether (50 ml) and stirred for 6 d at room temperature. After drying and concentration of the ethereal phase to 5 ml, a yield of 1.2 g (61%) of *(3h)* is obtained on cooling.

Received: July 16, 1979 [Z 311a IE]
German version: Angew. Chem. *91*, 860 (1979)

[1] *E. Vilsmaier, W. Tröger, W. Sprügel, K. Gagel*, Chem. Ber. *112*, 2997 (1979).
[2] a) *D. Cantacuzene, M. Tordeux*, Tetrahedron Lett. *1971*, 4807; b) *J. Szmuszkovicz, E. Cerda, M. F. Grostic, J. F. Zieserl, ibid. 1967*, 3969.
[3] *J. C. Blazejewski, D. Cantacuzene, C. Wakselman*, Tetrahedron *29*, 4233 (1973).
[4] *H. H. Wasserman, M. J. Hearn, B. Haveaux, M. Thyes*, J. Org. Chem. *41*, 153 (1976).
[5] *J. Smuszkovicz, D. J. Duchamp, E. Cerda, C. G. Chidester*, Tetrahedron Lett. *1969*, 1309.
[6] *H. H. Wasserman, M. S. Baird*, Tetrahedron Lett. *1971*, 3721.
[7] *R. K. Harris, R. A. Spragg*, Chem. Commun. *1966*, 314; *R. A. Spragg*, J. Chem. Soc. *B 1968*, 1128.
[8] *P. le Cam, J. Sandström*, Chem. Scr. *1*, 65 (1971).
[9] AA'XX' and ABXY signal patterns can also be clearly distinguished in the 90 and 60 MHz spectrum. We attribute the ABXY pattern to hindered rotation around the C N bond; the coupling constants found require the presence of essentially a single conformation at fast ring and N inversion.

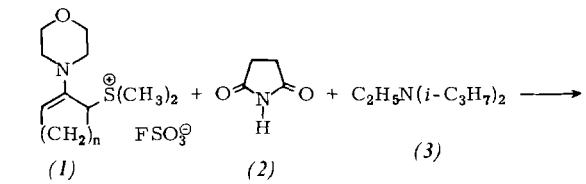
Morpholino(succinimido)bicyclo[*n*.1.0]alkanes from Enaminosulfonium Salts[**]

By *Elmar Vilsmaier* and *Claus Michael Klein*[*]

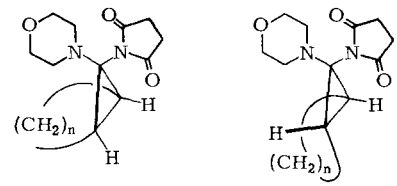
Starting from the enaminosulfonium salt *(1b)* and nucleophiles, we have prepared 7-morpholinobicyclo[4.1.0]heptanes whose stereochemistry can be determined by ^{1}H-NMR spectroscopy[1], and now wish to report about application of this method of synthesis and structural assignment to morpholinobicyclo[*n*.1.0]alkanes of various ring sizes taking succinimide as nucleophile.

Enaminosulfonium salts *(1a—e)* are treated with succinimide *(2)* in the presence of diisopropylethylamine *(3)* in anhydrous acetonitrile. After removal of the solvent and washing with aqueous potassium hydroxide solution (5%), colorless crystals are obtained in each case. On the basis of their ^{1}H-NMR, ^{13}C-NMR, and IR spectra, we assign the morpholino(succinimido)bicyclo[*n*.1.0]alkane structure *(4)* to these products. Compounds *(4)* can also be prepared by direct reaction of an enamine *(7)* with the succinimidosulfonium salt *(6)*[12], for *(6)* and *(7)* give an equimolar mixture of *(1)* and *(2)*.

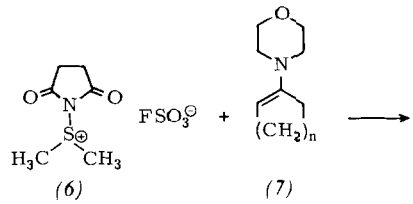
The ^{1}H-NMR spectra of 7-morpholinobicyclo[4.1.0]heptanes recorded at room temperature contain an AA'XX' system for *exo*-morpholine and an ABXY system for *endo*-morpholine[1]. Compounds *(4a—c)* give only an ABXY system which coalesces to an AA'XX' system above 120 °C (Table 1). Thus the morpholino group also proves to be a stereoindicator in these bicyclic systems; the *endo*-morpholino structure is to be assigned to compounds *(4a—c)*[3]. The coalescence temperature (T_c) is expectedly much lower for *(4d)* and *(4e)*.



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



(4) *(5)*



(6) *(7)*

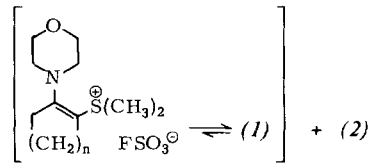


Table 1. Spectroscopic data of the morpholino(succinimido)bicyclo[*n*.1.0]alkanes of types *(4)* and *(5)*. δ values, solvent $CDCl_3$. T_c = coalescence temperature (in $C_2D_2Cl_4$).

	n	Yield [%]	M.p. [°C]	^{1}H-NMR (10 °C) NCH$_2$ [a] δ_A	δ_B	OCH$_2$ [a] δ_X	δ_Y	^{13}C-NMR NCH$_2$	OCH$_2$	quart. C	C=O	T_c [°C]/(ΔG^+ [kJ/mol]) Morpholine-AB	T_c Succinimide [b]
(4a)	3	60	187	2.39	2.81	3.71	3.45	50.7	67.2	57.5	177.9	120/(79.9)	30
(4b)	4	52	184	2.38	2.84	3.72	3.52	50.8	67.2	56.0	178.2	120/(79.6)	45
(4c)	5	52	193	2.42	2.65	3.72	3.52	50.8	67.2	59.7	178.0	112/(80.3)	—
(4d)	7	36	159	2.36	2.80	3.72	3.50	51.0	67.2	54.8	178.5	50/(66.1)	35
(4e)	8	48	144	2.65 (mc)		3.6 (mc) [c]		51.2	67.1	54.4	178.1	5/(54.8)	20
				2.28	2.89	3.70	3.48 [d]						
(5e)	8	39	112	2.13—2.87 (m) [e]		3.5 (mc) [c]		51.0	66.8	59.4	178.6 173.3	— [e]	—

[a] J [Hz]: J_{AB} = 11.5—14, J_{XY} = 9.6—11.6, $J_{AX} \approx 3$, $J_{BX} \approx 1$, J_{AY} = 10.3—11.9, $J_{BY} \approx 1.5$. [b] Above T_c, singlet at δ = 2.6; below T_c form of an AA'BB' system. [c] Typical morpholine signal. [d] At −50 °C. [e] Complex splitting of NCH$_2$ protons owing to chirality; coalescence detectable only for OCH$_2$ signal.

A rotation barrier can also be detected for the succinimidocyclopropane bond of *(4a—e)* by ^{1}H-NMR spectroscopy. Transition from the AA'BB' signal system to the singlet takes place just above room temperature. The ring size has only a slight effect on this process, thus indicating the uniform *exo* position of the succinimido group. Hence the *endo*-morpholine structures *(4d)* and *(4e)* are assigned to the compounds obtained by reaction of *(6)* with *(7d)* and *(7e)* respectively[4].

[*] Prof. Dr. E. Vilsmaier, Dipl.-Chem. C. M. Klein
Fachbereich Chemie der Universität
Paul-Ehrlich-Strasse, D-6750 Kaiserslautern (Germany)

[**] Enaminosulfonium Salts, Part 4.—Part 3: [1].

Depending upon the procedure adopted, two isomeric bicyclo[8.1.0]undecanes can be obtained from *(6)* and *(7e)*. Direct addition of *(3)* to a mixture of *(6)* and *(7e)* gives a colorless precipitate which proves to be pure *(4e)*. *cis*-Linkage of the two rings follows from the five signals observed for the ten-membered ring in the ^{13}C-NMR spectra [plane of symmetry in *(4)*]. If *(6)* and *(7e)* are allowed to stand for 48 h prior to addition of *(3)*, then 10% of *(4e)* is accompanied by 39% of an isomer. The *trans* product *(5e)* was deduced from the ^{13}C-NMR spectrum; the lack of symmetry in *(5e)* requires the occurrence of 11 signals for the 11 C atoms of the bicyclic system. Owing to chirality, *(5e)* shows a complex ^{1}H-NMR spectrum in the region of the morpholine NCH_2 protons; the OCH_2 signal corresponds to that of a normal morpholine molecule. In contrast to the situation in *(4e)*, the spectrum does not change down to $-20\,^\circ$C (Table 1). The purity of *(4e)* (>99%) and of *(5e)* (≈95%) was established by HPLC[5].

We assume that the compounds *(4a—e)* arise from *(1)* *via* bicyclic iminium salts (cf. [6]). They are preferentially attacked from the *exo* side (cf. [7]) and lead to the *endo*-morpholino bicyclic compounds *(4)*.

Procedure

Synthesis of *(4)*: To a stirred suspension of *S,S*-dimethylsuccinimidosulfonium fluorosulfate *(6)* (1.3 g, 5 mmol) in anhydrous acetonitrile (5 ml) is added compound *(7)* (5 mmol) at $-10\,^\circ$C. After 30 min at $-10\,^\circ$C, compound *(3)* (0.64 g, 5 mmol) is added. With *(7a—c)* the mixture is refluxed for 24 h, the solvent then being removed under vacuum and the residue washed twice with 5% aqueous KOH (2 × 30 ml) before being rubbed with pentane (20 ml) and dried in a vacuum. With *(7d—e)* stirring is continued for 18 h after addition of amine and the crystals filtered off under suction. They are successively washed with pentane (10 ml) and 5% aqueous KOH (30 ml), and then dried in a vacuum. A further crop of *(4d)* can be obtained by concentration of the acetonitrile solution.

Received: July 16, 1979 [Z 311 b IE]
German version: Angew. Chem. *91*, 861 (1979)

[1] *E. Vilsmaier, W. Tröger*, Angew. Chem. *91*, 860 (1979); Angew. Chem. Int. Ed. Engl. *18*, 798 (1979).
[2] *E. Vilsmaier, W. Tröger, W. Sprügel, K. Gagel*, Chem. Ber. *112*, 2997 (1979).
[3] Replacement of succinimido by phthalimido in *(4b)* accordingly does not affect the ^{1}H-NMR signals of the tetramethylene bridge.
[4] *Note added in proof* (September 9, 1979): X-ray structural analysis has confirmed the assignment *(4e)*.
[5] SP 8000 Spectra Physics, column 250 × 4.6 mm, silica gel 10 μm Li Chromosorb Si 100 Silica, chloroform 2 ml/min, ret. times: *(4e)*, 576 s; *(5e)*, 517 s.
[6] Cyclopropylidene- and 7-bicyclo[4.1.0]heptylidene-dimethylammonium salts have been isolated a) *E. Jongejan, W. J. M. van Tilborg, Ch. H. V. Dusseau, H. Steinberg, Th. J. de Boer*, Tetrahedron Lett. *1972*, 2359; b) *E. Jongejan, H. Steinberg, Th. J. de Boer*, Synth. Commun. *4*, 11 (1974); c) Rec. Trav. Chim. Pays-Bas *98*, 66 (1979).
[7] *K. Kitatani, T. Hiyama, H. Nozaki*, Bull. Chem. Soc. Jpn. *50*, 3288 (1977); *W. Kirmse, H. Jendralla*, Chem. Ber. *111*, 1857 (1978).

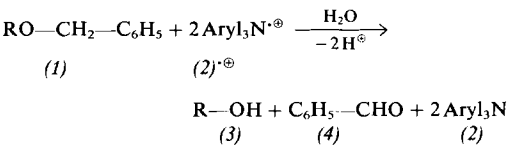
Oxidative Removal of the Benzyl Ether Protecting Group by Homogeneous Electron Transfer[1]

By *Werner Schmidt* and *Eberhard Steckhan*[*]

We recently reported the mild oxidative deprotection of *p*-methoxybenzyl ethers by homogeneous electron transfer with the tris(*p*-bromophenyl)amine cation radical, thus providing a convenient alternative to the usual reductive deprotection[2]. Internal electrochemical regeneration of the electron transfer agent permits use of only catalytic amounts of the reagent.

The benzyl ether function, however, is not attacked by this electron transfer agent.

We have now found a simple and relatively mild method for the oxidative removal of the benzyl ether protecting group with electron transfer agents of type *(2)*, whose cation radicals have a higher oxidation potential than the tris(*p*-bromophenyl)amine cation radical. A route is thus opened up for the selective protection and selective liberation of primary and secondary hydroxy functions (see [3]).



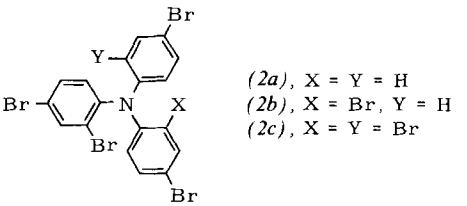


Table 1. Oxidative debenzylation of the ethers *(1)* by homogeneous electron transfer according to methods 1 and 2 (see Procedure).

(1), R	*(2)*	*(3)*, Yield [%] [d] Meth. 1	Meth. 2	b.p. [°C/torr] Lit. data
(1a) n-C_8H_{17}	*(2a)* [a]	10	5	
		90 [c]	95 [c]	
	(2b) [a]	95	30	95/18
			70 [c]	98/19 [7]
	(2c)	90	87	
(1b) n-$C_6H_{13}CH(CH_3)$	*(2b)* [a]		93	90/18
	(2c) [b]	95		87/20 [7]
(1c) Cyclohexyl	*(2c)* [b]	90	94	165/760
				161/760 [7]
(1d) n-$C_3H_7CHOH\,CH\,CH_2$ (C_2H_5)	*(2c)* [b]	45	45	95/1
				91–93/2 [8]

[a] In the presence of 2,6-dimethylpyridine. [b] In the presence of $NaHCO_3$. [c] Recovered benzyl ether *(1)*. [d] Material yield.

We have examined the cation radicals of the triarylamines *(2a)—(2c)* (synthesis, see [4]) having redox potentials of +1.42 *(2a)*, +1.56 *(2b)* and +1.74 V *(2c)*, measured against the normal hydrogen electrode (NHE), as electron transfer agents for the oxidative debenzylation of the ethers *(1a)—(1d)*.

In the preparative reaction the cation radical $(2)^{\cdot\oplus}$ can either be used in molar amounts as its readily obtainable[4] stable hexachloroantimonate (method 1) or it can be electrochemically generated and regenerated from catalytic amounts of *(2)* during the course of the reaction (method 2). In the presence of bases such as 2,6-dimethylpyridine or $NaHCO_3$ the reaction is considerably accelerated (see Table 1).

Benzyl octyl ether *(1a)* is a suitable example with which to monitor the effectiveness of the electron transfer agents. Owing to an inadequate redox potential, the cation radicals of

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

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1010-0801 $ 02.50/0*

(2a) and *(2b)* lead to only incomplete conversion of the benzyl ether *(1a)* according to method 2. The concentration of the benzyl ether cation radical in the electron transfer equilibrium is apparently so low that the follow-up chemical reactions are unable to shift the equilibrium sufficiently in favor of the products[5]. On the other hand, owing to the increased steady state concentration of the benzyl ether cation radical, *(2b)* leads by method 1 to complete conversion and almost quantitative yields of alcohol. *(2c)*, with a still higher redox potential, leads to excellent yields of alcohols in both methods, even in the absence of bases. The electrochemically determined irreversible oxidation potentials of the isomeric ethers *(1a)* (+2.50 V) and *(1b)* (+2.46 *vs.* NHE) differ by 40 mV. This potential difference is responsible for the fact that the secondary ether *(1b)* is quantitatively cleaved by the agent *(2b)* even according to method 2. Deprotection of benzyl 2-ethyl-3-hydroxyhexyl ether *(1d)* by the cation radical of *(2c)* leads to only moderate yields of the alcohol, since the oxidizing agent apparently attacks the secondary function in a side reaction.

From these findings it can be concluded that if the deprotection of alcohols is carried out in the presence of other oxidation-labile groups, a maximum selectivity is reached when the benzyl ether protecting group is removed from primary alcohols with *(2b)* according to method 1, whereas in the case of secondary alcohols method 2 can also be employed. In the absence of oxidation-labile functions *(2c)* is superior as electron transfer agent owing to its higher rate of reaction and ease of preparation.

General procedure

Method 1: A solution of the triarylammoniumyl hexachloroantimonate in CH_3CN is added dropwise to the solution of *(1)* (2 mmol) and 2,6-dimethylpyridine (0.212 g, 2 mmol) or $NaHCO_3$ (0.5 g, 6 mmol) in CH_3CN[6] until conversion of *(1)* is complete (GC control). On using *(2a)* or *(2b)* *ca.* 5 to 6 mmol, of the cation radical salt is necessary, on using *(2c)* *ca.* 8 mmol. The alcohols are isolated and identified as described in [2].

Method 2: In a divided beaker-type glass cell (20 °C, Pt anode, Pt cathode) a solution of *(2)* (2 mmol) in CH_3CN[6]/CH_2Cl_2 (5:1; 0.2 M $LiClO_4$) is used as anolyte; the catholyte consists of CH_3CN/1.0 M $LiClO_4$. After application of the redox potential of *(2a)*, *(2b)*, or *(2c)* the intense color of the cation radical appears. On addition of *(1)* (5 mmol) and 2,6-dimethylpyridine (0.535 g, 5 mmol) or $NaHCO_3$ (0.5 g, 6 mmol) the solution first decolorizes. After reappearance of the color of the cation radical and complete conversion (GC control) of *(1)* (consumption of *ca.* 0.020 F) the electrolysis is stopped.

Received: June 11, 1979 [Z 312a IE]
German version: Angew. Chem. *91*, 850 (1979)

[1] Part 7 of Indirect Electrochemical Processes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 6: *W. Schmidt, E. Steckhan*, J. Electroanal. Chem. *101*, 123 (1979).

[2] *W. Schmidt, E. Steckhan*, Angew. Chem. *90*, 717 (1978); Angew. Chem. Int. Ed. Engl. *17*, 673 (1978).

[3] *W. Schmidt, E. Steckhan*, Angew. Chem. *91*, 851 (1979); Angew. Chem. Int. Ed. Engl. *18*, 802 (1979).

[4] *W. Schmidt, E. Steckhan*, Chem. Ber., in press.

[5] For mechanistic details, see [2].

[6] For *(2a)* and *(2b)*: acetonitrile (Merck), water content 0.3—0.5%; for *(2c)*: acetonitrile (Merck, UVASOL), water content 0.03%.

[7] Handbook of Chemistry and Physics. 53rd Edit. Chemical Rubber Co., Cleveland, Ohio 1972.

[8] *R. L. Wear*, J. Am. Chem. Soc. *73*, 2390 (1951).

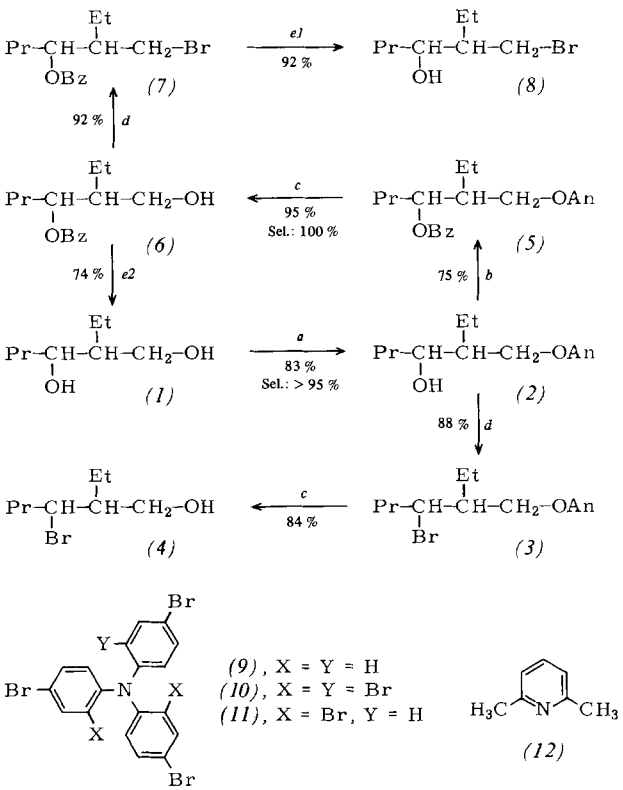
Selective Deprotection of Primary and Secondary Hydroxy Functions by Homogeneous Electron Transfer[1]

By *Werner Schmidt* and *Eberhard Steckhan*[*]

Both benzyl ether[2] and *p*-methoxybenzyl ether protecting groups[3] can be removed oxidatively if differently substituted triarylamine cation radicals are used as electron transfer agents. Owing to the ease of internal electrochemical regeneration of the agent only catalytic amounts of triarylamine are necessary. The *p*-methoxybenzyl ether group can be removed with the radical cation of tris(*p*-bromophenyl)amine *(9)*[3], whereas the benzyl ether function is not attacked by this agent. Removal of the benzyl ether function can, however, be achieved with the cation radicals of the amines *(10)*[2] and *(11)*[2]. We have now exploited this behavior for the directed functionalization and selective liberation of primary and secondary hydroxy functions.

This new method is a convenient and effective alternative for the directed protection/deprotection of primary and secondary hydroxy functions by cathodic cleavage of a 10-oxo-9-phenyl-9,10-dihydro-9-anthryl ether in the presence of a substituted benzyl ether[4], particularly in the case of reduction-labile compounds.

The efficiency of the method is demonstrated in Scheme 1 using as example the selective bromination of the primary and secondary OH groups in 2-ethyl-1,3-hexanediol *(1)*. The reaction sequence a, b, c, has also been effected with 1,3-butanediol: The yields (selectivities) were 75 (90), 69 and 90 (100%), respectively.



Scheme 1. Selective bromination of primary and secondary hydroxy groups of *(1)*. The material yields are given. An = *p*-methoxybenzyl, Bz = benzyl, Et = ethyl, Pr = *n*-propyl. For reaction steps a—e, see *Experimental*.

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

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1010-0802 $ 02.50/0

Since the oxidative removal of benzyl ether functions by homogeneous electron transfer both with molar amounts of triarylamine cation radicals (method 1)[2, 3] and with catalytic amounts of triarylamine and internal electrochemical generation and regeneration of the cation radical (method 2, indirect electrolysis)[2, 3] leads to comparably good results, only one method was used for every step in each case. In this way 3-(bromomethyl)-4-heptanol *(8)* could be prepared isomerically pure in a material yield of 50% *via* five steps from *(1)*. We obtained 3-bromo-2-ethyl-1-hexanol *(4)* in 61% yield *via* three steps. For comparison: In the reaction of *(1)* with molar amounts of Ph_3PBr_2 a 1:1 mixture of the bromo alcohols *(4)* and *(8)* was formed in a yield of 93%, together with 5% dibromo compound. In the case of these bromo alcohols all attempts at separation failed.

The completely selective removal of the *p*-methoxybenzyl ether protecting group in the presence of the benzyl ether protecting group offers new possibilities, especially in carbohydrate chemistry. Other methods for the removal are much less selective or even non-selective. For example, direct anodic oxidation[5] of *(5)* leads, despite potential control, to cleavage of both *p*-methoxybenzyl ether and benzyl ether. Moreover, the anode becomes passivated, the yields are poor, and the products contain numerous impurities[6].

Experimental[8]

(2) from *(1)* (Step *a*): To a solution of *(1)* (14.62 g, 100 mmol) in anhydrous dioxane (100 ml) is added 2.3 g (100 mmol) of Na and the mixture heated (reflux, stirring) for 4 h at 100 °C. After cooling to 30 °C, anisyl chloride (17.16 g, 110 mmol) is added dropwise. The mixture is treated with ether, neutralized with 2 N HCl, extracted three times with water and the ethereal phase dried over $MgSO_4$. Bulb-to-bulb distillation at 120 °C/0.05 torr furnishes 21.9 g (83%) of *(2)*. According to the ^{1}H-NMR spectrum the selectivity is at least 95%.

(5) from *(2)* (Step *b*): *(2)* (9.32 g, 35 mmol) is allowed to react with NaH in anhydrous dimethylformamide (DMF) and benzyl chloride, as described in [5c]. Bulb-to-bulb distillation at 140 °C/0.05 torr gives 9.29 g (75%) of *(5)*.

(6) from *(5)* and *(4)* from *(3)* (Step *c*): *(5)* (0.99 g, 3 mmol) or *(3)* (1.65 g, 5 mmol) is allowed to react with *(9)* (0.48 g, 1 mmol) and *(12)* (0.321 g, 3 mmol or 0.535 g, 5 mmol) according to the procedure described in [3], method 2. Bulb-to-bulb distillation affords 0.67 g (95%) of *(6)* or 0.87 g (84%) of *(4)*, respectively. Gas chromatographic and spectroscopic selectivity checking show that the benzyl ether function in *(6)* is completely retained.

(7) from *(6)* and *(3)* from *(2)* (Step *d*): *(6)* (0.43 g, 2 mmol) or *(2)* (1.33 g, 5 mmol) is brominated with Ph_3PBr_2 in anhydrous DMF according to the procedure given in [7]. Bulb-to-bulb distillation gives 0.55 g (92%) *(7)* or 1.45 g (88%) *(3)*, respectively.

(8) from *(7)* (Step *e1*): *(7)* (0.48 g, 1.6 mmol) is cleaved with *(10)*$^{\oplus}$$SbCl_6^{\ominus}$ (8.4 g, 8 mmol) and $NaHCO_3$ (0.5 g, 6 mmol) according to the method given in [2], method 1. Bulb-to-bulb distillation gives 0.31 g (92%) of *(8)*.

(1) from *(6)* (Step *e2*): *(6)* (0.24 g, 1 mmol) is cleaved with *(11)* (0.064 g, 0.1 mmol) and *(12)* (0.107 g, 1 mmol) according to the method in [2], method 2. Bulb-to-bulb distillation gives 0.11 g (74%) of *(1)*.

Received: June 11, 1979 [Z 312b IE]
German version: Angew. Chem. *91*, 851 (1979)

[1] Part 8 of Indirect Electrochemical Processes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 7: [2].
[2] *W. Schmidt, E. Steckhan*, Angew. Chem. *91*, 850 (1979); Angew. Chem. Int. Ed. Engl. *18*, 801 (1979).
[3] *W. Schmidt, E. Steckhan*, Angew. Chem. *90*, 717 (1978); Angew. Chem. Int. Ed. Engl. *17*, 673 (1978).
[4] *H. J. Schäfer, C. van der Stouwe*, Tetrahedron Lett. *1979*, 2643.
[5] Direct anodic oxidation of benzyl ethers, see a) *L. L. Miller, J. F. Wolf, E. A. Mayeda*, J. Am. Chem. Soc. *93*, 3306 (1971); b) *E. A. Mayeda, L. L. Miller, J. F. Wolf, ibid. 94*, 6811 (1972); c) *S. M. Weinreb, G. A. Epling, R. Comi, M. Reitano*, J. Org. Chem. *40*, 1356 (1975); d) *S. Czernecki, G. Gorson*, Tetrahedron Lett. *1978*, 4113.
[6] *W. Schmidt, E. Steckhan*, unpublished work.
[7] *G. A. Wiley, R. L. Hershkowitz, B. M. Rein, B. C. Chung*, J. Am. Chem. Soc. *86*, 964 (1964).
[8] All compounds gave correct analyses (C, H (Br)) and characteristic IR, ^{1}H-NMR and mass spectra.

BOOK REVIEWS

Solvent Effects in Organic Chemistry. Monographs in Modern Chemistry, Vol. 3, *C. Reichardt*. Verlag Chemie, Weinheim 1979. xi, 355 pp., 45 figs., 69 tables, linen, DM 108.00.

It is only recently that chemists have become aware of the great importance of solvents in all areas of organic chemistry. The reactivity series obtained in the mass spectrometer (*i.e.* in the absence of solvent), the activation of organometallic compounds by complexing ligands and the use of chiral solvents indicate pathways that lead beyond the questionings of previous decades. It is therefore greatly to be welcomed that the monograph "Solvent Effects in Organic Chemistry", the second edition of which appeared in 1973, is now available in a completely revised version. The relevant information, which is not easy to retrieve, has been evaluated (over 1200 references) and is presented in the proven format for organic chemists who are inclined toward the mechanistic and preparative aspects.

After an introduction to the physicochemical fundamentals of the interaction between solvent and solute (31 pages), where topics such as selective and micellar solvations are treated at reasonable length, there is a classification of solvents on this basis (19 pages), *e.g.* according to their polarity and their acceptor and donor properties (for electrons and hydrogen bonds).

The next two chapters are a fund of impressive examples of solvent effects on equilibria (25 pages) and in particular on reaction rates (109 pages), which can only be found to a limited extent from the subject index. These chapters will provide a wealth of new ideas for any organic chemist active in research or production.

The effects on acid-base and tautomeric equilibria, which to a certain extent have been known for a long time, are considered from modern viewpoints and amplified with recent examples. Among the qualitative and quantitative aspects the (in part) unexpectedly drastic solvent effects on S_N, E1,

and E2 reactions are discussed, where frequently specific solvations decide the issue. However, this chapter also includes a thorough discussion of the considerably weaker effects in radical and pericyclic reactions, together with their mechanistic consequences. The chapter has 451 references.

A further chapter (45 pages) deals with solvent effects on spectral properties. Starting with solvatochromism phenomena (UV/VIS), the author describes effects on IR, NMR, and ESR spectra, by which it is also often possible to detect specific solvations. This provides a logical transition to linear "free energy relationships" (54 pages), which are mainly derived from spectroscopic data for given model systems and which, possibly just because of their empirical nature, range over an astonishingly wide field of chemical reactivity. Here too the book shows the use and limitations of the Z and E_T values and AN and DN values, together with the value of multiparametric equations, some of which have only recently been developed.

An appendix gives brief information about the purification and possible applications of solvents, their spectroscopic and other physical data, and also their toxicity.

No other work currently available presents the confusing multiplicity of solvent effects as thoroughly, comprehensively, and critically as this one. Furthermore, it is intended for the organic chemist who wants to interpret these effects or to use them in planning his reactions. It is hoped that the high price will not hinder a wide readership of this book.

Siegfried Hünig [NB 481 IE]

Organometallic Mechanisms and Catalysis. By *J. K. Kochi.* Academic Press, New York 1978. xvii, 623 pp., $ 59.50.

It isn't very often that a reviewer has the good luck to be asked to write a critique about a book which he intended to purchase and I was, therefore, delighted when this volume landed on my desk—particularly in view of the price.

Organometallic chemistry and homogeneous catalysis can no longer be ignored by conventional organic and inorganic chemists: many organometallic compounds have either found direct practical application (*e.g.* organotin- and organolead compounds) or are routinely used as stoichiometric reagents in organic synthesis (*e.g.* organolithium- and organomagnesium compounds) or are involved as intermediates in metal catalyzed organic transformations some of which now form the basis of large industrial processes (*e.g.* organocobalt- and organonickel compounds in the hydroformylation and hydrocyanation of alkenes).

Although a number of reaction- or metal-specific books and reviews are available, it has become clear in the last few years that the role of organometallic species in organic synthesis could be profitably discussed from a unifying mechanistic standpoint and it is to fill this need that this book has been written.

Has the author succeeded? On the whole I think he has. He is certainly to be admired for not capitulating before the sheer volume of the material to be discussed. The book is divided into three related sections: part one deals with oxidation-reduction processes in which the metal undergoes a discrete change in oxidation state, part two is devoted to the chemistry of organometallic compounds with emphasis on reactions leading to cleavage of the metal-carbon bond, and part three is concerned with charge transfer interactions.

This arrangement enables a surprising amount of information to be classified while avoiding the frequently artificial distinction between main group- and transition-metal organometallic compounds. A first-class index makes it easy to find relevant material. The main difficulty facing the author is that concrete evidence is often lacking for many of the catalytic processes being considered and, in spite of his good intentions, the discussion all too often becomes metal-specific and generalizations have to be followed by a disclaimer. The most desirable effect which this book could have would be to stimulate further work towards greater mechanistic uniformity.

The book will be of greatest interest to chemists involved directly with organometallic compounds and catalysis but it should also be very profitable reading for all preparative organic chemists. Its greatest service will be to act as an orientation point in classifying new information. For me at least it will now be easier to keep an eye on what is happening in the wood while at the same time tending some of the trees.

P. W. Jolly [NB 477 IE]

The Chemistry of Functional Groups. The Chemistry of Diazonium and Diazo Groups. Edited by *S. Patai.* John Wiley & Sons, New York 1978. Part 1, xiv, 510 pp.; Part 2, xiv, pp. 511—1069; bound, together $ 130.00.

The last comprehensive survey of diazo and diazonium compounds (*H. Zollinger:* Diazo and Azo Chemistry) was published in 1961; the pertinent chapters of Houben-Weyl (10/3 and 10/4) were written in 1965 and 1968. The present two-volume work in the series "Chemistry of Functional Groups" is therefore most welcome.

Diazonium ions and diazo compounds do have a number of interfaces (they are related by acid-base equilibria in the aliphatic series), but differ greatly in their reactions. The two classes of compounds are therefore considered together in some of the chapters, but separately in others. The work opens with a theoretical survey (*J. B. Moffat*) which also embraces diazirines and diimides. Three chapters are concerned with the synthesis of diazonium salts (14, *K. Schank*) and of diazoalkanes and their carbonyl, phosphoryl, and sulfonyl derivatives (15, 17, *M. Regitz*). Further chapters are devoted to acid-base equilibria (2, *V. Štěrba;* 6, *J. F. McGarrity*), structural problems (3, *S. Sorriso;* 7, *H. M. Niemeyer*), and analytical procedures (5, *D. A. Ben-Efraim*). The section on thermochemistry (4, *R. Shaw*) does not appear very successful, being based on a value for the heat of formation of diazomethane which is most probably incorrect. Mechanistic questions are discussed with particular emphasis on photochemistry (9, *W. Ando*), electrochemistry (10, *J. Fry*), substituent effects (11, *E. S. Lewis*), kinetics (12, *A. F. Hegarty*), rearrangements (13, *D. Whittaker*), and the use of isotopes (16, *P. J. Smith* and *K. C. Westaway*). Special attention is focused on the synthetic application of diazonium salts (8, *D. S. Wulfman*) and diazo compounds (18, *D. S. Wulfman, G. Linstumelle,* and *C. F. Cooper*) by two large chapters with *ca.* 2400 references. This is where the chemist engaged in preparative work will gain well-founded information and critical suggestions concerning, for example, the choice of catalyst in the decomposition of diazo compounds.

Repetition is bound to occur in a book written by 19 authors (*e.g.* the Wolff rearrangement is mentioned in Chapters 3, 9, 13, and 18); and yet new aspects are often revealed precisely by such repetition. Some information turns up in unexpected places, *e.g.* ^{13}C-NMR data of diazo compounds in Chapters 11 and 16, but not in Chapter 5 and regrettably not in the index. Typographical errors are rare (*e.g.* pp. 374, 413, 607, 629, 726, 851, 855, 909, 932); errors of fact are even rarer (the statement on p. 13 that diazirine is more stable than diazomethane contradicts the heats of formation compiled in Tables 10 and 11; classification of the photochemical Bamford-Stev-

ens reaction as "photolysis of aliphatic diazonium ions" in Chapter 9 is surprising; the hypothesis of "hot" cations is attributed to the wrong authors on p. 574). Interspersion of an occasional *bon mot* provides amusement between formulae and tables: "It is not clear whether the catalyst plays an active role or represents a retreat to the chemistry of (Paracelsus) von Hohenheim" (p. 910). The subject index (24 pages) is comparatively exhaustive; the author index (66 pages) provides a visible measure of the relative ranking of the pundits (*Regitz* is a clear winner with 11.8 cm).

The high quality of most of the contributions, the high information content, and the careful editing recommend these volumes not only to subscribers to the series but to a wide circle of organic chemists engaged in mechanistic and preparative work.

Wolfgang Kirmse [NB 475 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Chemie der organischen Derivate des Hydrazins. By *B. V. Ioffe, M. A. Kuznecov,* and *A. A. Potechin.* Verlag Chimija, Leningrad 1979. 224 pp., paper 1 Rubel, 90 Kop.

A Theory of Biochemical Supersystems and its Application to Problems of Natural and Artificial Biogenesis. By *T. Ganti.* Akademiai Kiado, Budapest 1979. 136 pp., paperback.—ISBN 963-05-1719-1

Carbon-13 NMR Spectral Data. A "Living" COM-Microfiche Collection of Reference Material. Edited by *W. Bremser, L. Ernst, B. Franke, R. Gerhards,* and *A. Hardt.* Verlag Chemie, Weinheim 1979. 2nd edit. 32 pp., 108 microfiches with 18719 spectra of 14786 compound. Looseleaf file, DM 1100.00.—ISBN 3-527-25835-3

Landolt-Börnstein. Zahlenwerte und Funktionen aus Naturwissenschaft und Technik. Neue Serie. Gruppe III, Band 7. Edited by *K. H. Hellwege* and *A. M. Hellwege.* Springer-Verlag, Berlin 1979. xxvii, 452 pp., bound, DM 550.00.—ISBN 3-540-09039-8

Atom-Molecule Collision Theory. Edited by *R. B. Bernstein.* Plenum Press, New York 1979. xx, 779 pp., bound, $ 57.50.—ISBN 0-306-40121-5

Chemical Engineering, Vol. 5. By *J. M. Coulson* and *J. F. Richardson.* **Solutions to the Problems in Chemical Engineering, Vol. 2.** By *J. B. Backhurst* and *J. H. Harker.* Pergamon Press, New York 1979. vii, 255 pp., paper, $ 15.00.—ISBN 0-08-022952-2

Fluid Catalytic Cracking with Zeolite Catalysts. By *J. B. Venuto* and *E. T. Habib, Jr.* Marcel Dekker, Basel 1979. vi, 156 pp., bound, SFrs. 44.00.—ISBN 0-8247-6870-1

IUPAC: Carbohydrate Chemistry—9 (London 1978). Edited by *A. B. Foster.* Pergamon Press, New York 1979. pp. 1343—1476, bound, $ 30.80.—ISBN 0-08-022354-0

Advances in Structure Research by Diffraction Methods, Vol. 7. Unconventional Microscopy for Molecular Structure Determination. Edited by *W. Hoppe* and *R. Mason.* Vieweg & Sohn, Braunschweig 1979. 225 pp., bound, DM 84.00.—ISBN 3-528-08117-1

Developments in Polymerisation—2. Edited by *R. N. Haward.* Applied Science Publ., London 1979. xi, 285 pp., bound, $ 62.50.—ISBN 0-85334-821-9

Chemistry and Physics of Carbon, Vol. 15. Edited by *Ph. L. Walker, Jr.* and *P. A. Thrower.* Marcel Dekker, Basel 1979. xi, 299 pp., bound, SFrs. 82.00.—ISBN 0-8247-6816-7

Handbuch zur Anwendung der Nomenklatur organisch-chemischer Verbindungen. Edited by *W. Liebscher.* Akademie-Verlag, Berlin 1979. xix, 1076 S., bound, *ca.* DM 135.00.

Air Pollution Chemistry. By *J. D. Butler.* Academic Press, New York 1979. viii, 408 pp., bound, $ 52.50.—ISBN 0-12-147950-1

Amino-acids, Peptides and Proteins, Vol. 10. Senior Reporter: *R. C. Sheppard.* The Chemical Society, London 1979. xix, 537 pp., bound, DM 155.00.—ISBN 0-85186-094-X.—A volume of the series "Specialist Periodical Reports"

Spektren und Strukturen organischer Verbindungen. By *E. Fahr* and *M. Mitschke.* "taschentext" 61. Verlag Chemie/Physik-Verlag, Weinheim 1979. 130 pp., paper, DM 24.80.—ISBN 3-527-21027-X

Umweltforschungsreport 1977/78. Issued by the Umweltbundesamt Berlin. 233 pp., paper.

Gas Phase Ion Chemistry, Vol. 1. Edited by *M. T. Bowers.* Academic Press, New York 1979. xiii, 354 pp., bound, $ 39.50.—ISBN 0-12-120801-X

The Porphyrins, Vol. 7. Biochemistry, Part B. Edited by *D. Dolphin.* Academic Press, New York 1979. xxi, 550 pp., bound, $ 55.00.—ISBN 0-12-220107-8

The Chemistry of Heterocyclic Compounds, Vol. 25. Indoles, Part 3. Edited by *W. J. Houlihan.* John Wiley & Sons, New York 1979. x, 586 pp., bound, $ 93.00.—ISBN 0-471-05132-2

Porphyrin Chemistry Advances. Edited by *F. R. Longo.* Ann Arbor Science Publ., Ann Arbor 1979. vii, 368 pp., bound, £ 18.70.—ISBN 0-250-40229-7

Studienbücher Chemie: Einführung in die Kunststoffchemie. By *G. Rink.* Diesterweg/Salle/Sauerländer, Frankfurt 1979. x, 210 pp., paper, DM 14.90.—ISBN 3-7941-1468-X

Liquid Chromatographic Analysis of Food and Beverages, Vol. 2. Edited by *G. Charalambous.* Academic Press, New York 1979. xi, pp. 237—563, bound, $ 25.00.—ISBN 0-12-169002-4

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 11
November 1979
Pages 809–886

Bonding Properties of Cyclopropane and Their Chemical Consequences

By Armin de Meijere[*]

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

Among the cyclic compounds of carbon, cyclopropane and its derivatives are outstanding by virtue of their unusual structural, spectroscopic, and chemical properties. The cyclopropane ring more closely resembles the C=C double bond than the cyclobutane ring: it is a small ring with "double bond character". Cyclopropyl and vinyl groups interact with neighboring π-electron systems and p-electron centers; both cyclopropane derivatives and olefins form metal complexes, and add strong acids, halogens, and ozone; they both undergo catalytic hydrogenation and cycloadditions. While distinct differences in reactivity do exist—the double bond usually being more reactive than the three-membered ring—there are no fundamental differences in behavior.—Although cyclopropane derivatives have been known for more than 90 years, intensive studies have been limited to the past 25 years. The development of carbene chemistry has rendered cyclopropane derivatives far more readily accessible. In recent years, the synthetic potential of the small-ring function has been increasingly exploited. A considerable number of newly developed methods utilizing this approach clearly demonstrates that the reactivity of the cyclopropene ring, like that of the C=C double bond, qualify it as a "functional carbon group". This development is in full swing; we may therefore justifiably devote considerable effort to the study of cyclopropane chemistry.

1. The Chemical Bond in the Cyclopropane Ring

Olefins and cyclopropane derivatives are related in many ways[1]. The reason for this lies in the similarity of bonding in the C=C double bond and in the three-membered carbon ring. There are two equivalent descriptions for each system. According to the MO model of *Walsh*[2] (see Fig. 1), three occupied molecular orbitals (MOs) determine the nature of the C—C bonds of the three-membered ring. Of these, the orbit-

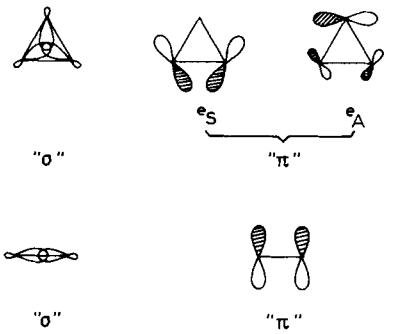


Fig. 1. Molecular orbital (MO) description of bonding in cyclopropane and ethylene.

[*] Prof. Dr. A. de Meijere
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1111-0809 $ 02.50/0

al of lowest energy (σ) is a linear combination of three sp^2-hybrid atomic orbitals (AOs), while the other two (e_S and e_A) are equal-energy linear combinations of three p-AOs differing only in their symmetry properties. This picture is strongly reminiscent of the commonest description of a C=C double bond by two occupied MOs, one linear combination each of two sp^2 AOs (σ-MO) and two p AOs (π-MO) (see Fig. 1). By analogy with the latter MOs, the Walsh e_S and e_A orbitals are also called π or "quasi π" orbitals of the three-membered ring.

The second kind of theoretical description is the valence bond (VB) model of cyclopropane, due originally to *Förster*[3] and refined by *Coulson*[4]. The C—C bonds are described as resulting from the overlapping of two sp^5-hybrid orbitals at each C atom (see Fig. 2). Since the directions of

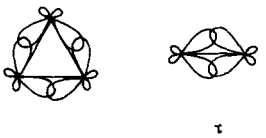


Fig. 2. Valence bond (VB) model of cyclopropane and ethylene.

the orbitals cannot coincide with the directions of bonding, but are directed outwards relative to the latter, the bonds create the impression of being bent. However, this merely expresses the experimentally established fact[5] that the density of the bonding electrons is greatest off the C—C connecting line. In the more common MO model this fact is reflected by the e_S and e_A orbitals in which the overlap region of the p AOs also lies off the C—C connecting lines (see Fig. 3)[6].

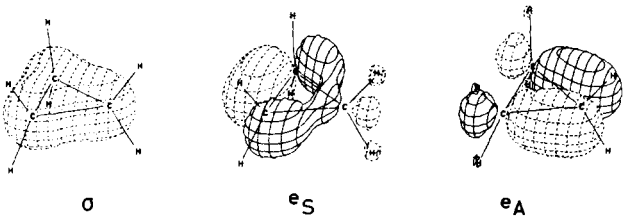


Fig. 3. Electron density distribution in the occupied molecular orbitals of cyclopropane responsible for the C—C bonds (according to [6]).

Another common feature of the two models is the participation of sp^2 hybrid orbitals of the C atoms in C—H bond formation. This is substantiated by experimental facts: for instance, the cyclopropyl C—H bonds (like vinylic C—H bonds) are shorter than normal aliphatic C—H bonds[7], and the ^{13}C-H coupling constants found for cyclopropane derivatives indicate 32% s character of the C—H bonding orbitals[8].

Furthermore, the C=C double bond can also be described, according to *Pauling*, by bent bonds[9]. As in the three-membered ring, the so-called "τ bonds" arise by overlapping of sp^5 hybrid orbitals of the C atoms off the C—C connecting line (see Fig. 2). For cyclopropane and ethylene, we have two completely equivalent models which can be transformed mathematically into each other[10]. The physical and chemical consequences can be explained equally well in principle by either model. However, the σ,π description of the double bond and the three-membered ring is more convenient for quantum mechanical calculations.

These analogies in bonding properties help us to understand similarities in chemical behavior; the regions of high electron density off the C—C connecting lines determine their reactivity towards electrophilic reagents[1, 11, 12]. This is also the reason why both of the bond systems can undergo electronic interaction with π or p-electron centers. It leads to an effect usually designated as conjugation, which is generally manifested in the physical and chemical properties of the corresponding compound. In the case of the C=C double bond, conjugation effects are known for systems containing in its immediate vicinity
a double bond or, more generally,
a CX multiple bond,
a cyclopropane ring,
a carbanion center,
a radical center, or
a carbenium ion center.

In principle, an interaction effect should be expected for combinations of each of these five groups with a cyclopropane ring. It is the intention of this article to describe model compounds with characteristic properties and thereby show how far this prediction is fulfilled.

It should first be mentioned that the extent of interaction in conjugated systems with a double bond and with a three-membered ring is highly dependent upon their conformation. In general, the interaction energy, and hence also the effect of conjugation on physical and chemical properties, is greatest when the axes of the mutually interacting orbitals are parallel to each other because the overlap between the orbitals is then at a maximum. Open-chain conjugated systems therefore preferentially adopt a conformation permitting such maximum interaction. Thus over 95% of the molecules of 1,3-butadiene exist in the antiperiplanar (*s-trans*) conformation having a planar carbon skeleton[13, 14]; the allyl anion, the allyl radical, and the allyl cation[15] are planar.

Owing to the special kind of anisotropic electron distribution in the cyclopropane ring (*vide supra*), its interaction with a suitable neighboring group is at a maximum when the p-orbital axis of the neighboring group is arranged parallel to the plane of the three-membered ring. For vinylcyclopropane, for instance, this is the case in the antiperiplanar con-

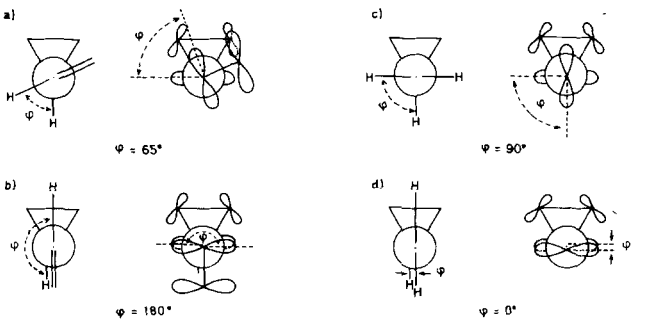


Fig. 4. Conformations of vinylcyclopropane: a) synclinal (*gauche*); b) antiperiplanar (*s-trans*). Conformations of the cyclopropylmethyl cation: c) perpendicular; d) bisected.

formation (see Fig. 4) and for the cyclopropylmethyl cation in the o-called bisected conformation.

The interaction energy in a system with a three-membered ring and a double bond is apparently lower than in one with

two conjugated double bonds because the more stable antiperiplanar conformation of vinylcyclopropane predominates only to the extent of 75% in the liquid and gaseous phase, corresponding to an energy difference of 4.6 kJ/mol relative to the less stable synclinal (*gauche*) form[16]. The maximum stabilization energy of a system with conjugated double bond and three-membered ring would correspond to the energy difference between the antiperiplanar form and a 90° conformation; this energy difference is somewhat greater than 4.6 kJ/mol (*vide infra*). In contrast, the energy difference between the lowest-energy bisected conformation of the cyclopropylmethyl cation and the energetically least favorable perpendicular conformation is much greater at 60—70 kJ/mol[17,18]. The gain in energy experienced by such a cation in an optimum geometry is of the same order of magnitude as the stabilization energy of an allyl or benzyl cation[19] relative to a primary alkyl carbenium ion. Thus the ability of the cyclopropyl group to stabilize a center of positive charge is comparable with, or even greater than, that of the vinyl and the phenyl group[20].

On comparing the vinyl and the phenyl group on the one hand with the cyclopropyl group on the other, it is essential to bear in mind a difference in geometry, which can play an important role primarily in conformationally rigid systems: as a rule, the four substituents attached to the two carbon atoms of a double bond are located in a plane (S) including the carbon atoms and oriented perpendicular to the plane (O) of the π-orbital axes (interplanar angle $\alpha = 90°$; cf. Fig. 5); however, four substituents attached to two C atoms of a cyclopropane ring define, together with the C atoms, two distinct planes (S^1 and S^2) enclosing an angle of *ca.* 120° and forming angles of *ca.* 60° with the plane of the three-membered ring, and thus also with that of the p-orbital axes (O) ($\alpha \approx 60°$, cf. Fig. 5).

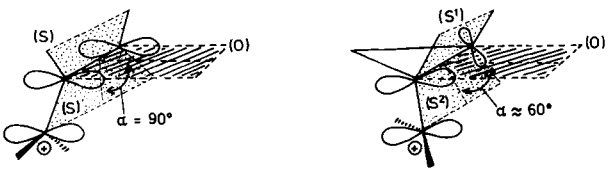


Fig. 5. Geometrical differences in the allyl and the cyclopropylmethyl cation at maximum orbital overlap [α = interplanar angle].

The modern description of the bonding properties of cyclopropane provides a theoretical basis for the classical concept of ring strain[21], which has been invoked to explain various typical reactions of small ring compounds: according to present-day ideas, ring strain is an expression of the sum of all bond energies in a molecule. The experimental value can be obtained for any cycloalkane from the difference between its heat of combustion and that of a long-chain unstrained *n*-alkane[22] with the same number of CH_2 groups (see Table 1). This definition is less misleading and yet more comprehensive that the original one proposed by *A. von Baeyer*[21], which assumed that only the C valence angles deviating from tetrahedral angles give rise to a strain in small rings which increases with decreasing ring size. In fact, we nowadays distinguish three causes of ring strain and thus three components contributing to the total strain: deformation of bond angles gives rise to angular strain (von Baeyer strain) and an eclipsed or at least imperfectly staggered arrangement of CH_2 groups causes torsional strain (Pitzer strain); the third contribution is due to transannular van der Waals interaction of nonbonded atoms.

Table 1. Strain energy of lower cycloalkanes $(CH_2)_n$ and ethylene.

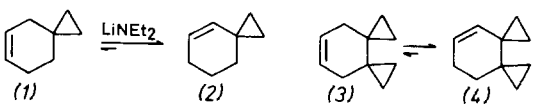
Cpd.	*n*	Bond angle deformation per CH_2 group	Heat of combustion per CH_2 group $\Delta H_{comb.}/n$ [kJ/mol]	Strain energy per molecule $\Delta H_{comb.} - n \cdot 6586$ [kJ/mol]
Ethylene	2	109.5°	705.4	93.6
Cyclopropane	3	49.5°	697.1	115.5
Cyclobutane	4	19.5° [a]	686.2	110.4
Cyclopentane	5	1.5° [a]	664.0	27.0
Cyclohexane	6	0°	658.6	0.0
n-Alkane	∞	0°	658.6	0.0

[a] Calculated for a planar ring, as assumed by *A. von Baeyer* [21].

The values of the strain energy (Table 1) show that the thermodynamic stability of a cyclopropane ring is lower than that of a C=C double bond; accordingly, cyclopropane derivatives are often observed to rearrange to more stable olefins on acid catalysis[11,23] or thermally at sufficiently high temperatures[24,25]. Nevertheless, three-membered rings show a pronounced tendency of formation; for example, certain eliminations leading to olefins can be applied with comparable success to the synthesis of cyclopropane derivatives from homologous substrates (γ-elimination)[26]. The numerous methods for generating carbenes[27] and their additions to C=C double bonds have greatly increased the possible preparations of three-membered rings[28]. The recently developed generation of dichlorocarbene from chloroform and concentrated aqueous sodium hydroxide under phase transfer catalysis[29] has reduced the expenditure of effort and financial resources to such an extent that two of the principle obstacles on the way to an industrial utilization of cyclopropane chemistry have been removed.

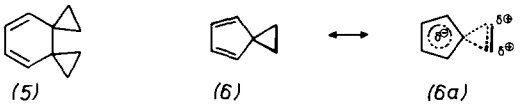
2. Effects of Conjugation between Cyclopropane and Multiple Bonds

Staley has estimated from the position of the equilibrium which is established in the presence of strong bases between spiro[2.5]oct-5-ene *(1)* and spiro[2.5]oct-4-ene *(2)* at room temperature that conjugation between the C=C double bond and the cyclopropane ring effects a stabilization of *ca.* 5.0 kJ/mol[30]. Dispiro[2.0.2.4]dec-8-ene *(3)* can accordingly undergo more than 80% rearrangement to the more stable conjugated isomer *(4)*[31].



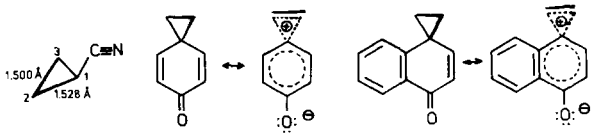
Conjugation in compounds of types *(2)* and *(4)* is manifested not only in their greater thermodynamic stability but also in their UV, NMR, IR, and PE spectra. The bathochromic shift of the longest wavelength UV absorption band

of a 1,3-diene chromophore is *ca.* 15 nm per three-membered ring, given optimum conformation of the system, as is almost accomplished in dispiro[2.0.2.4]deca-7,9-diene *(5)*[31,32]. For spiro[2.4]hepta-4,6-diene *(6)*, having the vinylcyclopropane units fixed in the antiperiplanar conformation in the planar



(5) *(6)* *(6a)*

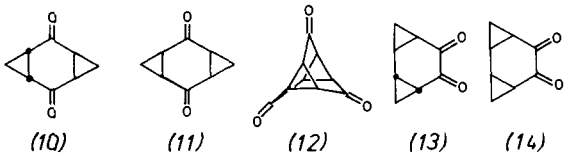
five-membered ring[33], *Clark* and *Fiato* have deduced partial delocalization of the cyclopropyl bond electrons into the five-membered ring [as in *(6a)*] from the exceptional downfield position of the NMR signals due to the cyclopropyl protons[34]. However, this assumption could not be confirmed by way of the bond lengths of *(6)*. In the five-membered ring they correspond to those of cyclopentadiene and in the three-membered ring to those of cyclopropane[33]. The electron-donating capacity of the cyclopropyl group apparently becomes effective only when stimulated by electron withdrawal by a π-acceptor substituent, such as a polar CX multiple bond[35]. Thus a significant lengthening of the C^1—C^2 bond, and a corresponding shortening of the C^2—C^3 bond have been determined experimentally for cyclopropanecarbonitrile *(7)*, just as predicted theoretically on the basis of the Walsh MO model[36]. (The C—C bond length in cyclopropane is 1.510 Å.)



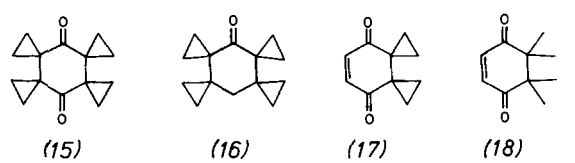
(7) *(8)* *(8a)* *(9)* *(9a)*

Thus it appears reasonable that the ^{1}H-NMR and UV data of spiro[2.5]octa-4,7-dien-6-one *(8)*[37] and its benzo derivative *(9)*[38] are best interpreted in terms of a significant contribution of the zwitterionic resonance structures *(8a)* and *(9a)*[38].

The magnitude of the bathochromic shift of the n-π^* band in the UV spectrum[39] and the shift of the νC=O band to lower wave numbers in the IR spectrum[40] of cyclopropyl ketones as an expression of the conjugation between the cyclopropyl and the carbonyl group is critically dependent upon the geometry of the system[41]. In cyclopropyl-conjugated diketones, the effect of through-space and through-bond interaction between the carbonyl groups is also important; the data collected for compounds *(10)*—*(18)* are impressive illustrations (see Tables 2).



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



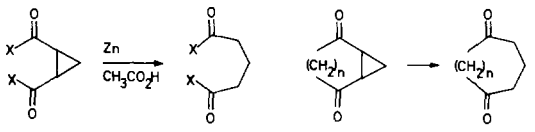
(15) *(16)* *(17)* *(18)*

Table 2. Selected UV and IR data of some cyclopropyl-conjugated cyclohexanediones and reference systems.

Compound	UV, n-π^* (EtOH) λ_{max} [nm] (ε_{max})	IR (KBr) νC=O [cm^{-1}]	Ref.
(10)	271 (57)	1712, 1686	[42]
(11)	280 (47)	1701, 1578	[42]
(12)	[a]	1700	[43]
1,4-Cyclohexanedione	281 (29)	1724	[44]
(13)	373 (27)	1685	[45]
(14)	360 (90)	1695	[45]
3,4,5,6-Tetramethyl-1,2-cyclohexanedione	380 (11)	1709	[45]
(15)	271 (135)	1688	[44]
(16)	279 (169)	1667	[44]
(17)	348	1670	[46]
(18)	365	1682	[46]

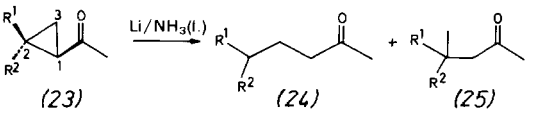
[a] Not measured.

The particularly facile reductive cleavage of the cyclopropyl C—C bond in 1,4-dicarbonyl compounds of types *(19)* and *(21)* may be regarded as a chemical consequence of cyclopropyl-carbonyl conjugation and of the low C—C bond energy. This mode of reaction, which leads to 1,5-dicarbonyl compounds *(20)* and *(22)*[47], can be used to advantage, *e.g.*, for ring expansion[48].



(19) *(20)* *(21)* *(22)*

Reductive ring cleavage of conjugated cyclopropyl monoketones can also be accomplished with lithium in liquid ammonia[49]. In monocyclic conformationally mobile systems such as *(23)*, the type of substitution will determine which of the cyclopropyl bonds overlaps with the π orbital of the C=O group in the energetically most favorable conformation and is thus preferentially opened (see Scheme 1)[50]. In annelated bicyclic systems the fixed geometry leads to a stereoselective ring opening, which has been successfully utilized to reduce (+)-caran-2-one *(26)* to (−)-carvomenthane *(27)*[51] and to produce the intermediate *(29)* from *(28)* in a total synthesis of the spirosesquiterpene (+)-α-chamigrene *(30)*[52].

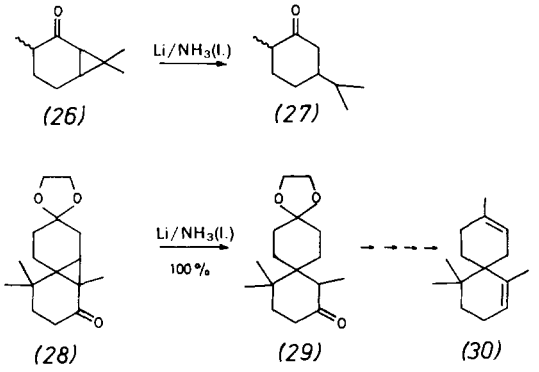


(23) *(24)* *(25)*

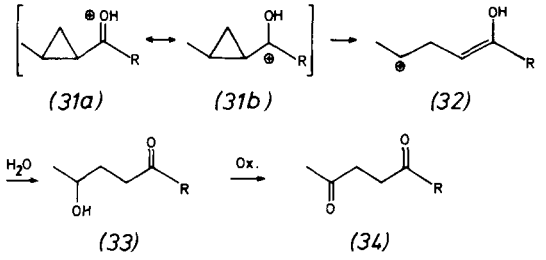
(a), $R^1=R^2=CH_3$	76	:	24
(b), $R^1=CH_3$, $R^2=H$	95	:	5
(c), $R^1=H$, $R^2=CH_3$	6	:	94

Scheme 1. Ring opening of cyclopropyl methyl ketones *(23)* depending upon type of substitution [50].

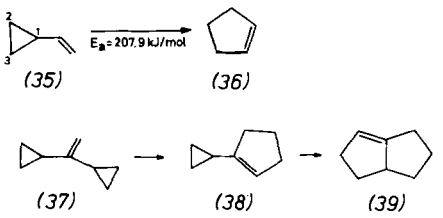
In protonated cyclopropyl ketones *(31)*, the electron-donating capacity of the cyclopropyl group is exploited by a neighboring carbenium ion center. In keeping with their cyclopropylmethyl cation structure (see Section 6), compounds



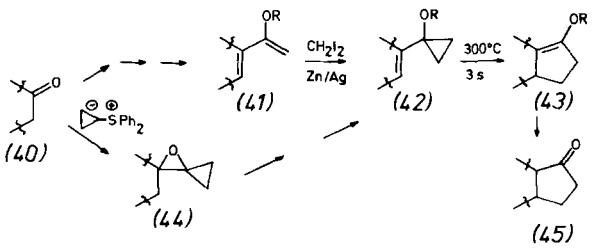
(31) form homoallyl systems *(32)* by ring opening; this mode of reaction is the basis of a synthetic method for 1,4-diketones *(34)* which result from trapping of *(32)* with water and subsequent oxidation[53].

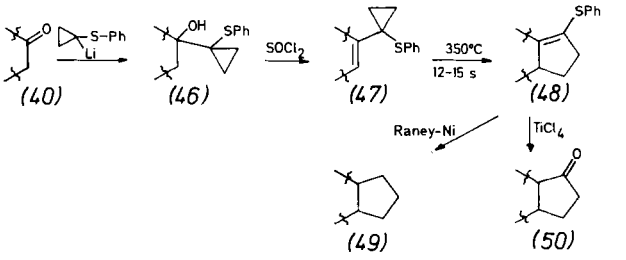


Conjugation of C=C double bonds with cyclopropyl groups also affects chemical properties. The simplest compound of this kind, vinylcyclopropane *(35)*, undergoes a relatively facile and uniform thermal rearrangement (Arrhenius activation energy $E_a = 207.9$ kJ/mol) to cyclopentene *(36)*[54]; numerous substituted vinylcyclopropanes[24,25] behave analogously [*e.g. (37)→(38)→(39)*] provided they are not fixed in



an antiperiplanar or anticlinal conformation that is unfavorable for this ring closure. This kind of rearrangement serves as the principle underlying techniques of fusing cyclopentane rings onto cyclic ketones *(40)* (see Scheme 2)[55,56]. The decisive intermediates are 1-vinylcyclopropyl trimethylsilyl ethers *(42)*, obtained according to *Conia et al.*[55] by Simmons-Smith cyclopropanation of 2-trimethylsilyloxy-1,3-dienes *(41)* or according to *Trost et al.*[56] *via* the oxaspiropentanes *(44)*.

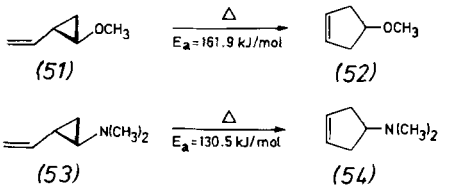




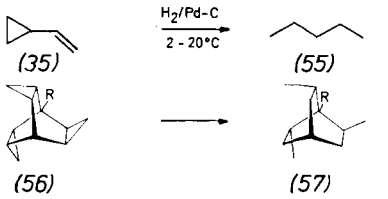
Scheme 2. Methods of fusing cyclopentane to cyclic ketones *(40)*, R = $(CH_3)_3Si$.

Being stereocontrolled, the alternative method *via* the phenylthio-substituted systems *(47)* and *(48)* also developed by *Trost et al.*[57] may be advantageous. The trimethylsiloxy and phenylthio groups in *(42)* and *(47)*, respectively, facilitate thermal rearrangement as compared to the parent system.

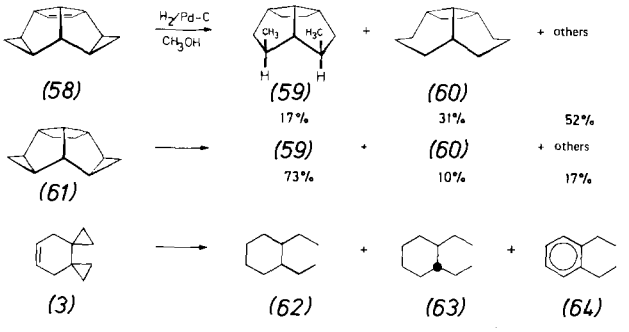
A comparable effect is observed with a methoxy ($E_a = 161.9$ kJ/mol) or a dimethylamino group ($E_a = 130.5$ kJ/mol) in position 2 of the vinylcyclopropane [see *(51)* and *(53)*][58].



On catalytic hydrogenation, vinyl-conjugated cyclopropyl groups are generally more readily cleaved than isolated ones[59]; moreover, vinyl as well as carbonyl and phenyl groups lead to regioselective opening of the C^1—C^2 bond, while it is mainly the C^2—C^3 bond which is opened in the case of alkyl-substituted cyclopropanes[60].

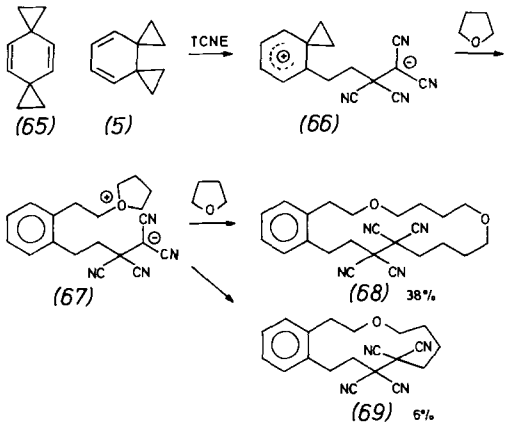


Vinylcyclopropane *(35)* is hydrogenated to *n*-pentane *(55)* over palladium in methanol at 2—20 °C and at normal pressure[61]; in contrast, the trishomobarrelene derivatives *(56)* undergo hydrogenation to the stereochemically interesting 2,6,7-trimethylbicyclo[2.2.2]octyl derivatives *(57)* (R = ethyl, 1-methylcyclopropyl, methoxy) only at elevated hydrogen pressure (≥5 bar) in the presence of platinum dioxide/glacial acetic acid[62]. In oligocyclic systems having essentially rigid geometry, however, non-conjugated C=C double bonds may also affect the regioselectivity and ease of cyclopropyl ring opening. The unsaturated pentacycle *(58)* takes up hydrogen far more rapidly than the corresponding saturated pentacycle *(61)*, and gives a much higher proportion of the fully unexpected[59,60] product *(60)*[63] than does *(61)*. Compound *(3)* completely fails to give the expected[59,60] 1,1,2,2-tetramethylcyclohexane, but instead affords *cis*- *(62)* and *trans*-1,2-diethylcyclohexane *(63)*, as well as 1,2-diethylbenzene *(64)* alongside a small amount of saturated dispiro[2.0.2.4]decane[64].

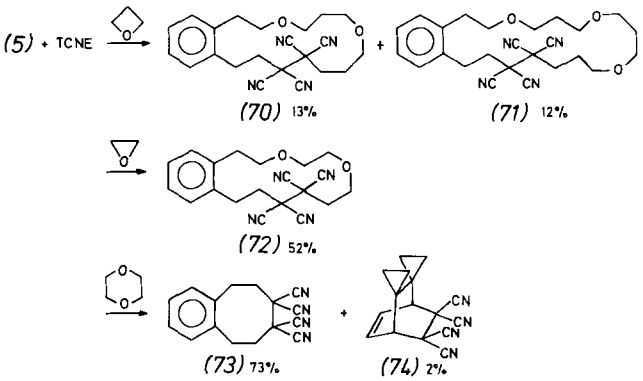


Thus in molecules such as *(58)* and *(3)* the olefinic group is the better "ligand" for the catalyst surface, and therefore plays a major role in determining how the overall molecule is adsorbed on the catalyst surface and which cyclopropyl bond subsequently undergoes preferential cleavage.

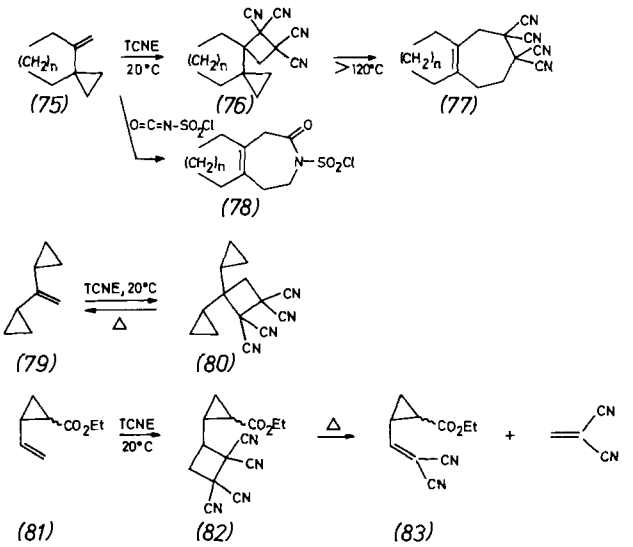
The interaction between the bonding orbitals of a cyclopropyl group and the π orbitals of neighboring C=C double bonds raises the energy of the highest occupied MO (HOMO) of such a conjugated system. This corresponds to a lowering of the π-ionization potential, as has been established by photoelectron spectroscopy for the compounds *(2)*, *(4)*, *(5)*[31], *(6)*[65], *(65)*[66], and other examples[67]. The ionization potential of dispirodecadiene *(5)* is especially low at 7.74 eV. This is apparently responsible for the unusual mode of reaction of *(5)* with tetracyanoethylene (TCNE).



The major product (38%) of a reaction in tetrahydrofuran (THF) at room temperature is the 1:1:2 cycloadduct *(68)* of *(5)*, TCNE, and THF[68]. Since TCNE readily takes up an electron to form the radical anion[69], electron transfer from *(5)* to TCNE is probably the initial step of this reaction. After recombination of the pair of radical ions from *(5)* and TCNE the zwitterion *(66)* is formed, which ultimately cyclizes to the 18-membered ring *(68)* after incorporation of two molecules of THF *via (67)* and a further intermediate. Careful work-up of the reaction mixture afforded a further product (6%)[70] shown by its ^{1}H-NMR spectrum to have the structure *(69)* with a 13-membered ring, which must have arisen by cyclization of *(67)*. This reaction can be extended to the preparation of further macrocyclic ethers. In the presence of an excess of oxetane, *(5)* and TCNE give a mixture of *(70)* (13%) and *(71)* (12%) having a 16- and a 20-membered ring, respectively, in addition to polymeric material[70]. Similarly, the more highly strained oxirane is cyclooligomerized by *(66)* even at $-20\,^{\circ}C$: the major product (52% yield) is 11,12-benzo-1,4-dioxa-11-cyclotetradecene-7,7,8,8-tetracarbonitrile *(72)*[70].

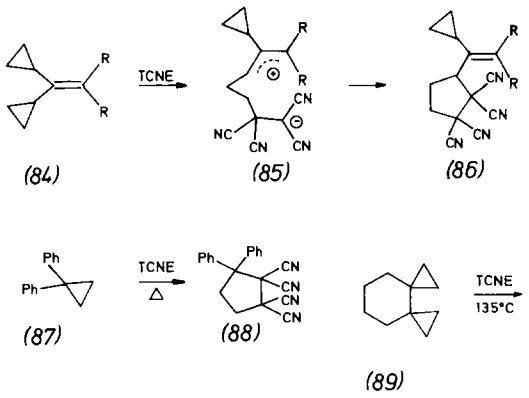


In contrast, the strain-free cyclic ether dioxane does not participate in the reaction; as a polar solvent it instead prolongs the lifetime of the zwitterion *(66)* and permits its cyclization to the benzocyclooctene derivative *(73)* (73% yield)[70]. The bicyclo[2.2.2]octene derivative *(74)* is formed merely as a by-product (2%) by normal Diels-Alder addition to the 1,3-diene unit in *(5)*. In contrast, this "normal" type of adduct is formed exclusively with all dienophiles[71-73] which are not also sufficiently strong oxidizing agents for *(5)*, like TCNE or certain substituted *p*-benzoquinones[73]. Compound *(73)* is formally a $[_{\sigma}2+_{\sigma}2+_{\sigma}2]$cycloadduct of TCNE and the synperiplanar-fixed bicyclopropyl unit. Analogous additions of TCNE to synperiplanar-fixed vinylcyclopropane systems have also been reported[74, 75].



Unlike *(5)*, however, the spirovinylcyclopropanes *(75)*, $n=1$ or 2, initially react by way of a [2+2]cycloaddition to give isolable cyclobutane derivatives *(76)*, which rearrange to cycloheptene derivatives *(77)* only at elevated temperature[75]. Prior electron transfer is not essential in this case because chlorosulfonyl isocyanate reacts analogously with *(75)* to give the seven-membered ring *(78)*[76] whereas this cyclophile gives a normal Diels-Alder adduct of type *(74)* with *(5)*[77]. Instead it is the conformation of the vinylcyclopropane system which is of prime importance. The adducts *(80)* and *(82)* of the sterically undefined cyclopropylethylenes

(79) and *(81)*[78] undergo exclusive cycloreversion to *(79)* and *(83)* on heating[75].



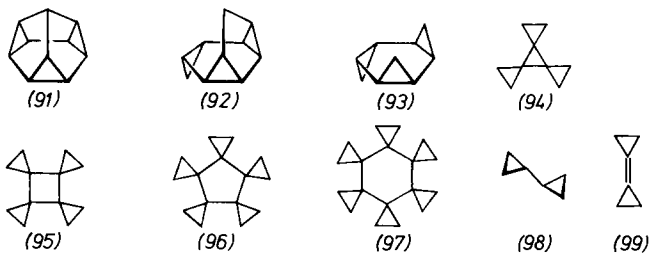
(84) *(85)* *(86)* *(87)* *(88)* *(89)* *(90)*

Cyclopropylethylenes having a sufficiently low ionization potential, such as *(84)*, R = cyclopropyl or phenyl, react like *(5)* in the initial steps; however, the zwitterion *(85)* preferentially cyclizes to the cyclopentane derivative *(86)*[79]. As shown by the examples *(88)*[80] and *(90)*[81], TCNE also undergoes cycloaddition to phenyl- and cyclopropyl-conjugated cyclopropanes such as *(87)* and *(89)*, probably without intermediate formation of radical ions.

Further transformation of such tetracarbonitriles, formed by TCNE addition to olefins and cyclopropanes, has hardly been utilized so far in spite of the potential they offer. Thus under alkaline conditions, *(72)* can readily be hydrolyzed to the tetracarboxylic acid[70]; in the absence of acid-labile groups, acid-catalyzed hydrolysis with simultaneous decarboxylation is possible[82].

3. Cyclopropyl-Cyclopropyl Interaction

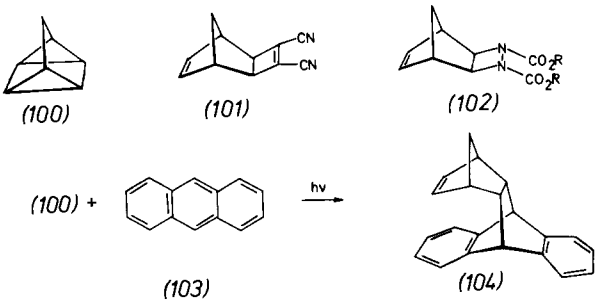
Although the electronic interaction between neighboring cyclopropyl groups does not appear to exert any substantial effect on the UV/VIS spectrum of corresponding compounds[31,83,84], it is manifested in the PE spectra in accord with theoretical concepts. Of particular value for such studies were compounds such as *(3)*, *(4)*, *(5)*, *(89)*[31], the tris-σ-homobenzenes *(91)*[85], *(92)*[86], and [*n*]rotanes *(94)*—*(97)*[87]



(91) *(92)* *(93)* *(94)* *(95)* *(96)* *(97)* *(98)* *(99)*

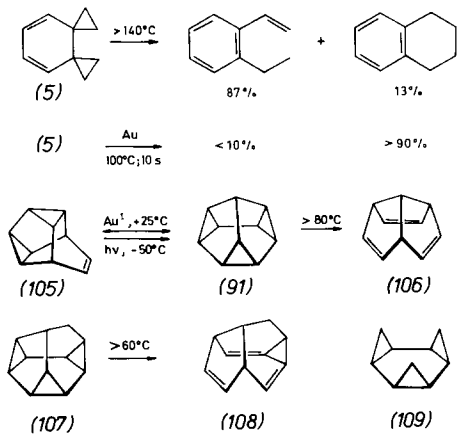
containing bicyclopropyl groups in uniformly defined conformations. However, comparable information was also provided by the PE spectrum of bicyclopropyl *(98)* which exists in two equilibrium conformations[88]. The resonance integrals serving as a measure for the interaction between neighboring 2p atomic orbitals of conjugated cyclopropyl groups vary from $\beta = -1.50$ eV for *(95)* through $\beta = -1.73$ eV for *(91)*, *(92)*, *(93)*, *(98)* up to $\beta = -2.05$ for *(94)*. The highest value, $\beta = -2.14$ eV, was found for bicyclopropylidene *(99)*[87], because the distance between the two cyclopropyl groups in this compound is smaller than in all other systems owing to the linkage *via* a double bond.

The proximity of two cyclopropyl groups is surely a determining factor in the cycloaddition of TCNE to a three-membered ring of *(89)* to give *(90)*[81]; however, bicyclopropyl *(98)* does not react under comparable conditions. The same unusual type of cycloaddition as that of TCNE to the bicyclopropyl unit of *(5)* to give *(66)* has so far been found for only one other class of compounds: quadricyclane *(100)*[89] and quadricyclane derivatives[90] react with dicyanoacetylene, azodicarboxylate, or other reactive dienophiles to form cycloadducts of the type *(101)*[89a] and *(102)*[89b], respectively. A photochemical $[_\pi 4 + _\sigma 2 + _\sigma 2]$cycloaddition of anthracene *(103)* to *(100)* giving *(104)* has also been reported[91].



(100) *(101)* *(102)* *(100)* + *(103)* *(104)*

Uncatalyzed and catalyzed thermal rearrangements of *(5)* and *(91)*—*(93)* are also determined by the proximity of cyclopropyl groups in various ways. While the purely thermal reaction of *(5)*—probably *via* intermediate diradicals—yields 87% *o*-ethylstyrene and only 13% tetralin[71], the gold-catalyzed reaction[92] gives more that 90% tetralin, the product of a bicyclopropyl group cyclization. The same kind of rearrangement is catalyzed by gold and gold(I) complexes in the case of diademane *(91)*; in the presence of dicyclopentadienegold(I) chloride, *(91)* isomerizes even a room temperature to snoutene *(105)*[92] from which it is in turn formed by photochemical interamolecular $[_\pi 2 + _\sigma 2]$cycloaddition[83b,93].

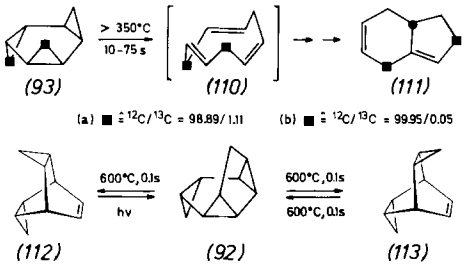


(5) *(5)* *(105)* *(91)* *(106)* *(107)* *(108)* *(109)*

In the absence of catalyst, however, *(91)* rearranges above 80 °C with cleavage of all its three-membered rings to triquinacene *(106)*[83b,94]. This type of cycloreversion, which has an activation energy of only 132.2 kJ/mol[95] in the case of *(91)*, is common to all *cis*-tris-σ-homobenzene derivatives[96]. All experimental evidence indicates a concerted $[_\sigma 2_s + _\sigma 2_s + _\sigma 2_s]$cy-

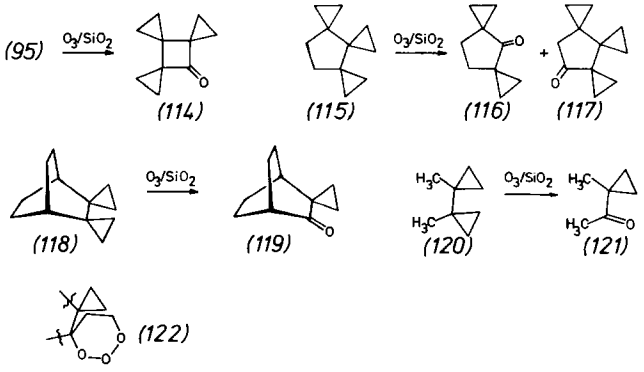
cloreversion. If the three cyclically conjugated cyclopropyl groups of a *cis*-tris-σ-homobenzene are better oriented for overlap of the Walsh orbitals than in *(91)*, as is the case in 1,6-homodiademane *(107)*[93,97], the isomerization proceeds even more readily ($E_a = 118.4$ kJ/mol). Thence it could be estimated that the hitherto unknown parent hydrocarbon *(109)* should just be stable at room temperature[97].

Although the overlap between neighboring p orbitals in two out of three bicyclopropyl groups is very small in *trans*-tris-σ-homobenzene *(93)*, it rearranges formally according to the same scheme; however, this reaction requires an activation energy of 175.7 kJ/mol[98]. Thus, under the conditions employed, the initial product, *viz.* the highly strained *cis,trans,trans*-1,4,7-cyclononatriene *(110)*[98b], could not be



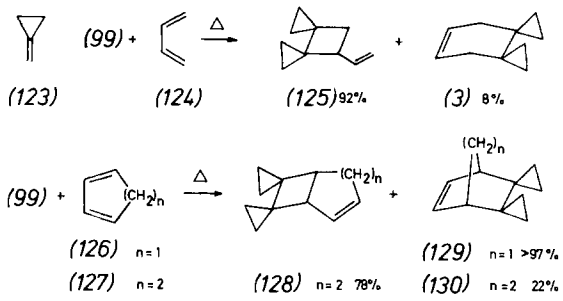
isolated but detected only by the isotopic labeling pattern in the final product *(111b)* from *(93b)*[98a]. Only when an additional bridge is present, as in *(92)* does the system avoid the excessive strain energy in the bridged intermediates of type *(110)* and instead undergoes $[_\sigma 2 + _\pi 2]$cycloreversion probably proceeding *via* diradicals at higher temperatures, giving the isomeric bishomobarrelenes *(112)* and *(113)*[99], from which it was in turn generated photochemically[99] and thermally[100].

Although the [*n*]rotanes *(94)*—*(97)* would appear predestined for a number of interesting chemical transformations, hardly anything of this kind is known about them. This is partly due to the tedious synthetic pathways leading to them before more convenient alternative approaches were developed[101]. The [4]rotane *(95)* obtainable by dimerization of the bicyclopropylidene *(99)*, which is now readily accessible[102], undergoes oxidative degradation to trispiro[2.0.2.0.2.1]decan-10-one *(114)* by ozone on silica gel[103]. It is not the ring strain of a spiro[2.3]hexane system which plays a crucial role, but instead the activation of a spirocyclopropyl group by at least one neighboring cyclopropyl group, for the hydrocarbons *(115)*, *(118)*, and *(120)* are degraded analogously to the ketones *(116)* [alongside *(117)*], *(119)*, and *(121)*, respectively[103]. Moreover, this mode of reaction is not

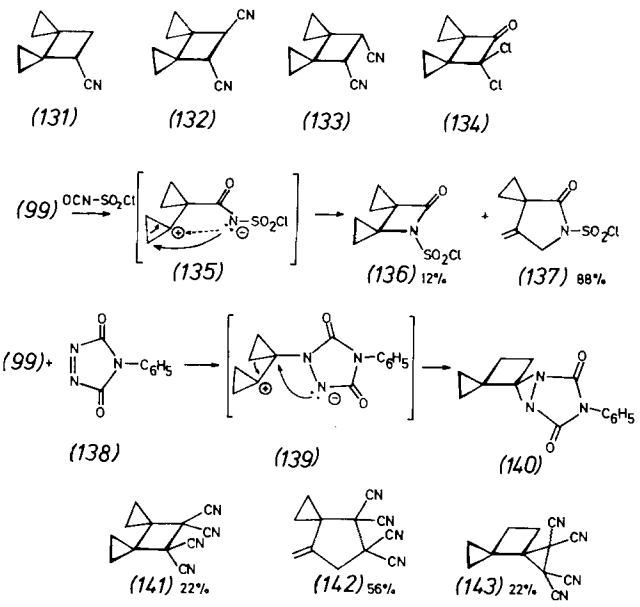


a consequence of an initial silica gel-catalyzed isomerization to an olefin[103]; rather the ozone directly attacks a cyclopropyl C—C bond, possibly with cycloaddition to give a rather unstable 1,2,3-trioxane of type *(122)*, as has been proved for highly strained σ bonds[104].

Because of the double bond-like properties of the cyclopropane ring (see Section 1), methylenecyclopropane *(123)* and bicyclopropylidene *(99)* sometimes react like cumulenes. The ready dimerization of *(123)*[105] and *(99)*[106] are pertinent examples. Cycloadditions of the more reactive compound *(99)*[106] to double bonds of other reactants provide an entry



to compounds having spirobicyclopropyl groups. Reaction with conjugated dienes such as 1,3-butadiene *(124)* and 1,3-cyclohexadiene *(127)* give mainly the cyclobutane derivatives *(125)* and *(128)*, respectively, together with the [2+4]cycloadducts *(3)* and *(130)*[107]. Only cyclopentadiene *(126)* reacts with *(99)* to give exclusively the formal [2+4]adduct *(129)*[107]. Compound *(99)* does not add to electron-rich olefins[108], but very readily to some double bond systems bearing strong electron acceptors as substituents. Thus *(99)* reacts with acrylonitrile to give the cyclobutanecarbonitrile derivative *(131)*, and with fumaronitrile to give a mixture of the isomers *(132)* and *(133)*; dichloroketene forms the "normal" [2+2]adduct *(134)*[108]. In contrast, chlorosulfonyl iso-

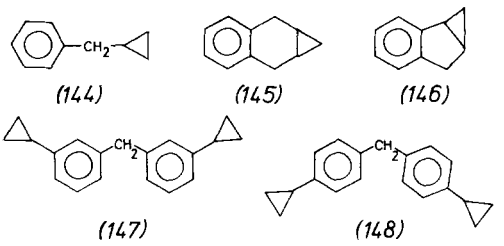


cyanate affords, alongside a small amount of *(136)*, mainly *(137)*, possibly by cyclopropylallyl rearrangement of the intermediate zwitterion *(135)*. *N*-Phenyltriazolinedione behaves differently: the intermediate *(139)* apparently undergoes cyclopropylmethyl-cyclobutyl ring expansion and sub-

sequent cyclization to the four-membered ring derivatives *(140)*. TCNE experiences all three kinds of addition, as shown by the products *(141)*, *(142)* (major product), and *(143)*[108]. Simple methylenecyclopropanes also undergo a formally analogous reaction[109].

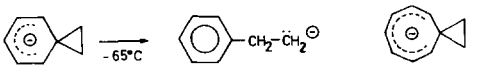
4. Stabilization of Carbanions by Cyclopropyl Groups

Owing to its bonding properties, a cyclopropyl group should, in principle, have a mesomeric and an inductive stabilizing effect on a carbanion[110]. However, *Perkins et al.* have deduced from measurements of hydrogen/deuterium exchange rates for benzylcyclopropane *(144)*, 3,4-benzobicyclo[4.1.0]heptene *(145)*, 2,3-benzobicyclo[3.1.0]hexene *(146)*, and reference compounds that the benzyl anions obtained from *(144)*, *(145)*, and *(146)* are, at best, only slightly more stable than the corresponding anions having no α-cyclopropyl groups[111]. This conclusion, *i. e.* that cyclopropyl substituents have hardly any effect on the stability of carbanions was confirmed by *Streitwieser*[112] on the basis of the kinetic acidities of *(147)* and *(148)*.



(144) *(145)* *(146)* *(147)* *(148)*

The widely differing stabilities of the spiro[2.5]octadienyl *(149)* and spiro[2.7]decatrienyl anion *(151)* reported by *Staley et al.*[113] also convincingly demonstrate the cyclopropyl group to be a poor π-electron acceptor but a very good π donor: the anion *(149)* in which the cyclopropyl group is spiro-linked to a 6 π system and in which it can only act as an ac-



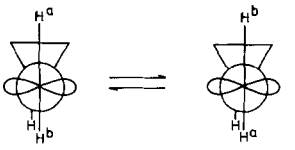
(149) *(150)* *(151)*

ceptor undergoes fast rearrangement at as low a temperature as −65 °C to the aromatic phenethyl anion *(150)*. In contrast, *(151)* in which the spirocyclopropyl group acts as a π donor, as in spiro[2.4]heptadiene *(6)*, is itself already "aromatic" according to the ring current criterion[113b] and therefore stable up to −30 °C.

5. Relative Stabilities of Cyclopropylmethyl Radicals

Although studies on the generation and transformation of cyclopropylmethyl radicals and their relative stabilities are not very numerous[114], they are far better represented than those on cyclopropylcarbanions. This would indicate that cyclopropyl-substituted radicals have a greater potential.

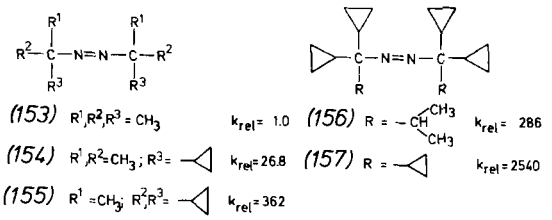
ESR studies have shown that cyclopropylmethyl radicals prefer the bisected conformation *(152)* with optimum overlap between the radical p orbital and the cyclopropyl Walsh orbital[115]; however, the CH_2 rotation responsible for the exchange process *(152a)*⇌*(152b)* is subject to a barrier of only <12.5 kJ/mol[115]. This is much smaller than in the case of



(152a) *(152b)*

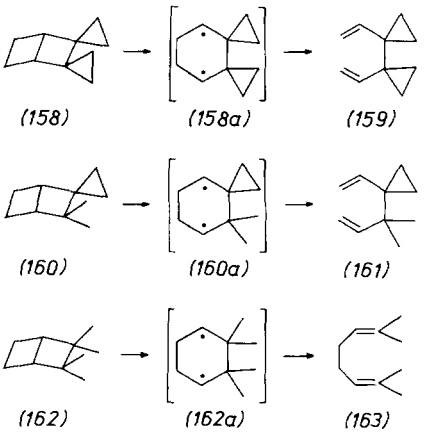
the cyclopropylmethyl cation[17,18] indicating that a radical is stabilized less by an α-cyclopropyl substituent than a carbenium ion.

Kinetic studies on the decomposition of azoalkanes *(153)*—*(157)* led *Martin* and *Timberlake* to essentially the same conclusion[116]. Any replacement of a methyl by a cy-



clopropyl group in *(153)* increases the rate of thermolysis, on average by a factor of 14. The steric influence due to the difference in sizes of these groups plays a subordinate role, as shown by comparison of the values obtained for *(156)* and *(157)*. However, in the case of *(155)*, *(156)*, and *(157)*, apparently not all the cyclopropyl groups can simultaneously adopt an optimum conformation for interaction with the incipient radical center in the transition state.

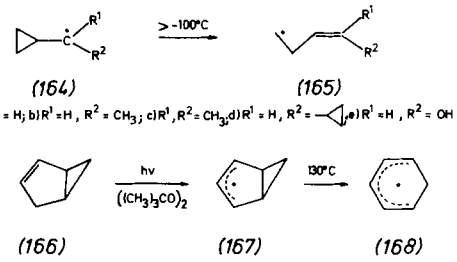
This difficulty is largely avoided in the bicyclo[2.2.0]hexane derivatives *(158)*, *(160)*, and *(162)*: their thermolysis leads initially to conformationally uniform 1,4-cyclohexanediyls *(158a)*, *(160a)*, and *(162a)*, respectively[117]. It was estimated from the differences in activation energy for the over-



(158) *(158a)* *(159)*
(160) *(160a)* *(161)*
(162) *(162a)* *(163)*

all reactions leading to *(159)*, *(161)*, and *(163)* that the stabilization energy of a cyclopropylmethyl radical with an optimum conformation is *ca.* 12 kJ/mol[117].

Simple cyclopropylmethyl radicals *(164)*—generated from methylcyclopropanes by hydrogen abstraction with *tert*-butoxy radicals—undergo very fast rearrangement to homoallyl radicals *(165)*, in some cases even at *ca.* −100 °C[118]. In contrast, the bicyclo[3.1.0]hexenyl radical *(167)* generated in the



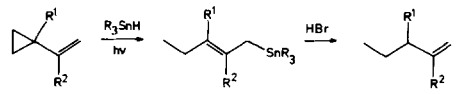
(164) (165)

a) $R^1,R^2 = H$; b) $R^1 = H$, $R^2 = CH_3$; c) $R^1,R^2 = CH_3$; d) $R^1 = H$, $R^2 =$; e) $R^1 = H$, $R^2 = OH$

(166) (167) (168)

same way from *(166)* is stable up to at least +70 °C; it isomerizes to the cyclohexadienyl radical *(168)* only at +150 °C[119].

The facile ring cleavage of cyclopropylmethyl radicals is the basis of a method for the chemospecific reductive ring opening of vinylcyclopropanes *(169)*. Photochemically initiated hydrostannylation leads *via* 1,4-addition to trialkylal-

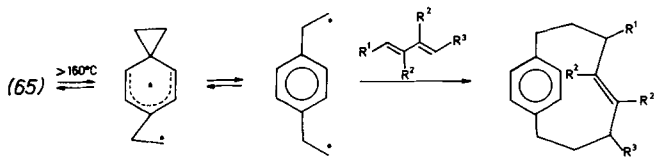


(169) (170) (171)

$R^1,R^2 = H, CH_3$ R = CH_3, n-Bu

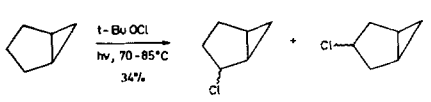
lylstannanes *(170)* which are transformed by hydrogen bromide into the alkenes *(171)* in more than 80% yield[120].

Dispiro[2.2.2.2]deca-4,9-diene *(65)* is an interesting special case. The second step of its double ring cleavage *via (172)* to the diradical *(173)*, which is fast above 160 °C, belongs to the class of cyclopropylmethyl to homoallyl rearrangements; the yield of the [8]paracyclophane derivatives *(174)* (30—84%) on cycloaddition of *(173)* or *(172)* to conjugated dienes are surprisingly high[121].



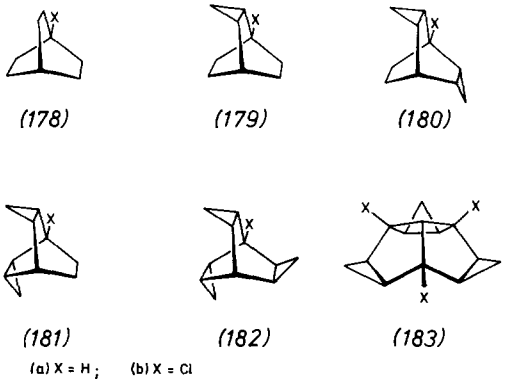
(172) (173) (174)

In spite of the pronounced tendency of α-cyclopropyl-substituted radicals to undergo ring opening, cyclopropyl hydrocarbons can be selectively derivatized by free radical attack. For instance, comparatively mild chlorination can be accomplished with *tert*-butyl hypochlorite on irradiation, especially at low temperatures[122–124]. Thus, at 70—85 °C, bicyclo[3.1.0]hexane *(175)* gives a mixture of 78% of *(176)* and 22% of *(177)* in 34% yield[122a]. Low temperature photochlorination (−40 °C) of the hydrocarbons *(179a)—(182a)* gave good yields of the bridgehead chlorides *(179b)—(182b)* completely free of secondary products due to rearrangement of the radical intermediate[18,123].



(175) (176) 78% (177) 22%

The same applies to the preparation of the trichloride *(183b)* from *(183a)*[124]. Even in tricyclo[3.2.2.0^{2,4}]nonane *(179a)*, bridgehead attack is favored by a factor of more than



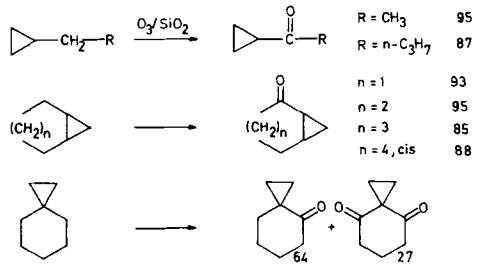
(178) (179) (180)

(181) (182) (183)

(a) X = H; (b) X = Cl

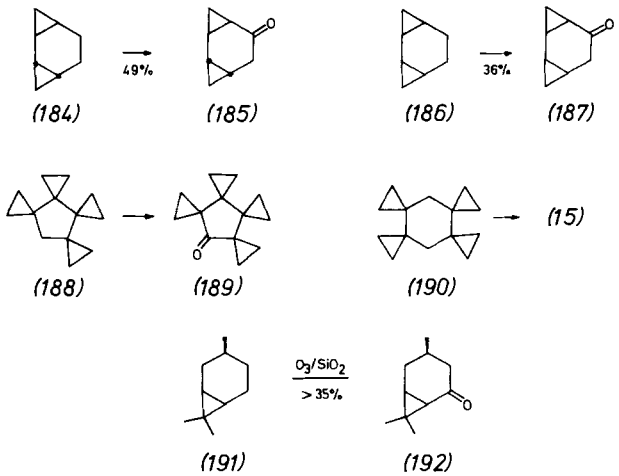
2 relative to bicyclo[2.2.2]octane *(178a)*; it becomes more and more dominant as the number of α-annelated cyclopropane rings increases, and is practically the only reaction in trishomobarrelene *(182a)*. This is due not only to the weak yet definite radical stabilization by α-cyclopropyl groups; the strong electron donating effect of the cyclopropane ring on electron-deficient centers (see Section 6) also plays a role since the transition state of hydrogen abstraction by *tert*-butoxy radicals (and by electronegative radicals in general) exhibits partial charge separation[125].

This combined effect also becomes operative on attack of C—H bonds by ozone; it is responsible for the selective oxidation[103,127] of sites adjacent to a cyclopropane ring on dry ozonation[126], for ozone behaves as a dipolar 1,3-diradical[128]. This new method for the synthesis of cyclopropyl ketones from cyclopropyl hydrocarbons (see Scheme 3) is a



Scheme 3. Relative yields of α-ketones on ozonation of cyclopropyl hydrocarbons as percentages (without considering unreacted starting material).

convenient addition to the list of previous reactions[28]. The method also provides an entry to compounds which are otherwise inaccessible or accessible only with difficulty. Ex-



amples of such compounds are *exo- (185)* and *endo*-tricyclo[5.1.0.0^{2,4}]octan-5-one *(187)* from *(184)* and *(186)*, respectively, and the monoketone *(189)* and the diketone *(15)* as convenient precursors of [5]- *(96)*[129] and [6]rotane *(97)*[127b].

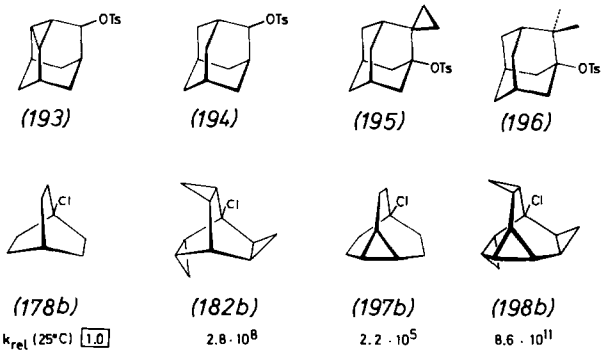
The new one-step preparation of *cis*-caran-5-one *(192)* from *cis*-carane *(191)*[130] is faster and gives better yields than other multistep procedures[131]. Further applications of this oxidation in the field of terpenes are conceivable and would appear promising.

6. Electron-Donating Effect of the Cyclopropyl Group

Undoubtedly the most versatile and hence most interesting "cyclopropyl function" results on combination of the three-membered carbocycle with a neighboring electron-deficient center. Several reviews[1,132–135] witness to the wealth of publications about such systems. The basis of a directed synthetic application of this function is, *inter alia*, a detailed knowledge of structure/stability and structure/reactivity relationships of cationic cyclopropylmethyl systems.

Studies by several research groups, especially those on systems of uniform, defined conformation, have revealed the relationship between the stability of a cyclopropylmethyl cation and its conformation[17,18,136–138].

In the didehydroadamantyl derivative *(193)* we see a system of this kind in the bisected conformation (see Fig. 4) with a parallel arrangement of the interacting orbitals. Therefore, *(93)* solvolyzes 2.5×10^8 times faster than 2-adamantyl tosylate *(194)*[136a] under the same conditions. For a perpendicular orientation of the cyclopropane Walsh orbital and the carbenium ion p orbital, such as encountered in the adamantane-2-spirocyclopropane system *(195)*, the solvolysis rate is reduced by a factor of 365 relative to the reference system *(196)*, *i.e.* the cyclopropyl group has an inductive electron-attracting effect in this case and destabilizes the intermediate carbenium ion[17]. The overall range of rate ratios of $\approx 10^{11}$ between *(193)/(194)* and *(195)/(196)* corresponds to a



difference in free energy of $\Delta G_{298} \approx 68$ kJ/mol between the bisected ($\varphi = 0°$) and the perpendicular ($\varphi = 90°$) conformation of the cyclopropylmethyl cation.

Essentially rigid intermediate conformations ($\varphi = 50$—$60°$) are found in the bridgehead cations of the polycyclic systems *(179)*—*(182)* and *(198)*. The S_N1 solvolysis rates of all the bridgehead chlorides *(179b)*—*(182b)* and *(198b)* are accordingly much higher that those of the reference compounds *(178b)* and *(197b)* which do not contain cyclopropyl groups in an α position relative to the bridgehead[18,138]. Owing to the cumulative effect of three such groups, the ratios of *(182b)* to *(178b)* and of *(198b)* to *(197b)* are particularly large at 2.8×10^8 and 3.9×10^6, respectively. Although it is a bridgehead chloride, *(198b)* is some 1.6×10^5 times more reactive than *tert*-butyl chloride: *(198)* thus exhibits the greatest bridgehead reactivity found so far for any system[139].

Detailed analysis of the solvolysis rates of *(178b)*—*(182b)*, paying due attention to all relevant structural factors, has shown that the dependence of the relative stabilization energy E_φ of a cyclopropylmethyl cation upon the torsional angle φ is reproduced very well by the $\cos^2 \varphi$ function

$$E_\varphi = E_{\varphi=0} \cos^2 \varphi$$

where $E_\varphi = 75$ kJ/mol[18]. Apart from the value for maximum stabilization ($E_{\varphi=0}$) the function exactly corresponds to the curve calculated for this angular dependence by the CNDO method[140] (see Fig. 6).

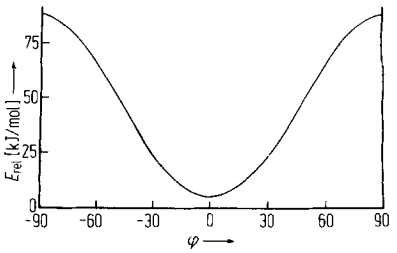


Fig. 6. Change in energy of a cyclopropylmethyl cation with conformation calculated by the CNDO method (φ = torsional angle, see Fig. 4) (according to [140]).

As a logical consequence of the enhanced bridgehead reactivity of *(179b)*—*(182b)* and *(198b)*, the corresponding "free" bridgehead cations can be readily generated[18] by

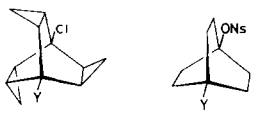
Table 3. Examples of known bridgehead derivatives of trishomobarrelene *(182)* and trishomobullvalene *(198)*. Isolated yields given.

Starting material	Reagent/ method	Product	Yield [%]	Ref.
Trishomobarrelene (182), bridgehead substituent:				
Cl	H_2O/Dioxane	OH	91	[143]
Cl	CH_3OH/CH_3ONa	OCH_3	95	[144]
Cl	NH_3/Et_2O	NH_2	90	[143]
Cl	$NaN_3/ZnCl_2/CS_2$	N_3	95	[144]
Cl	KCN/CuI/NMP [a]	CN	69	[144]
H	O_3/SiO_2	OH	73	[144]
OH	$SOCl_2$/Polym. base [b]	Cl	95	[144]
OH	HBr/H_2O	Br	81	[144]
OH	HI/H_2O	I	92	[144]
OH	$ClFCH-CF_2NEt_2$	F	40	[144]
Cl	Ag_2CO_3/H_2O	[c]	92	[145]
I	1) *t*-BuLi, 2) CO_2	CO_2H	60	[144]
OH	$Al(CH_3)_3$	CH_3	88	[144]
Cl	*i*-C_3H_7MgBr	*i*-C_3H_7	54	[144]
Cl	*cyclo*-C_3H_5MgBr	*cyclo*-C_3H_5	53	[144]
Cl	C_6H_5MgBr	C_6H_5	72	[144]
Cl	Imidazole (Im-H)	Im	91	[144]
Trishomobullvalene (198), bridgehead substituent:				
H	*t*-BuOCl/*hν*	Cl	30	[143, 146]
H	O_3/SiO_2	OH	60	[144]
OH	HCl/H_2O/Acetone	Cl	100	[147]
OH	KCN/CF_3CO_2H	CN	90	[147]
Cl	NH_3/Et_2O	NH_2	82	[143]

[a] *N*-Methylpyrrolidone. [b] (Diethylaminomethyl)polystyrene. [c] Bistrishomobarrelenyl ether.

present-day techniques[141]. Their ^{1}H- and ^{13}C-NMR spectroscopic data suggest considerable delocalization of the positive charge into the cyclopropyl groups, as has been demonstrated for cyclopropylmethyl cations in other conformations[142]. The cations can generally be efficiently trapped by nucleophilic reagents, regenerating bridgehead derivatives. In no case was skeletal rearrangement observed. Thus, on use of suitable reagents, nucleophilic substitution reactions provide access to almost any bridgehead derivative, especially of the trishomobarrelene *(182)* and the trishomobullvalene system *(198)* (see Table 3).

Unlike trishomobullvalene *(198a)*, trishomobarrelene *(182a)* has two equivalent reactive bridgehead sites; it therefore preferentially forms 1,5-dichlorotrishomobarrelene *(199a)* on treatment with an excess of *tert*-butyl hypochlorite[123]. Owing to the inductive effect of the second chlorine substituent, *(199a)* is significantly less reactive than the monochloride *(182b)*[123]. The logarithms of the solvolysis rates of a series of 5-substituted 1-chlorotrishomobarrelenes *(199a)—(199i)*[147]; correlate well with the inductive substit-

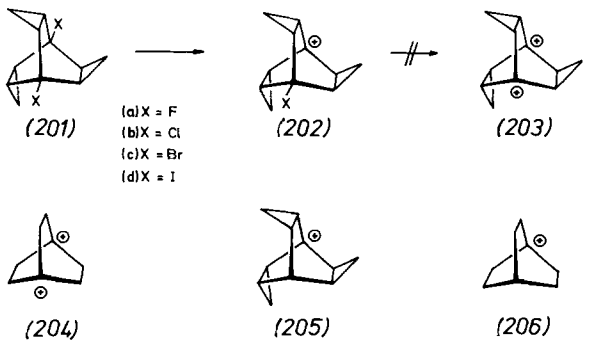


(199) *(200)* Ns = p-$NO_2C_6H_4SO_3$

(a) Y = Cl, *(b)* Y = CH_3, *(c)* Y = C_2H_5, *(d)* Y = *i*-C_3H_7, *(e)* Y = C_6H_5, *(f)* Y = CO_2CH_3, *(g)* Y = OCH_3, *(h)* Y = CF_3, *(i)* Y = CN

uent constants σ_{CH_2} of the Taft equation[148], and even better with the σ_q^I constants introduced by *Grob*[149]. The slope of the regression line, *i.e.* the reaction constant ρ_q^I (at 25 °C), is *ca.* 50% greater than that for 4-substituted 1-bicyclo[2.2.2]octyl *p*-nitrobenzenesulfonates *(200)*[150]. Hence the ability to transmit inductive substituent effects must be considerably greater for cyclopropane C—C σ bonds that for normal C—C σ bonds, as would be expected from their greater p character[10]. In contrast, transmission of mesomeric effects by the cyclopropane ring is much poorer than by a C=C double bond[151].

With regard to the results obtained for *(199a)—(199i)*, the substantially stronger electron withdrawal of a carbenium ion center should also be efficiently transmitted through the cyclopropyl C—C bonds in this system. This may be the reason why it has been impossible so far to generate the trishomobarrelene dication *(203)* from any of the dihalides *(201)*. In all cases only the monohalomonocations *(202)* were detectable[152] although, according to MINDO/3 calculations[153], the extent of stabilization for *(203)* with respect to

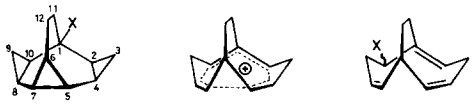


(201) *(202)* *(203)*

(204) *(205)* *(206)*

the known bicyclo[2.2.2]octyl dication *(204)*[154] should be the same as that for the monocation *(205)* relative to the kinetically unstable *(206)*[155].

Cationic cyclopropylmethyl systems in general are known[132–134] to rearrange to homoallyl systems *via* ring opening or to cyclobutyl systems *via* ring expansion[156]. Neither of these types of rearrangement occurs in the bridgehead cyclopropylmethyl systems mentioned above, apparently because of extensive ring strain in the potential products. The dihydro-*exo,exo*-bishomobullvalene system *(207)*[157] is an exception, since the reaction of the alcohol *(207b)* with thionyl chloride in the presence of diethylaminomethyl-polystyrene even at room temperature yields a rearranged chloride shown by its ^{1}H- and ^{13}C-NMR spectra[158] to have the structure *(209c)*.

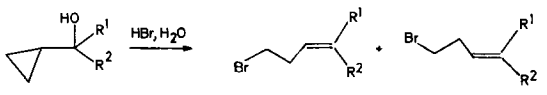


(207) *(208)* *(209)*

(a) X = H ; (b) X = OH ; (c) X = Cl

Apparently the intermediate carbenium ion behaves, like *(208)*, as a bridged trishomocycloheptatrienyl cation which is attacked by the nucleophile preferentially in positions 2 and 10, respectively.

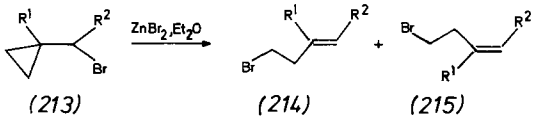
Therefore *(209)* is the result of a threefold cyclopropylmethylhomoallyl rearrangement. This type of reaction plays a major role in the synthetic utilization of the cyclopropyl ring function (see above). *Julia*'s olefin synthesis[159] is a classical example of these methods; it has found wide application in the preparation of isoprenoids[160–162].



(210) *(211)* *(212)*

(a) R^1 = Alkyl, R^2 = H
(b) R^1 = Alkyl, R^2 = CH_3

90–95% 5–10%



(213) *(214)* *(215)*

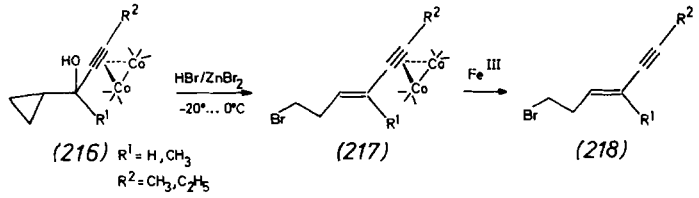
R^1 = CH_3, C_2H_5
R^2 = Alkyl, Alkenyl

96–97% 3–4%

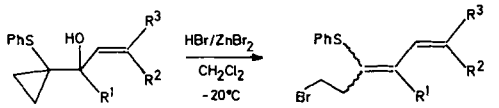
According to the original procedure[159a,b] a cyclopropylmethanol *(210)* is treated with 48% hydrobromic acid; secondary alcohols *(210a)* give the (*E*)-configurated olefins *(211a)* with 90 to 95% stereoselectivity. Treatment of tertiary alcohols *(210b)* with magnesium halides in ether also give the (*E*)-olefins *(211b)* in excellent yields[160]. On the other hand, the modified procedure of *Johnson et al.*[161] leads to trisubstituted (*E*)-olefins *(214)* stereoselectively upon treatment of the secondary cyclopropylmethyl bromides *(213)* with zinc bromide in ether. Stereoselectivity is also observed if one of the two alkyl groups in *(210)* carries a phenylsulfonyl group[159e].

Interesting variants of the *Julia* method are the stereoselective production of conjugated enynes *(218)* as precursors for conjugated *E,Z*-dienes from alkynylcyclopropylmethanols *via* their dicobaltcarbonyl complexes *(216)* as interme-

diates[163], as well as the acid-catalyzed rearrangement of (phenylthiocyclopropyl)vinylmethanols *(219)* to functionalized conjugated dienes *(220)*, which are versatile intermediates in synthesis[164].

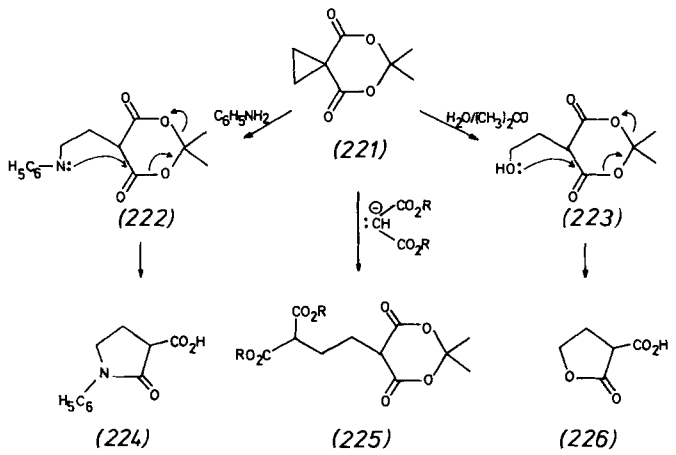


(216) $R^1 = H, CH_3$; $R^2 = CH_3, C_2H_5$ *(217)* *(218)*



(219) *(220)*

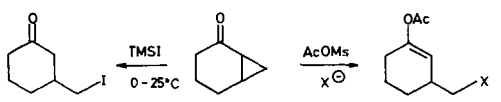
The "homologous Michael reaction", *i.e.* the ring opening of cyclopropylcarbonyl compounds by nucleophiles, which has been developed extensively in recent years[165,166], is derived from the same reaction principle. If sufficiently activated by two electron-withdrawing groups (especially as in *(221)*), such compounds can add various nucleophilic reagents[167]. The primary adducts of primary amines (*e.g.* *(222)*) or water *(223)* readily cyclize to the five-membered heterocycles *(224)* and *(226)* respectively, which, like the adducts of carbanions [*e.g.* *(225)*], can serve as intermediates in the synthesis of natural products[165].



(222) *(221)* *(223)*

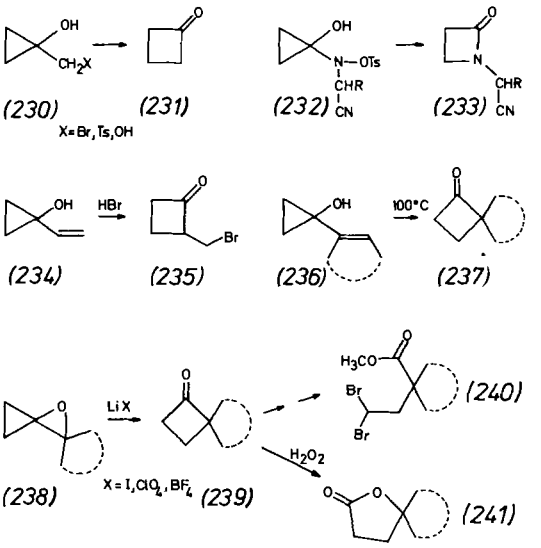
(224) *(225)* *(226)*

Monoactivated cyclopropanes do not react the same way except in special cases[165]. Nucleophilic additions to such systems do, however, occur smoothly with the assistance of an electrophile[168–171] (see Section 2[53]). In this way, cyclo-



(227) *(228)* *(229)*

propyl ketones are cleaved under mild conditions by trimethylsilyliodide (TMSI) to γ-iodoketones [*e.g.* *(228)*→*(227)*[170]] or by acetylmethanesulfonate (AcOMs) together with nucleophiles to give δ-substituted enol acetates [*e.g.* *(228)*→*(229)*][171].



(230) *(231)* *(232)* *(233)* *(234)* *(235)* *(236)* *(237)* *(238)* *(239)* *(240)* *(241)*

These are a few examples only for the various possibilities of the cyclopropylmethyl homoallyl ring opening reaction. Nonetheless the second type of cyclopropylmethyl rearrangement, *i.e.* the ring expansion to cyclobutane derivatives, was essential for a number of new synthetic reactions[172–175]. All the (1-hydroxycyclopropyl)methyl derivatives *(230)* yield cyclobutanone *(231)* under appropriate conditions[172]. A β-lactam synthesis developed by *Wasserman et al.* [*e.g.* *(232)*→*(233)*] is based on the same reaction principle[173]. 1-Vinylcyclopropanol *(234)* reacts with electrophilic reagents to yield derivatives of 2-methylcyclobutanone, *e.g.* *(235)*[174]. 1-Vinylcyclopropanols *(236)* can also be rearranged thermally to cyclobutanones *(237)*[172]. The greatest flexibility is offered by the oxaspiropentanes *(238)*—readily available according to *Trost et al.*[56,57,175] from aldehydes and ketones—because of their rearrangements to cyclobutanones *(239)*, which can be utilized in the synthesis of a variety of compounds such as *(240)* and *(241)*[175].

The wide spectrum of possible applications of electron-deficient cyclopropylmethyl groups has only been suggested by these examples. Finally, it should be pointed out how the electron-donating ability of the cyclopropyl group can be utilized in mechanistic problems. *Tidwell et al.* have carefully investigated electrophilic additions to alkenes and observed that the rate enhancement by a cyclopropyl substituent is proportional to the amount of positive charge localized on the α-carbon atom in the transition state[176]. In a reversed sense, the cyclopropyl substituent can therefore be used as a sensitive probe into the transition state structure of an electrophilic addition[176].

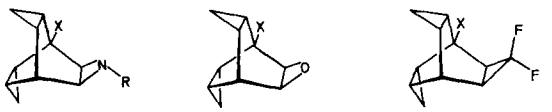
7. Heterocyclic Analogues of Cyclopropane

While discussing the characteristics of the cyclopropane ring one is automatically tempted to compare them with those of simple heterocyclic three-membered rings, especially since their bonding properties can be described by the same model as that used for the cyclopropane ring[2,177]. As far as the chemistry of aziridines and oxiranes is concerned, reference is made to the relevant handbooks[178]. In this context, only the interesting question about the electron-donating ability of aziridyl and oxiryl groups, which has remained

unanswered for a long time in spite of elaborate studies[179/181], will be discussed briefly.

Previous kinetic and mechanistic investigations on aziridylmethyl[179,180a] and oxirylmethyl derivatives[181a] did not give a clear-cut picture, because in all cases so far ring opening reactions and neighboring group participation of the heteroatom played an important role. In contrast to this, the 1-chloro-3-methyl-3-azatrishomobarrelene *(242b)* and the 1-chloro-3-oxatrishomobarrelene *(243b)* solvolyze exclusively to unrearranged bridgehead derivatives *(242c, d)* and *(243c, d)*[182], respectively. Their solvolysis rates therefore yield reliable information pertaining to the question of how an intact three-membered heterocycle influences the relative stability of an adjacent carbenium ion center.

Taking into account all the structural details, the exact analysis of the rate data (see Table 4) shows that in these systems with their rigid conformations the electron-donating ability of an unsubstituted aziridyl group is about 13 times weaker than that of a cyclopropyl group, whereas the oxiryl group even exhibits a strong electron-withdrawing effect. The decreasing donating ability of the hetero-three-membered rings correlates with the increasing electronegativity of the heteroatoms, which lowers the energy of its highest occupied Walsh molecular orbital[184]. Electron-withdrawing substituents at the cyclopropyl group as in *(244b)* act in the same way (see Table 4)[182].



(242) R = CH_3 *(243)* *(244)*

(a) X = H ; (b) X = Cl ; (c) X = OH ; (d) X = OEt

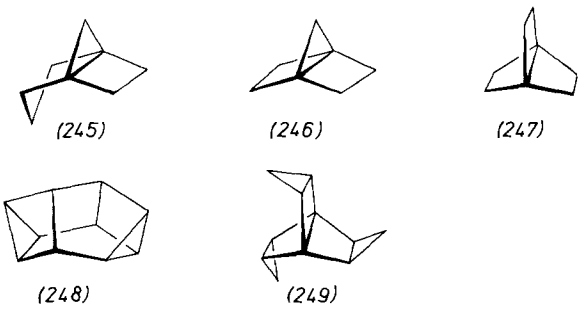
Table 4. Rate constants and free energies of activation of heterologous 1-chlorotrishomobarrelenes and reference compounds [182].

Cpd.		k_{25} [s^{-1}]	k_{rel}	$\Delta G^{\neq}_{25}$ [kJ/mol]	$\Delta G^{\neq}_{25}$ [kJ/mol]
(181b)	real	$5.8 \cdot 10^{-6}$	0.15	—	—
(181b)	hypothet. [a]	$8.9 \cdot 10^{-7}$	1.0	107.5	0.0
(182b)		$5.8 \cdot 10^{-4}$	650	91.6	−15.9
(244b)		$4.2 \cdot 10^{-6}$	4.7	103.8	− 3.7
(242b)	R = CH_3	$1.4 \cdot 10^{-5}$	16	100.6	− 6.9
(242b)	R = H [b]	$1.4 \cdot 10^{-6}$	1.6	106.3	− 1.2
(243b)		$3.8 \cdot 10^{-8}$	0.04	115.5	+ 8.0

[a] Calculated for a hypothetical model showing the same degree of skeletal twisting in its transition state as found for *(182b)* (see [18]). [b] Calculated from the value for the *N*-methyl compound with a factor of 10^{-1} to account for the methyl group [183].

8. Outlook

It is obvious that the aspects of small ring chemistry presented here cannot be discussed extensively, and they have not even been completely investigated yet. New polycyclic small ring compounds which have already been prepared or only trapped as short-lived intermediates will help to delineate the limits of the carbon atom's bonding ability and the possibilities of reactivity enhancement by ring strain. This is exemplified by the molecules *(245)—(249)*. In the so-called small ring propellanes *(245)—(247)* the p character of the central C—C single bond must be unusually high because all four bonds on the two quaternary carbons are arranged as in an "inverted" tetrahedron[185,186]. Like the π bonds in olefins, these central bonds therefore easily add a variety of reagents. However, the most important factor determining the reactivity of these propellanes is the high total strain energy, which is largely liberated upon opening the central bond. In this way, the [3.2.1]propellane *(245)*[187] with a strain energy *(SE)* of about 250 kJ/mol[188] rapidly adds halogens, acids, and even atmospheric oxygen. So far the [2.2.1]propellane *(246)*[189] and the [2.2.2] parent system[190] (*SE* about 330 kJ/mol[191] in each case) have only been postulated as intermediates based on the isolation of their addition products.



(245) *(246)* *(247)*

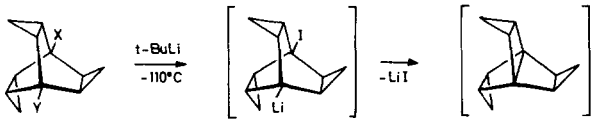
(248) *(249)*

However, one cannot generally relate a high total strain energy of a molecule to its thermal instability and draw conclusions about its ability to exist at room temperature. For instance, *(245)* is thermally quite stable although it adds electrophiles quite easily. This difference is even more pronounced in the case of barettane *(248)* with $SE \geq 449$ kJ/mol[191]: in the presence of a catalyst *(248)* adds hydrogen extremely rapidly to the most highly strained σ bonds of its two bicyclo[2.1.0]pentane units; yet, on the other hand, it is completely stable up to 200 °C[192]. In contrast to the isomeric diademane *(91)* (*SE* about 427 kJ/mol)[191], *(248)* does not have a low energy reaction path to a thermodynamically more stable rearrangement product at its disposal.

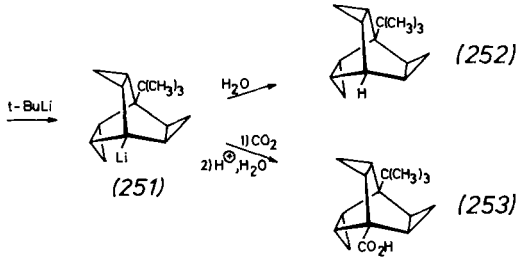
The still hypothetical propellane *(249)* seems to approach the limits of what is conceivable on the basis of current bonding theory. Its three bicyclopentane units which all share the same central bond contribute to a total strain energy of at least 670 kJ/mol[191], the portion of about 328 kJ/mol which would be released upon opening the central bond very closely resembles the energy of a normal C—C single bond. It remains questionable, therefore, whether *(249)* can exist at all with a central "bond", even if one takes into account that a certain stabilizing interaction may occur between the bridgehead p orbitals and the cyclopropyl Walsh orbitals.

Nevertheless, there are experimental findings which suggest an intermediacy of *(249)* or its diradical or zwitterionic equivalent respectively[193]. The 1-*tert*-butyl derivative *(250)* is formed at −110 °C from 1,5-diiodotrishomobarrelene *(201d)* and *tert*-butyllithium after aqueous work-up. Since a direct *tert*-butylation of *(201d)* can be excluded—though the more reactive 1-iodotrishomobarrelene is smoothly metalated under the same conditions it does not yield a trace of *(252)*—it is more probable that in fact *(249)* is formed *via (250)*.

An addition of *tert*-butyllithium to the central bond in *(249)*, which would be reasonable in view of its high strain energy, leads to *(252)*, the intermediacy of which was proved by its carboxylation to *(253)*. Final proof for the intermediate formation of the symmetrical *(249)*, which would be possible, for instance, by use of a trishomobarrelene derivative *(201e)*



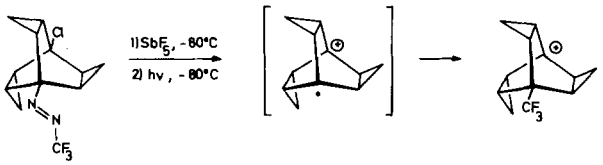
(201) (d) X = Y = I (e) X ≠ Y (250) (249)



(251) (252) (253)

with two different leaving groups in optically active form[194], is still pending.

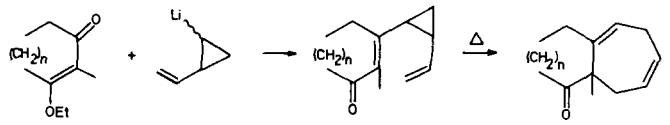
Better chances for a direct spectroscopic proof should exist for the radical cation *(255)* which is closely related to *(249)*, because the substantial cation-stabilizing effect of the cyclopropyl group (*vide supra*) comes into play and the conceivable "bond" between the two bridgeheads[195] would be a one-electron bond and thereby longer than that in *(249)*. It is an open question what the lifetime of *(255)* may be, if it occurs as an intermediate in the sequence *(254)*→*(257)*[193]. In this case, the use of optically active starting material[196] would again be of help.



(254) (255) (256)

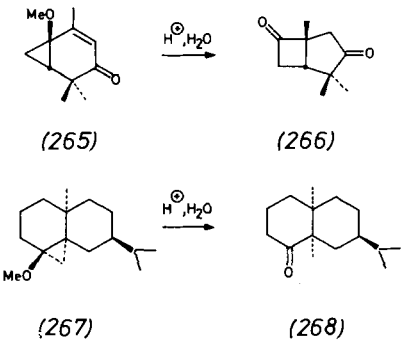
Thus more and more new model compounds can be conceived which will provide ever more detailed knowledge about the "bonding properties of the cyclopropane ring and their chemical consequences". The development of new synthons, which utilize these properties, will build upon that knowledge. Even nowadays, synthetic applications of the small ring functions are beginning to play a major role.

(261) constitutes a useful method for the annelation of cycloheptane rings[198].



(261) (262) (263) (264)

Wenkert et al. demonstrated an elegant utilization of the methoxycyclopropyl function in important steps of the total synthesis of (+)-grandisol [*(265)*→*(266)*], of (−)-valeranone [*(265)*→*(268)*], and of other sesquiterpenes[199].

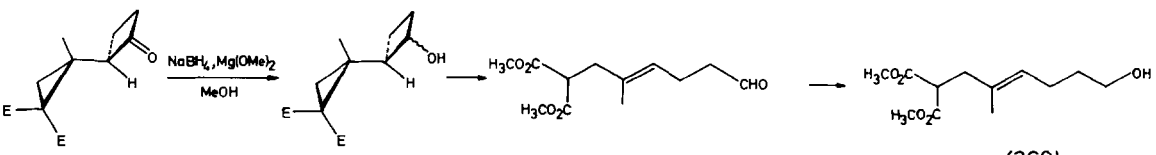


(265) (266) (267) (268)

These and many other examples[200,165,163] point the way for the directed utilization of three-membered ring synthons.

The authors' own work cited in this article was only made possible by the dedication and ingenuity of a group of enthusiastic co-workers. Their namens are given in the relevant references. Particular thanks go to Professor W. Lüttke, Göttingen, for provision of excellent working conditions during the decisive initial phase. Financial support by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, the State of Lower Saxony, and Hoechst AG, Frankfurt/Main, and BASF AG, Ludwigshafen, is gratefully acknowledged.

Received: August 23, 1979 [A 293 IE]
Supplemented: September 26, 1979
German version: Angew. Chem. *91*, 867 (1979)



(257) E = $CO_2C(CH_3)_3$ (258) (259) (260)

Systems of type *(257)* can be constructed by standard methods, *e.g.* from α,β-unsaturated carbonyl compounds. Their fragmentation, accompanied by a strain energy release of about 230 kJ/mol, proceed under mild conditions and stereospecifically to give 1,6- and 1,7-difunctionalized molecules such as *(259)* and *(260)*, which can serve as starting materials for the syntheses of acyclic terpenes[197].

The thermal rearrangement of the adducts *(263)* of 2-vinylcyclopropyllithium *(262)* to 3-alkoxy-2-cycloalkenones

[1] Cf. *M. Charton* in *J. Zabricky:* The Chemistry of Alkenes. Interscience, London 1970, Vol. 2, pp. 511 ff.
[2] *A. D. Walsh*, Trans. Faraday Soc. *45*, 179 (1949); *T. M. Sugden*, Nature *160*, 367 (1947); cf. also: *W. W. Schoeller*, Tetrahedron *29*, 929 (1973).
[3] *Th. Förster*, Z. Phys. Chem. (Leipzig) *B 43*, 58 (1939).
[4] *C. A. Coulson, W. E. Moffit*, J. Chem. Phys. *15*, 151 (1947); Phil. Mag. *40*, 1 (1949).
[5] *A. Hartmann, F. L. Hirschfeld*, Acta Crystallogr. *20*, 80 (1966); *C. J. Fritchie, Jr., ibid. 20*, 27 (1966).
[6] *W. L. Jorgensen, L. Salem:* The Organic Chemist's Book of Orbitals. Academic Press, New York 1973, pp. 146 f.
[7] See [1], p. 524.

[8] *N. Muller, D. E. Pritchard,* J. Chem. Phys. *31*, 768 (1959).
[9] *L. Pauling,* J. Am. Chem. Soc. *53*, 1367 (1931); *J. C. Slater,* Phys. Rev. *37*, 481 (1931).
[10] Cf. *W. A. Bernett,* J. Chem. Educ. *44*, 17 (1967), references cited therein.
[11] Cf. *C. J. Collins,* Chem. Rev. *69*, 543 (1969); *C. C. Lee,* Prog. Phys. Org. Chem. *7*, 129 (1970); *C. H. De Puy,* Fortschr. Chem. Forsch. *40*, 73 (1973).
[12] Concerning the stereochemistry, see *C. H. De Puy, A. H. Andrist, P. C. Fünfschilling,* J. Am. Chem. Soc. *96*, 948 (1974); *R. T. LaLonde, A. D. Debboli,* J. Org. Chem. *38*, 4228 (1973).
[13] *R. W. Lipnick, E. W. Garbisch, Jr.,* J. Am. Chem. Soc. *95*, 6370 (1973), references cited therein; cf. *M. E. Squillacote, R. Sheridan, O. L. Chapman, F. A. L. Anet, ibid. 101*, 3657 (1979), and references cited therein.
[14] *P. N. Skanche, J. E. Boggs,* J. Mol. Struct. *16*, 179 (1973), references cited therein.
[15] Cf., *e.g. A. Streitwieser, C. H. Heathcock:* Introduction to Organic Chemistry. MacMillan, New York 1976, pp. 529 ff.
[16] *A. de Meijere, W. Lüttke,* Tetrahedron *25*, 2047 (1969); *H. Günther, H. Klose, D. Wendisch, ibid. 25*, 1531 (1969); *V. R. Salares, W. F. Murphy, H. J. Bernstein,* J. Raman Spectrosc. *7*, 147 (1978); cf. also *H. Braun, W. Lüttke,* J. Mol. Struct. *31*, 97 (1976).
[17] *B. R. Ree, J. C. Martin,* J. Am. Chem. Soc. *92*, 1660 (1970); *V. Buss, R. Gleiter, P. v. R. Schleyer, ibid. 93*, 3927 (1971); *D. S. Kabakoff, E. Namanworth, ibid. 92*, 3234 (1970).
[18] *A. de Meijere, O. Schallner, C. Weitemeyer, W. Spielmann,* Chem. Ber. *112*, 908 (1979), references cited therein.
[19] *G. A. Olah, R. J. Spear,* J. Am. Chem. Soc. *97*, 1539 (1975), references cited therein.
[20] *H. Volz, J.-H. Shin, H. J. Streicher,* Tetrahedron Lett. *1975*, 1297; *H. C. Brown, M. Ravindranathan, E. N. Peters,* J. Org. Chem. *42*, 1073 (1977), and references cited therein.
[21] *A. von Baeyer,* Ber. Dtsch. Chem. Ges. *18*, 2278 (1885).
[22] *J. W. Knowlton, F. D. Rossini,* J. Res. Natl. Bur. Stand. *43*, 113 (1949); cf. *L. N. Ferguson,* J. Chem. Educ. *47*, 46 (1970).
[23] Cf., *e.g., R. T. LaLonde, L. S. Forney,* J. Org. Chem. *29*, 2911 (1964); *K. B. Wiberg, A. de Meijere,* Tetrahedron Lett. *1969*, 519.
[24] *H. M. Frey,* Adv. Phys. Org. Chem. *4*, 147 (1966); *H. M. Frey, R. Walsh,* Chem. Rev. *69*, 103 (1969).
[25] *M. R. Willcott, R. L. Cargill, A. B. Sears,* Prog. Phys. Org. Chem. *9*, 25 (1972).
[26] Cf. [28], pp. 89 ff.
[27] *M. Jones, Jr., R. A. Moss:* Carbenes. Vol. 1, 2. Wiley-Interscience, New York 1973, 1975; *W. Kirmse:* Carbene, Carbenoide und Carbenanaloge. Verlag Chemie, Weinheim 1969.
[28] *D. Wendisch* in Houben-Weyl-Müller: Methoden der Organischen Chemie. 4th Edit. Thieme, Stuttgart 1971, Vol. IV/3.
[29] a) *W. P. Weber, G. W. Gokel:* Phase Transfer Catalysis in Organic Chemistry. Springer, Heidelberg 1977; b) *C. M. Starks, C. Liotta:* Phase Transfer Catalysis. Principles and Techniques. Academic Press, New York 1978; c) *E. V. Dehmlow, S. S. Dehmlow:* Phase Transfer Catalysis. Verlag Chemie, Weinheim, in press.
[30] *S. W. Staley,* J. Am. Chem. Soc. *89*, 1532 (1967).
[31] *A. de Meijere,* Chem. Ber. *107*, 1684 (1974).
[32] Cf. *C. H. Heathcock, S. R. Poulter,* J. Am. Chem. Soc. *90*, 3766 (1968).
[33] *J. F. Chiang, C. F. Wilcox, Jr.,* J. Am. Chem. Soc. *95*, 2885 (1973).
[34] *R. A. Clark, R. A. Fitao,* J. Am. Chem. Soc. *92*, 4737 (1970).
[35] *R. Pearson, Jr., A. Choplin, V. W. Laurie,* J. Chem. Phys. *62*, 4859 (1975); *R. Pearson, A. Choplin, V. W. Laurie, J. Schwartz, ibid. 62*, 2949 (1975), references cited therein.
[36] *R. Hoffmann,* Tetrahedron Lett. *1970*, 2907; *H. Günther, ibid. 1970*, 5173.
[37] *R. Baird, S. Winstein,* J. Am. Chem. Soc. *85*, 567 (1963).
[38] *P. Rys, P. Skrabal, H. Zollinger,* Tetrahedron Lett. *1971*, 1797.
[39] Survey in: *J. P. Pete,* Bull. Soc. Chim. Fr. *1967*, 357.
[40] *G. W. Cannon, A. A. Santilli, P. Shenian,* J. Am. Chem. Soc. *81*, 1660 (1959).
[41] Cf. also *S. A. Monti,* J. Org. Chem. *35*, 380 (1970).
[42] *J. Heller, A. Yogev, A. S. Dreiding,* Helv. Chim. Acta *55*, 1003 (1972); *J. E. Heller, A. S. Dreiding, B. R. O'Connor, H. E. Simmons, G. L. Buchanan, R. A. Raphael, R. Taylor, ibid. 56*, 272 (1973).
[43] *I. A. McDonald, A. S. Dreiding,* Helv. Chim. Acta *56*, 2523 (1973).
[44] *E. Proksch, A. de Meijere,* Tetrahedron Lett. *1976*, 4851.
[45] *M. Engelhard, W. Lüttke,* Chem. Ber. *110*, 3759 (1977), and references cited therein.
[46] *I. Erden, D. Kaufmann, A. de Meijere,* to be published.
[47] *E. Wenkert, J. E. Yoder,* J. Org. Chem. *35*, 2985 (1970); *P. G. Gassman, X. Creary,* J. Chem. Soc. Chem. Commun. *1972*, 1214; see also *J. Dekker, E. J. C. Martins, J. A. Krüger, A. J. Goosen,* Tetrahedron Lett. *1974*, 3721, footnote [1b].
[48] *E. J. Corey, H. J. Burke,* J. Am. Chem. Soc. *78*, 174 (1956).
[49] a) *R. Fraisse-Jullien, C. Frejaville,* Bull. Soc. Chim. Fr. *1968*, 4449; b) *W. G. Dauben, R. E. Wolf,* J. Org. Chem. *35*, 374 (1970).
[50] Apart from the ketones *(24)* and *(25)* the corresponding secondary alcohols were also formed; they could be oxidized to *(24)* and *(25)*, respectively, in the reduction mixture.
[51] *T. Norin,* Acta Chem. Scand. *19*, 1289 (1965); *W. G. Dauben, E. J. Deviny,* J. Org. Chem. *31*, 3794 (1966).
[52] *J. D. White, S. Torii, J. Nogami,* Tetrahedron Lett. *1974*, 2879.
[53] *T. Nakai, E. Wada, M. Okawara,* Tetrahedron Lett. *1975*, 1531.
[54] a) *M. C. Flowers, H. M. Frey,* J. Chem. Soc. *1961*, 3547; b) concerning the mechanism, see: *G. D. Andrews, J. E. Baldwin,* J. Am. Chem. Soc. *98*, 6705, 6706 (1976), and references cited therein.
[55] *C. Girard, P. Amice, J. P. Barnier, J. M. Conia,* Tetrahedron Lett. *1974*, 3329; *J. M. Conia,* Pure Appl. Chem. *43*, 317 (1975).
[56] *B. M. Trost, M. J. Bogdanowicz,* J. Am. Chem. Soc. *95*, 289, 5311 (1973); *M. J. Bogdanowicz, B. M. Trost,* Tetrahedron Lett. *1972*, 887; *B. M. Trost, S. Kurozumi, ibid. 1974*, 1929.
[57] *B. M. Trost, D. E. Keeley,* J. Am. Chem. Soc. *98*, 248 (1976).
[58] *H. G. Richey, Jr., D. M. Shull,* Tetrahedron Lett. *1976*, 575.
[59] Cf. [1], pp. 588 ff., and [28], pp. 656 ff.
[60] *C. Gröger, H. Musso,* Angew. Chem. *88*, 415 (1976); Angew. Chem. Int. Ed. Engl. *15*, 373 (1976); *R. L. Augustine, E. J. Rearden, Jr.,* J. Org. Chem. *39*, 1627 (1974), and references cited therein.
[61] *B. A. Kazanskii, M. Y. Lukina, L. G. Salnikova,* Dokl. Akad. Nauk SSSR *115*, 301 (1957).
[62] *B. Schrader, A. de Meijere,* Tetrahedron Lett., in press.
[63] *D. Bosse, A. de Meijere,* Tetrahedron Lett. *1975*, 871.
[64] *D. Kaufmann,* Dissertation, Universität Göttingen 1976.
[65] *R. Gleiter, E. Heilbronner, A. de Meijere,* Helv. Chim. Acta *54*, 1029 (1971).
[66] *P. Asmus, M. Klessinger, L.-U. Meyer, A. de Meijere,* Tetrahedron Lett. *1975*, 381.
[67] *J. Spanget-Larsen, R. Gleiter, M. R. Detty, L. A. Paquette,* J. Am. Chem. Soc. *100*, 3005 (1978).
[68] *D. Kaufmann, A. de Meijere, B. Hingerty, W. Saenger,* Angew. Chem. *87*, 842 (1975); Angew. Chem. Int. Ed. Engl. *14*, 816 (1975).
[69] Cf. *N. Kushibiki, H. Yoshida,* J. Am. Chem. Soc. *98*, 268 (1976), and references cited therein.
[70] *B. König, A. de Meijere,* unpublished.
[71] *A. de Meijere,* Chem. Ber. *107*, 1702 (1974).
[72] *D. Kaufmann, A. de Meijere,* Tetrahedron Lett. *1979*, 779.
[73] *D. Kaufmann, A. de Meijere,* unpublished; 2,5-dichloro-3,6-dicyano-*p*-benzoquinone and 2,5-dibromo-*p*-benzoquinone have been tested so far, *D. Kaufmann,* Diplomarbeit, Universität Göttingen 1971.
[74] *J. E. Baldwin, R. K. Pinschmidt, Jr.,* Tetrahedron Lett. *1971*, 935; *S. Sarel, A. Felzenstein, J. Yovell,* J. Chem. Soc. Chem. Commun. *1973*, 859.
[75] a) *S. Sarel, A. Felzenstein, J. Yovell,* J. Chem. Soc. Chem. Commun. *1974*, 753; b) *A. Felzenstein, S. Sarel, J. Yovell, ibid. 1975*, 918.
[76] *S. Sarel, A. Felzenstein, J. Yovell,* Tetrahedron Lett. *1976*, 451.
[77] *R. Näder, B. König, A. de Meijere,* unpublished; *R. Näder,* Dissertation, Universität Göttingen 1978.
[78] Cf. *F. Effenberger, W. Podszun,* Angew. Chem. *81*, 1046 (1969); Angew. Chem. Int. Ed. Engl. *8*, 976 (1969); *S. Nishida, I. Moritani, E. Tsuda, T. Teraji,* Chem. Commun. *1969*, 781.
[79] *S. Nishida, I. Moritani, T. Teraji,* Chem. Commun. *1971*, 36; *S. Nishida,* Angew. Chem. *84*, 309 (1972); Angew. Chem. Int. Ed. Engl. *11*, 328 (1972).
[80] *T. Martini, J. A. Kampmeier,* Angew. Chem. *82*, 216 (1970); Angew. Chem. Int. Ed. Engl. *9*, 236 (1970).
[81] *D. S. Magrill, J. Altmann, D. Ginsburg,* Isr. J. Chem. *7*, 479 (1969).
[82] *L. A. Paquette, S. V. Ley, W. B. Farnham,* J. Am. Chem. Soc. *96*, 312 (1974).
[83] Cf. a) *L. I. Smith, E. R. Rogier,* J. Am. Chem. Soc. *73*, 3840 (1951); b) *A. de Meijere, D. Kaufmann, O. Schallner,* Angew. Chem. *83*, 404 (1971); Angew. Chem. Int. Ed. Engl. *10*, 417 (1971); c) *M. Engelhard, W. Lüttke, ibid. 84*, 346 (1972) and *11*, 310 (1972), respectively; *M. Engelhard,* Dissertation, Universität Göttingen 1974; d) *L. Fitjer, J. M. Conia,* Angew. Chem. *85*, 349, 832 (1973); Angew. Chem. Int. Ed. Engl. *12*, 334, 761 (1973); e) *J. M. Denis, P. LePerchec, J. M. Conia,* Tetrahedron *33*, 399 (1977).
[84] The relatively long wavelength UV absorption previously attributed to the [5]rotane *(96)* (*J. L. Ripoll, L. C. Limasset, J. M. Conia,* Tetrahedron *27*, 2431 (1971)) proved to be an artefact attributable to a persistent impurity: *E. Proksch, B. Schrader, A. de Meijere, J.-P. Barnier, J. M. Conia,* Tetrahedron Lett., in press.
[85] *E. Heilbronner, R. Gleiter, T. Hoshi, A. de Meijere,* Helv. Chim. Acta *56*, 1594 (1973).
[86] *J. Spanget-Larsen, R. Gleiter, A. de Meijere, P. Binger,* Tetrahedron *35*, 1385 (1979).
[87] a) *R. Gleiter, R. Haider, J. M. Conia, J.-P. Barnier, A. de Meijere, W. Weber,* J. Chem. Soc. Chem. Commun. *1979*, 130; b) *R. Gleiter, R. Haider, J. M. Conia, J.-P. Barnier, E. Proksch, A. de Meijere,* to be published.
[88] *P. Asmus, M. Klessinger,* Angew. Chem. *88*, 343 (1976); Angew. Chem. Int. Ed. Engl. *15*, 310 (1976).
[89] a) *C. D. Smith,* J. Am. Chem. Soc. *88*, 4273 (1966); b) *N. Rieber, J. Alberts, J. A. Lipsky, D. M. Lemal, ibid. 91*, 5668 (1969).
[90] *G. Kaupp, H. Prinzbach,* Chem. Ber. *104*, 182 (1971); *H. Prinzbach, J. Rivier,* Angew. Chem. *79*, 1102 (1967); Angew. Chem. Int. Ed. Engl. *6*, 1069 (1967).

[91] *T. Sasaki, K. Kanematsu, I. Ando, O. Yamashita,* J. Am. Chem. Soc. *98*, 2686 (1976).

[92] *L.-U. Meyer, A. de Meijere,* Tetrahedron Lett. *1976*, 497; *L.-U. Meyer,* Dissertation, Universität Göttingen 1976.

[93] *D. Kaufmann, H.-H. Fick, O. Schallner, W. Spielmann, L.-U. Meyer, A. de Meijere,* Justus Liebigs Ann. Chem., in press.

[94] *A. de Meijere, D. Kaufmann, O. Schallner,* Tetrahedron Lett. *1973*, 553.

[95] *L.-U. Meyer, A. de Meijere,* Chem. Ber. *110*, 2545 (1977).

[96] *H. Prinzbach, D. Stusche, M. Breuninger, J. Markert,* Chem. Ber. *109*, 2823 (1976), and earlier work cited therein; *E. Vogel, H. J. Altenbach, E. Schmidbauer,* Angew. Chem. *85*, 862 (1963); Angew. Chem. Int. Ed. Engl. *12*, 838 (1973), and earlier work cited therein.

[97] a) *W. Spielmann, H.-H. Fick, L.-U. Meyer, A. de Meijere,* Tetrahedron Lett. *1976*, 4057.

[98] a) *W. Spielmann, D. Kaufmann, A. de Meijere,* Angew. Chem. *90*, 470 (1978); Angew. Chem. Int. Ed. Engl. *17*, 440 (1978); b) *J. Spanget-Larsen, R. Gleiter, ibid. 90*, 471 (1978) and *17*, 441 (1978), respectively.

[99] *A. de Meijere, D. Kaufmann, O. Schallner,* Tetrahedron Lett. *1974*, 3835.

[100] *D. Kaufmann, A. de Meijere,* Tetrahedron Lett. *1974*, 3831.

[101] a) *A. H. Schmidt, U. Schirmer, J.-M. Conia,* Chem. Ber. *109*, 2588 (1976); b) *L. Fitjer,* Angew. Chem. *88*, 804 (1976); Angew. Chem. Int. Ed. Engl. *15*, 763 (1976); c) *E. Proksch, A. de Meijere,* Tetrahedron Lett. *1976*, 4851.

[102] Cf. [101a] and *W. Weber, A. de Meijere,* Synthesis, in press.

[103] *E. Proksch, B. Schrader, M. Zarth, T. Liese, A. de Meijere,* Tetrahedron Lett., in press.

[104] *T. Preuss, E. Proksch, A. de Meijere,* Tetrahedron Lett. *1978*, 833.

[105] *P. Binger,* Angew. Chem. *84*, 483 (1972); Angew. Chem. Int. Ed. Engl. *11*, 433 (1972).

[106] *P. LePerchec, J. M. Conia,* Tetrahedron Lett. *1970*, 1587.

[107] *D. Kaufmann, A. de Meijere,* Angew. Chem. *85*, 151 (1973); Angew. Chem. Int. Ed. Engl. *12*, 159 (1973).

[108] *W. Weber, I. Erden, A. de Meijere,* to be published.

[109] Dipolar intermediates of type *(135)* and *(139)* appeared unlikely owing to the slight solvent effect: *R. Noyori, N. Hayashi, M. Katô,* J. Am. Chem. Soc. *93*, 4949 (1971).

[110] Cf. [1], pp. 563 f. and references cited therein.

[111] *M. J. Perkins, P. Ward,* Chem. Commun. *1971*, 1134; J. Chem. Soc. Perkin Trans. I *1974*, 667.

[112] *A. Streitwieser, Jr.* (Berkeley, Calif.), personal communication.

[113] a) *S. W. Staley, G. M. Cramer, W. G. Kingsley,* J. Am. Chem. Soc. *95*, 5025 (1973); b) *S. W. Staley, W. G. Kingsley, ibid. 95*, 5804 (1973).

[114] Cf. [1], pp. 564 ff. and references cited therein.

[115] *P. J. Krusic, P. Meakin, J. P. Jesson,* J. Phys. Chem. *75*, 3438 (1971); cf. *N. L. Bauld, J. D. McDermed, C. E. Hudson, Y. S. Rim, J. Zoeller, R. D. Gordon, J. S. Hyde,* J. Am. Chem. Soc. *91*, 6666 (1969).

[116] *J. C. Martin, J. W. Timberlake,* J. Am. Chem. Soc. *92*, 978 (1970).

[117] *D. Kaufmann, A. de Meijere,* Tetrahedron Lett. *1979*, 787.

[118] *J. K. Kochi, P. J. Krusic, D. R. Eaton,* J. Am. Chem. Soc. *91*, 1877, 1879 (1979); cf. *M. Suzuki, S. I. Murahashi, A. Sonoda, I. Moritani,* Chem. Lett. *1974*, 267.

[119] *R. Sustmann, F. Lübbe,* Tetrahedron Lett. *1974*, 2832; cf. also Chem. Ber. *109*, 444 (1976).

[120] *M. Ratier, M. Pereyre,* Tetrahedron Lett. *1977*, 2273.

[121] *T. Tsuji, T. Shibata, Y. Hienuki, S. Nishida,* J. Am. Chem. Soc. *100*, 1806 (1978).

[122] a) *P. K. Freeman, F. A. Raymond, J. C. Sutton, W. R. Kindley,* J. Org. Chem. *33*, 1448 (1967); b) *P. K. Freeman, R. S. Raghavan, G. L. Fenwick,* J. Am. Chem. Soc. *94*, 5101 (1972); c) *P. K. Freeman, T. D. Ziebarth, R. S. Raghavan, ibid. 97*, 1875 (1975).

[123] *A. de Meijere, C. Weitemeyer, O. Schallner,* Chem. Ber. *110*, 1504 (1977).

[124] *W. Spielmann, C. Weitemeyer, I.-N. Huang, A. de Meijere, F. Snatzke, G. Snatzke,* Isr. J. Chem. *15*, 99 (1976/77).

[125] Cf., *e.g., W. A. Pryor:* Free Radicals. McGraw-Hill, New York 1966, pp. 170 ff.

[126] *E. Keinan, Y. Mazur,* Synthesis *1976*, 523; *Z. Cohen, E. Keinan, Y. Mazur, A. Ulman,* J. Org. Chem. *41*, 2651 (1976), and references cited therein.

[127] a) *E. Proksch, A. de Meijere,* Angew. Chem. *88*, 802 (1976); Angew. Chem. Int. Ed. Engl. *15*, 761 (1976); b) Tetrahedron Lett. *1976*, 4851; c) cf. also *A. de Meijere,* Nachr. Chem. Tech. Lab. *27*, 177 (1979).

[128] *L. B. Harding, W. A. Goddard III,* J. Am. Chem. Soc. *100*, 7180 (1978).

[129] Cf. [84] *(A. de Meijere et al.).*

[130] *M. Zarth,* Diplomarbeit, Universität Göttingen und Hamburg 1979.

[131] *W. Cocker, P. V. R. Shannon, P. A. Staniland,* J. Chem. Soc. *C 1967*, 485, 915.

[132] *M. Hanack, H. J. Schneider,* Angew. Chem. *79*, 709 (1967); Angew. Chem. Int. Ed. Engl. *6*, 666 (1967); Fortschr. Chem. Forsch. *8*, 554 (1967).

[133] *H. G. Richey, Jr.* in *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions. Interscience, New York 1972, Vol. 3, p. 1201.

[134] *K. B. Wiberg, B. A. Hess, Jr., A. J. Ashe III* in [133], p. 1295.

[135] *J. Haywood-Farmer,* Chem. Rev. *74*, 315 (1974).

[136] a) *J. E. Baldwin, W. D. Foglesong,* J. Am. Chem. Soc. *90*, 4303, 4311 (1968); b) *K. B. Wiberg, T. Nakahira, ibid. 93*, 5193 (1971), and references concerning this question cited therein.

[137] *Y. E. Rhodes, V. F. DiFate,* J. Am. Chem. Soc. *94*, 7582 (1972).

[138] *B. Andersen, O. Schallner, A. de Meijere,* J. Am. Chem. Soc. *97*, 3521 (1975).

[139] *(198b)* reacts *ca.* 10 times faster than 1-chlorobicyclo[3.3.3]undecane (1-chloromanxane). *W. Parker, R. L. Tranter, C. I. F. Watt, W. K. Chang, P. v. R. Schleyer,* J. Am. Chem. Soc. *96*, 7121 (1974).

[140] *K. B. Wiberg, J. G. Pfeiffer,* J. Am. Chem. Soc. *92*, 553 (1970).

[141] Cf., *e.g., G. A. Olah, G. Liang, J. R. Wiseman, Jr., J. A. Chong,* J. Am. Chem. Soc. *94*, 4927 (1972).

[142] Cf. *G. A. Olah, G. Liang, K. A. Babiak, T. K. Morgan, Jr., R. K. Murray, Jr.,* J. Am. Chem. Soc. *98*, 576 (1976), and earlier work cited therein.

[143] *O. Schallner,* Dissertation, Universität Göttingen 1974.

[144] *B. Schrader,* Dissertation, Universität Göttingen 1977.

[145] *O. Schallner, B. Schrader, W. Spielmann, P. Gölitz,* unpublished.

[146] *A. de Meijere, O. Schallner, C. Weitemeyer,* Angew. Chem. *84*, 63 (1972); Angew. Chem. Int. Ed. Engl. *11*, 56 (1972).

[147] *W. Spielmann,* Dissertation, Universität Göttingen 1976.

[148] *R. W. Taft, Jr.* in *M. S. Newman:* Steric Effects in Organic Chemistry. Wiley, New York 1956.

[149] *C. A. Grob,* Angew. Chem. *88*, 621 (1976); Angew. Chem. Int. Ed. Engl. *15*, 569 (1976).

[150] *C. A. Grob, R. Rich,* Tetrahedron Lett. *1978*, 663.

[151] Cf. *L. D. Kispert, C. Engelmann, C. Dyas, C. U. Pittmann, Jr.,* J. Am. Chem. Soc. *93*, 6948 (1971); *R. S. Brown, T. C. Traylor, ibid. 95*, 8025 (1973); *C. F. Willox, L. M. Loew, R. Hoffmann, ibid. 95*, 8192 (1973), and references cited therein.

[152] *O. Schallner, G. D. Mateescu, A. de Meijere,* to be published; cf. *A. de Meijere, O. Schallner,* Angew. Chem. *85*, 400 (1973); Angew. Chem. Int. Ed. Engl. *12*, 399 (1973).

[153] Doz. Dr. *P. Bischof,* Heidelberg, personal communication.

[154] *G. A. Olah, G. Liang, P. von R. Schleyer, E. M. Engler, M. J. S. Dewar, R. C. Bingham,* J. Am. Chem. Soc. *95*, 6829 (1973).

[155] *G. A. Olah, G. Liang,* J. Am. Chem. Soc. *93*, 6872 (1971).

[156] Cf. *M. Geisel, C. A. Grob, W. Santi, W. Tschudi,* Helv. Chim. Acta *56*, 1046, 1055 (1973), and references cited therein.

[157] Systematic name: pentacyclo[4.4.2.$0^{2,4}$.$0^{5,7}$.$0^{8,10}$]dodecane.

[158] *E. Proksch, A. de Meijere,* unpublished; cf. *E. Proksch,* Dissertation, Universität Göttingen 1977.

[159] a) *M. Julia, S. Julia, R. Guégan,* Bull. Soc. Chim. Fr. *1960*, 1072; b) *M. Julia, S. Julia, S.-Y. Tchen, ibid. 1961*, 1849; c) *M. Julia, S. Julia, B. Stalla-Bourdillon, C. Descoins, ibid. 1964*, 2533; d) *M. Julia, C. Descoins, C. Risse,* Tetrahedron Suppl. *8*, 443 (1966); e) *M. Julia, J. M. Paris,* Tetrahedron Lett. *1974*, 3445.

[160] *J. P. McCormick, D. L. Barton,* J. Chem. Soc. Chem. Commun. *1975*, 303.

[161] *S. F. Brady, M. A. Ilton, W. S. Johnson,* J. Am. Chem. Soc. *90*, 2882 (1968).

[162] See, *e.g.,* a) *B. H. Braun, M. Jacobson, M. Schwarz, P. E. Sonnet, N. Wakabayashi, R. M. Waters,* J. Econ. Entomol. *61*, 866 (1968); b) *W. S. Johnson, T. Li, D. J. Faulkner, S. F. Campbell,* J. Am. Chem. Soc. *90*, 6225 (1968); c) *K. A. Parker, W. S. Johnson,* Tetrahedron Lett. *1969*, 1329; d) *H. Wolf, U. Mätzel, E.-J. Brunke, E. Klein, ibid. 1979*, 2339.

[163] *C. Descoins, D. Samain,* Tetrahedron Lett. *1976*, 745.

[164] *R. D. Miller, D. R. McKean, D. Kaufmann,* Tetrahedron Lett. *1979*, 587.

[165] *S. Danishefsky,* Acc. Chem. Res. *12*, 66 (1979).

[166] *R. V. Stevens,* Pure Appl. Chem. *51*, 1317 (1979).

[167] a) *S. Danishefsky, R. K. Singh,* J. Am. Chem. Soc. *97*, 3239 (1975); b) *R. K. Singh, S. Danishefsky,* J. Org. Chem. *41*, 1668 (1976).

[168] a) *G. Stork, P. Grieco,* J. Am. Chem. Soc. *91*, 2407 (1969); b) *G. Stork, M. Marx, ibid. 91*, 2371 (1969); c) *G. Stork, M. Gregson, ibid. 91*, 2373 (1969).

[169] *E. J. Corey, R. D. Balanson,* Tetrahedron Lett. *1973*, 3153.

[170] *R. D. Miller, D. R. McKean,* Tetrahedron Lett. *1979*, 2305.

[171] *M. Demuth, P. R. Raghavan,* Helv. Chim. Acta *62*, in press (1979).

[172] *J. Salaun, B. Garnier, J. M. Conia,* Tetrahedron *30*, 1413 (1974), and further references cited therein.

[173] *H. H. Wasserman, E. A. Glazer, M. J. Hearn,* Tetrahedron Lett. *1973*, 4855; *H. H. Wasserman, E. Glazer,* J. Org. Chem. *40*, 1505 (1975).

[174] *H. H. Wasserman, R. E. Cochoy, M. S. Baird,* J. Am. Chem. Soc. *91*, 2375 (1969); *H. H. Wasserman, H. W. Adickes, O. Espejo de Ochoa, ibid. 93*, 5586 (1971).

[175] *B. M. Trost,* Acc. Chem. Res. *7*, 85 (1974); *B. M. Trost, M. Preckel, L. M. Leichter,* J. Am. Chem. Soc. *97*, 2224 (1975); *B. M. Trost, D. E. Keeley, H. C. Arndt, M. J. Bogdanowicz, ibid. 99*, 3088 (1977), and further references cited therein.

[176] *D. G. Garrat, A. Modro, K. Oyama, G. H. Schmid, T. T. Tidwell, K. Yates,* J. Am. Chem. Soc. *96*, 5295 (1974); *K. Oyama, T. T. Tidwell, ibid. 98*, 947 (1976); *I. C. Ambidge, S. K. Dwight, C. M. Rynard, T. T. Tidwell,* Can. J. Chem. *55*, 3086 (1977), and references cited therein.

[177] *C. A. Coulson, T. H. Goodwin,* J. Chem. Soc. *1962*, 2851 and earlier work; cf. *D. T. Clark,* Theor. Chem. Acta *10*, 111 (1968).

[178] *O. C. Dermer, G. E. Ham:* Ethylenimine and Other Aziridines. Academic Press, New York 1969; *S. Winstein, R. B. Henderson* in *R. C. Elderfield:*

Heterocyclic Chemistry, Vol. I. Wiley, New York 1950; *R. E. Parker, N. S. Isaacs,* Chem. Rev. *59*, 737 (1959).
[179] *J. A. Deyrup, C. L. Moyer,* Tetrahedron Lett. *1968*, 6179; *J. A. Deyrup, C. L. Moyer, P. S. Dreyfus,* J. Org. Chem. *35*, 3428 (1970); V. R. Gaertner, Tetrahedron Lett. *1968*, 5919; J. Org. Chem. *35*, 3952 (1970).
[180] a) *G. Szeimies,* Chem. Ber. *106*, 3695 (1973); b) *G. Szeimies, K. Mannhardt, M. Junius, ibid. 110*, 1792 (1977).
[181] Cf. a) *D. L. Whalen,* J. Am. Chem. Soc. *92*, 7619 (1970); b) *W. C. Danen, ibid. 94*, 4835 (1972), and references cited therein.
[182] *C. Weitemeyer, A. de Meijere,* unpublished; cf. *C. Weitemeyer,* Dissertation, Universität Göttingen 1976.
[183] Cf. *P. von R. Schleyer, G. W. Van Dine,* J. Am. Chem. Soc. *88*, 2321 (1966); *R. S. Brown, T. G. Traylor, ibid. 95*, 8025 (1973).
[184] Cf. *H. Basch, M. B. Robin, N. A. Kuebler, C. Baker, D. W. Turner,* J. Chem. Phys. *51*, 52 (1969); *M. Rohmer, B. Roos,* J. Am. Chem. Soc. *97*, 2025 (1975).
[185] Cf. *D. Ginsburg:* Propellanes, Structure and Reactions. Verlag Chemie, Weinheim 1975, and references published therein.
[186] a) *W. D. Stohrer, R. Hoffmann,* J. Am. Chem. Soc. *94*, 739 (1972); b) *M. L. Herr,* Tetrahedron *33*, 1897 (1977).
[187] *K. B. Wiberg, G. J. Burgmaier,* Tetrahedron Lett. *1969*, 317; J. Am. Chem. Soc. *94*, 7396 (1972); *P. G. Gassman, A. Topp, J. W. Keller,* Tetrahedron Lett. *1969*, 1093.
[188] *K. B. Wiberg, E. D. Lupton, Jr., G. J. Burgmaier,* J. Am. Chem. Soc. *91*, 3372 (1969).
[189] *K. B. Wiberg, W. F. Bailey, M. E. Jason,* J. Org. Chem. *41*, 2711 (1976); *P. E. Wood, W. F. Bailey, K. B. Wiberg,* J. Am. Chem. Soc. *99*, 268 (1977).
[190] *K. B. Wiberg, G. A. Epling, M. Jason,* J. Am. Chem. Soc. *96*, 912 (1974); *J. J. Dannenberg, T. M. Provic, C. Hutt, ibid. 96*, 914 (1974); *K. B. Wiberg, W. E. Pratt, W. F. Bailey, ibid. 99*, 2297 (1977).
[191] Estimated with the usual assumption of additivity of strain contributions of the subunits. Cf. *L. N. Ferguson:* Highlights of Alicyclic Chemistry. Franklin Publ. Co., Palisade, N. J. 1973.
[192] *D. Bosse, A. de Meijere,* Chem. Ber. *111*, 2223 (1978).
[193] *P. Gölitz, A. de Meijere,* unpublished; *P. Gölitz,* Dissertation, Universität Göttingen 1978.
[194] In the optically active derivatives of type *(201e)* [147] prepared so far, X and Y were not good enough leaving groups.
[195] ESR studies on the question of delocalization of the radical electron in *(255)* are being conducted in collaboration with *M. McBride* and *M. Saunders* (Yale University, New Haven, Conn. (USA)).
[196] Cf. *W. Spielmann, A. de Meijere,* Angew. Chem. *88*, 446 (1976); Angew. Chem. Int. Ed. Engl. *15*, 429 (1976).
[197] *B. M. Trost, W. J. Frazee,* J. Am. Chem. Soc. *99*, 6124 (1977).
[198] *P. A. Wender, M. P. Filosa,* J. Org. Chem. *41*, 3490 (1976).
[199] *E. Wenkert, D. A. Bergers, N. F. Golob,* J. Am. Chem. Soc. *100*, 1263 (1978); *E. Wenkert, B. L. Buckwalter, A. A. Craveiro, E. L. Sanchez, S. S. Sathe, ibid. 100*, 1267 (1978); cf. also *Y. Ito, T. Saegusa,* J. Org. Chem. *42*, 2326 (1977); *Y. Ito, T. Sugaya, M. Nakatsuka, T. Saegusa,* J. Am. Chem. Soc. *99*, 8366 (1977).
[200] See, *e.g.* a) *J. W. ApSimon:* The Total Synthesis of Natural Products. Vol. 1—3. Wiley-Interscience, New York 1973, 1977; b) *K. Nakanishi, T. Goto, S. Ito, S. Natori, S. Nozoe:* Natural Products Chemistry. Kodansha Ltd., Tokyo/Academic Press, New York 1975; c) *D. Seebach,* Angew. Chem. *91*, 259 (1979); Angew. Chem. Int. Ed. Engl. *18*, 239 (1979).

Conformational Analysis by Photoelectron Spectroscopy

By Martin Klessinger and Paul Rademacher[*]

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

The conformation of organic molecules may be determined by means of photoelectron (PE) spectroscopy if there are orbital interactions present which depend on a dihedral angle. Straightforward application of the method requires that all ionization bands of interest can be assigned unambiguously and that inductive effects and secondary orbital interactions do not occur or can be accounted for appropriately. In many cases, this method complements conventional methods of conformational analysis. PE conformational analysis is particularly suited to compounds containing vicinal lone pairs or π systems.

1. Introduction

In order to completely describe the structure of an organic molecule one has to specify not only the *constitution* and the *configuration,* but also the *conformation.* While the constitution merely indicates which atoms are connected, different spatial arrangements of the bonds with respect to a given atom or group of atoms (*e.g.* a C=C double bond, a ring, *etc.*) lead to different configurations which may be converted into each other only by breaking and reforming one or several bonds.

According to *Barton*[1] the conformations of a molecule of given constitution and configuration "are those arrangements in space of the atoms of the molecule which are not superposable upon each other". A molecule can therefore assume an infinite number of conformations by varying its bond lengths and bond angles. In practice, however, only those arrangements of atoms are usually considered as different conformations which are obtained by rotation about single bonds. Different conformations are populated according to their energy contents. While the few "stable" conformations of a molecule are of principal interest, energy rich forms may be of special importance in connection with chemical reactivity.

As the various stable conformers of a molecule can be interconverted by means of relatively low-energy processes (rotation about single bonds, inversion of nonplanar groups), they may be isolated at room temperature only in exceptional cases. The borderline between conformational and configurational isomerism is not rigid; a value of 80 kJ/mol may be assumed for practical purposes.

Conformational analysis as a branch of stereochemistry is concerned with physical and chemical properties of different conformers of a given molecule. The principles of conformational analysis[2,3], the historical development[3,4], as well as experimental[3] and theoretical[3,5] methods have been dealt

[*] Prof. Dr. M. Klessinger
Organisch-Chemisches Institut der Universität
Orléansring 23, D-4400 Münster (Germany)
Prof. Dr. P. Rademacher
Fachbereich Chemie der Universität
Universitätsstrasse 5—7, D-4300 Essen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1111-0826 $ 02.50/0

with extensively in a number of monographs and review papers.

Geometry and symmetry of a given conformer may be obtained by static methods, primarily by diffraction methods and spectroscopic methods such as IR/Raman and NMR spectroscopy, but also by the measurement of dipole moments. Activation energies of conformational interconversions are determined by means of dynamic methods such as calorimetry, acoustic relaxation, as well as microwave spectroscopy for barriers of 2—20 kJ/mol and especially dynamic NMR spectroscopy for barriers of 20—100 kJ/mol. A great number of interesting conformational problems in organic chemistry has been solved particularly by this last method in recent years.

Owing to the complexity of the internal motion of polyatomic organic molecules, the elucidation of the conformational properties of a given compound will often require a combination of various experimental and theoretical methods; complete potential energy diagrams for internal rotations and ring inversions as well as so-called conformational maps of molecules with several possibilities of internal conversion may be derived only by theoretical methods.

2. Theoretical Foundations of Conformational Analysis by PE Spectroscopy

2.1. The Koopmans Approximation

Photoelectron (PE) spectroscopy[6] permits the determination of vertical ionization potentials $IP(i)$, which according to *Koopmans'* theorem[7]

$$IP(i) = -\varepsilon_i \tag{1}$$

may be set equal to negative orbital energies $-\varepsilon_i$. PE spectroscopy is therefore suitable for the investigation of orbital interactions[8]. It was realized quite early that orbital interactions and therefore also PE spectra may be conformation-dependent[9].

Conformational analysis by PE spectroscopy is based upon the validity of *Koopmans'* theorem or *Koopmans'* approximation[10] as well as upon the possibility of assigning the observed ionization bands to distinct orbitals. For large organic molecules an unambiguous assignment can usually be given only for a few bands at lower energies which are well separated from neighboring bands.

Within this energy range *Koopmans'* theorem is valid to a fairly good approximation: each ionization potential corresponds to an orbital energy and *vice versa* since a single product of orbitals is a sufficiently accurate wave function of the system; it is only at higher energies that an adequate description of an ionic state will also require orbital products which, within the simple MO model, correspond to excited configurations of the ion. Due to this configuration interaction (CI) more states may appear than are to be expected from the orbital energies, so that the intensity of an ionization may be distributed as shown in Figure 1 over several bands as a result of so-called shake-up and shake-off processes[13].

Furthermore, correlation and reorganization effects which arise from changes in the number of electron pairs and from changes in the effective field for the individual electrons re-

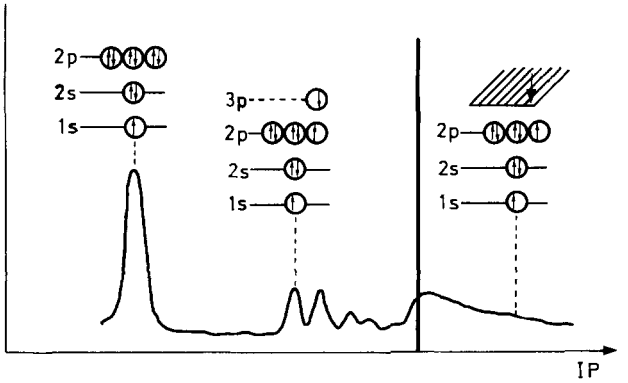


Fig. 1. Schematic representation of a PE spectrum including shake-up and shake-off processes for a core ionization of a neon atom. The solid vertical line represents the ionization limit.

spectively more or less cancel each other for valence electrons[11,12]. Deviations from *Koopmans'* approximation are observed mainly in the case of ionizations from strongly localized orbitals[14] as a consequence of electron reorganization. However, even these deviations may be neglected if only relative orbital energies for different conformers are of interest, and if the character of the corresponding orbital does not change on going from one conformer to the other. In the following it is therefore assumed that an interpretation of the PE spectra based on the assumption of the validity of *Koopmans'* theorem is justified.

2.2. Orbital Interactions

2.2.1. Calculation of Orbital Energies as Functions of Dihedral Angles

The orbital energies for different conformations of a molecule may in principle be calculated by varying one (or sev-

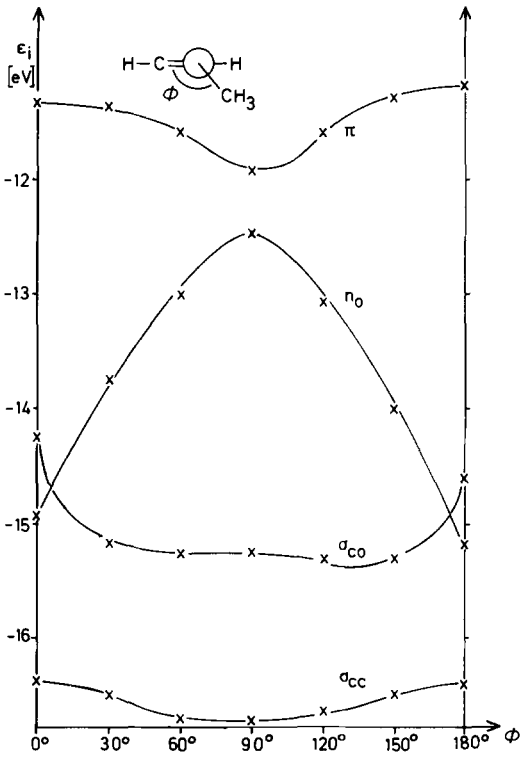
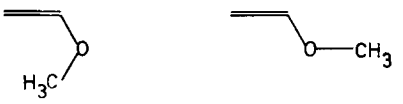


Fig. 2. Calculated energies (CNDO/S) of the four highest occupied orbitals of methyl vinyl ether *(1)* and their dependence on the dihedral angle ϕ. *(1a)*, $\phi = 0°$; *(1b)*, $\phi = 180°$.

eral) dihedral angles and simultaneously readjusting all other geometric parameters. Thus for methyl vinyl ether *(1)* the orbital energies are obtained as functions of the dihedral angle ϕ as shown in Figure 2[15]. Such calculations make it possible to decide which ionization potentials may be used for conformational analysis. However, if the dihedral angle is to be determined by comparing the observed difference ΔIP of ionization potentials with the calculated difference $\Delta\varepsilon$ of orbital energies an extremely high accuracy of calculation is required. In such cases an empirical parametrization of the theoretically determined relation between ΔIP and the dihedral angle ϕ is preferable[16] (cf. Section 3.2).

2.2.2. Orbital Interactions between Molecular Fragments

One of the main disadvantages of the direct calculation of orbital energies may be seen in the fact that this method, although making possible predictions of the conformational dependence of orbital energies, in general does not explain the origin of the orbital interactions. Thus it is not obvious from the calculated orbital energies in Figure 2 why ΔIP should differ for the planar *syn- (1a)* and *anti* conformer *(1b)* of methyl vinyl ether.



(1a), $\Phi = 0°$ *(1b)*, $\Phi = 180°$

Detailed information about conformation-dependent orbital interactions is obtained on starting from orbitals localized in subsystems or fragments of the molecule, *e.g.* in the case of methyl vinyl ether *(1)* from the orbitals of the vinyl group and the oxygen lone pair as well as the methyl group. An SCF calculation based on such localized fragment orbitals yields the same results as a conventional SCF calculation based on AOs, but as these results are expressed in terms of fragment orbitals it is immediately seen which orbitals interact with each other and to what extent.

For the interpretation of the orbital interactions it is furthermore very illustrative to split the orbital interactions into two parts, which may be called "inductive" and "conjugative" interactions, and which are obtained by first considering the orbitals of one fragment in the field of all the other fragments and taking into account the bonding interactions between the fragments only in a second step. Within the LCFO-SCF-MO method (LCFO = *l*inear *c*ombination of *f*ragment *o*rbitals)[17] which has been especially developed for the interpretation of PE spectra, the inductive effects of the first step may be evaluated quantitatively on the basis of the generalized product functions approach[18] together with the strong orthogonality condition[19] which is automatically satisfied if the ZDO approximation is being applied. This procedure makes it possible to determine the conjugative interactions using for the orbital energies of the fragments experimental ionization potentials and electron affinities corrected by the calculated inductive perturbations. Interactions of fragment orbitals can thus be evaluated directly and in very good agreement with experimental data. The method was first developed within the π approximation and applied to the interaction of π systems[20], and afterwards extended to include σ systems[21], where *e.g.* in the case of the union of two methane fragments to yield ethane, changes in the number of nuclei and electrons have to be taken into account.

Calculations according to the LCFO method show that in general only very few antibonding orbitals of the fragments are needed for a sufficiently accurate description of the combined system. For unpolar systems, as *e.g.* for the interaction of the π systems of two unsaturated alternant hydrocarbons or for the interaction of two alkyl groups, all antibonding orbitals may be neglected. In this case the LCFO model reduces to the interaction of bonding (or occupied) orbitals and becomes identical with the LCBO model in the HMO approximation, which was first introduced by *Hall*[22] and which in a great number of different investigations has proved very useful for the interpretation of PE spectra[23].

2.2.3. Summary and Examples

The results of calculations based on the LCFO method may be taken as a justification of the LCBO method, but at the same time they indicate clearly the limits of this approach. These results can be summarized as follows:

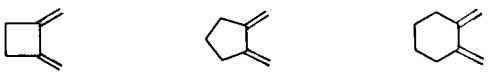
The influence of conformational effects on the PE spectrum may be discussed on the basis of the LCBO model by means of angularly dependent orbital interactions, if

a) inductive perturbations of the fragment orbitals,
b) secondary orbitals interactions, and
c) interactions with unoccupied orbitals

either do not occur or else can be taken into account appropriately. Points b) and c) are of special importance as they can also be angularly dependent.

Some examples may illustrate these three points:

For 1,2-dimethylenecyclobutane *(2)*[24] and 1,2-dimethylenecyclopentane *(3)*[25] the difference $\Delta IP_{1,2}$ of the first two ionization potentials, which could be assigned to π orbitals, is about the same as for 1,3-cyclohexadiene[26]; these compounds contain a coplanar π system. For 1,2-dimethylenecyclohexane *(4)*[27] on the other hand $\Delta IP_{1,2}$ is only half that



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

value, as the chair conformation of the cyclohexane ring leads to a dihedral angle $\phi \approx 55°$ between the double bonds and therefore to a reduced conjugative interaction. The simple LCBO model is applicable and leads to $\Delta IP_{1,2} = 2\beta = 2\beta_0 \cos\phi$, if $\beta = \beta_0 \cos\phi$ is the angle-dependent resonance integral for the π-π interaction; the inductive effect can be estimated, from a comparison of the mean value of the π bands of 1,2-dimethylenecyclohexane with the first ionization potential of methylenecyclohexane[28], to be ≈ 0.3 eV.

In methyl vinyl ether *(1)* the difference between the splitting $\Delta IP_{1,2}$ for the *syn (1a)* and the *anti* conformer *(1b)* may be explained by secondary orbital interactions as shown in Figure 3: through-space interactions between the π_{CH_3} and π_{CC} orbitals destabilize the second MO, which is essentially the lone pair n_O of the oxygen, and stabilize the highest MO, which is predominantly π_{CC} in character. As this interaction is larger for the *syn* conformer than for the *anti* conformer for

geometrical reasons, $\Delta IP_{1,2}$ is smaller for the former than for the latter[29].

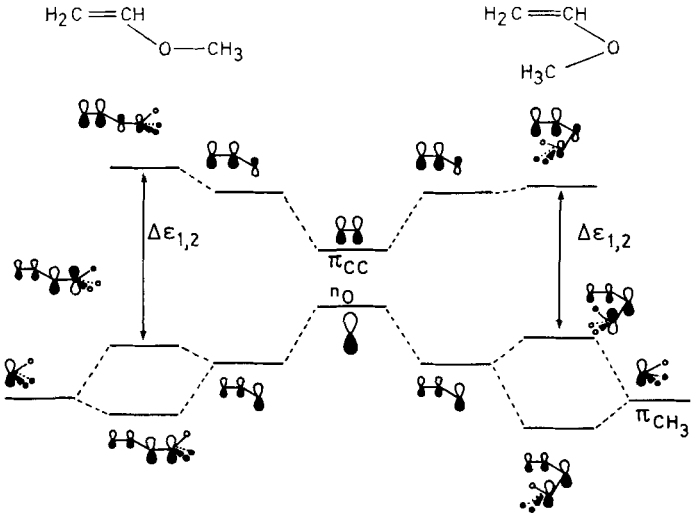


Fig. 3. Orbital interaction diagram of methyl vinyl ether *(1)* in the LCBO approximation. Center: energies of the π_{CC} and n_O orbitals without ($\phi=90°$) and with interaction ($\phi=0°$ or 180°). Left: influence of the π_{CH_3} orbital in the *anti* form *(1b)* ($\phi=180°$). Right: with additional through-space π_{CC}/π_{CH_3} interactions in the *syn* form *(1a)* ($\phi=0°$).

Finally, α,β-unsaturated carbonyl compounds[30] illustrate the inapplicability of the LCBO model as a result of interactions with antibonding orbitals. This may be seen from the fact that in contrast to expectations based on the LCBO model, the first ionization potential is higher for acrolein than for ethylene, corresponding to a stabilization of the π_{CC} MO due to the interaction with the lower lying π_{CO} MO.

3. Conformational Analysis by PE Spectroscopy

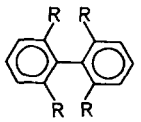
Conformation-dependent interactions are observed primarily between neighboring atoms. The corresponding orbitals may be lone-pair orbitals or p orbitals of π systems. PE spectroscopy may therefore be used to study conformational problems which can be interpreted by

a) n/n interactions,
b) π/π interactions, and
c) n/π interactions.

3.1. Biphenyls

The first example of a systematic conformational analysis by PE spectroscopy was presented by *Maier* and *Turner* in their study of biphenyls[9].

In the crystalline state, the two benzene rings of biphenyl *(5)* are coplanar, with an optimal delocalization of π electrons. In the gase phase, however, biphenyl is not planar but twisted with respect to the central CC bond by *ca.* 45°. The magnitude of this twisting depends on the substituents: for



(5) R = H

(6) R ≠ H

ortho substitution as in *(6)* the barrier to internal rotation can be large enough (≥80 kJ/mol) to permit the isolation of different conformers (atropisomerism)[31].

From Figure 4 it is seen that the pairwise splittings of the occupied MOs π_1 to π_6 of *(5)*, which may be constructed schematically from the π MOs of benzene, show different variations with the torsional angle ϕ. As expected, the effects are largest for the pair π_3 and π_6, for which the LCBO method yields

$$\Delta\varepsilon=\varepsilon(\pi_6)-\varepsilon(\pi_3)=2B\cos\phi \qquad (2)$$

for the splitting, with $2B$ being the maximal value for coplanar arrangement of the benzene rings ($\phi=0°$).

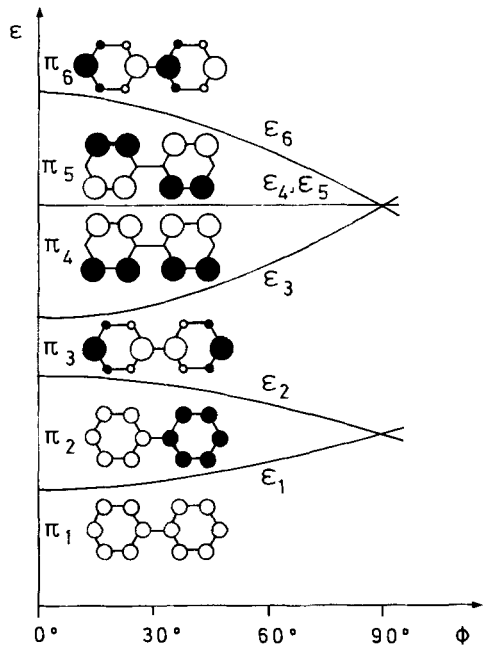


Fig. 4. Schematic representation of the occupied π MOs π_1 to π_6 of biphenyl *(5)* and the variation of the orbital energies ε_1 to ε_6 with the torsional angle ϕ.

Maier and *Turner* proved the validity of this relation using biphenyls of known structure, for which they obtained values of $\Delta IP=IP(\pi_6)-IP(\pi_3)$ and $\cos\phi$ which clearly confirm the linear relation of eq. (2). From this calibration line, torsional angles ϕ of a large number of biphenyls could be determined from their PE spectra.

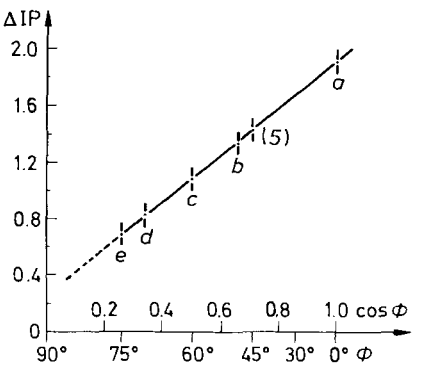


Fig. 5. Splitting $\Delta IP=IP(\pi_6)-IP(\pi_3)$ corresponding to the π MOs π_3 and π_6 for biphenyls of known conformation as a function of $\cos\phi$. *(5)*, biphenyl; *a*, fluorene; *b*, 2-fluoro-; *c*, 2,2'-difluoro-; *d*, perfluoro-; *e*, 2,2'-dibromobiphenyl.

As far as experimental data are available, the values of ϕ thus obtained are in excellent agreement with the result of other methods.

The straight line shown in Figure 5 may be expressed as

$$\Delta IP = 1.65 \cos\phi + 0.35 \text{ [eV]} \quad (3)$$

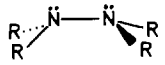
In contrast to eq. (2), this line does not pass through the origin of the coordinate system. This is due to secondary interactions between π and σ orbitals, which cannot be neglected, especially for large torsional angles.

This method was applied analogously to the conformational analysis of related systems like bipyridyls[9], bithienyls[32], and bipyrroyls[33].

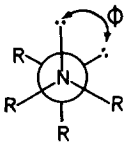
3.2. Systems with n/n Interactions

3.2.1. Hydrazines

Hydrazines *(7)* are the simplest possible compounds with vicinal lone pairs of electrons. The unusual conformational

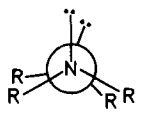


(7)

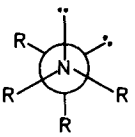


properties of such systems have been the subject of numerous theoretical and experimental investigations[34–38]. In particular, the preference for the *gauche* conformation ($\phi \approx 90°$) by the parent compound N_2H_4 and nearly all open-chain derivatives *(7)* was difficult to rationalize for a long time[35]. This property is not due to a specific "repulsion" or "attraction" of the lone-pair electrons, but results from the interaction with vicinal antibonding orbitals (n/σ*- or n/π* interaction)[36].

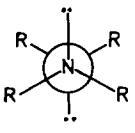
Undoubtedly, the most interesting aspect of the conformation of hydrazines is the magnitude of the torsional angle ϕ. The conformers *(7a)*, *(7b)*, and *(7c)* may be distinguished by



syn (C_{2v})
(7a)



gauche (C_2)
(7b)



anti (C_{2h})
(7c)

their symmetry. According to experimental[34] and theoretical[36] results for hydrazine and methylhydrazine, *(7b)* corresponds to the minimum of the torsional potential, while *(7a)* as well as *(7c)* are related with maxima of approximately 50 and 15 kJ/mol. Substituents obviously have only minor effects upon the torsional potential curve. Thus structure determinations and spectroscopic investigations on *(7)* with R = H, CH_3, CF_3, and SiH_3 always yielded *gauche* forms as stable conformers[34,39]. The only exception is tetrafluorohydrazine, for which an *anti/gauche* mixture has been observed[34].

The accurate experimental determination of ϕ for *(7)* is a very tedious task and usually necessitates complete structure analysis, since methods such as IR and NMR spectroscopy reveal at most the symmetry of *(7)* but not the value of the angle ϕ.

Substantial progress in this field was achieved on introduction of PE spectroscopy, which provided elegant solutions to many interesting conformational problems of hydrazines[16,40–51]. The procedure is based upon the correlation of the splitting ΔIP of the ionization potentials of the lone-pair electrons with the torsional angle ϕ. The two n MOs of *(7)*, n_+ and n_-, are obtained by linear combination of the n orbitals n_1 and n_2 (approximately sp^3-hybridized orbitals) localized on the nitrogen atoms:

$$n_+ = (n_1 + n_2)/\sqrt{2} \quad (4)$$
$$n_- = (n_1 - n_2)/\sqrt{2}$$

The variation of the orbital energies $\varepsilon(n_+)$ and $\varepsilon(n_-)$ on internal rotation as calculated by quantum chemical methods is drawn schematically in Figure 6.

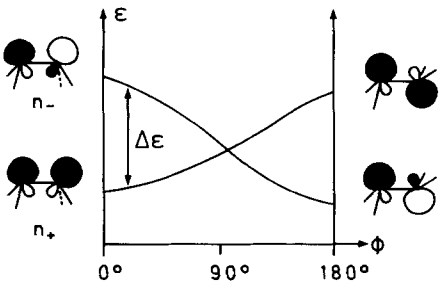


Fig. 6. Variation of the orbitals energies $\varepsilon(n_+)$ and $\varepsilon(n_-)$ of hydrazines with the torsional angle ϕ.

From these results a value of $\Delta IP = 0$ is to be expected for $\phi \approx 90°$, *i.e.* for the perpendicular arrangement of n_1 and n_2 with minimal overlap, while at 0° and 180° maximum values should be observed for ΔIP. Although the correlation between $\Delta IP = -\Delta\varepsilon = \varepsilon(n_+) - \varepsilon(n_-)$ and ϕ is undoubtedly affected by the substituents R and other structural parameters, it is justifiable, to a good approximation, to use a single relation similar to eq. (3) in all cases[16]. From the data of hydrazines of known structure, the relation

$$\Delta IP = 2.20 \cos\phi - 0.25 \text{ [eV]} \quad (5)$$

was obtained.

For unsymmetric hydrazines, n_+ and n_- may differ in energy due to the non-equivalence of n_1 and n_2, even in the case of vanishing interaction, by an amount $\Delta\varepsilon_0$ (Fig. 7)

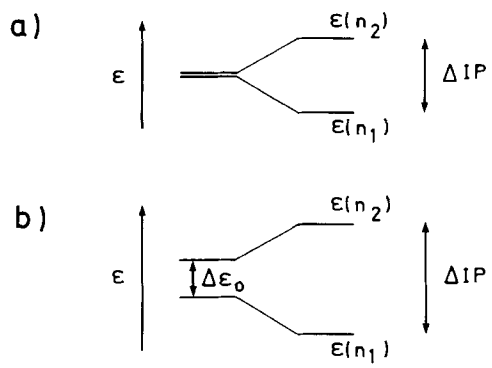
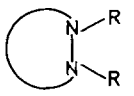


Fig. 7. Splitting $\Delta\varepsilon$ for the n orbitals of (a) symmetrically and (b) unsymmetrically substituted hydrazines *(7)*.

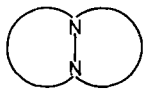
which has to be subtracted from the measured ΔIP prior to use of eq. (5)[16,42–44].

With the correspondingly corrected ΔIP values angles between *ca.* 90 and *ca.* 100° are obtained for acyclic hydrazines in all cases, definitely indicating the *gauche* conformation of these compounds.

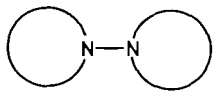
Equation (5) has been applied not only to acyclic hydrazines *(7)* but also to cyclic *(8)* and bicyclic *(9)* compounds and to bi(cycloamines) *(10)*, as well as to molecules containing two or three hydrazine groups *(11)—(14)*. Thus a variety



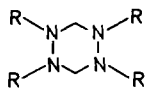
(8)



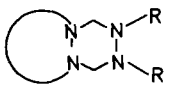
(9)



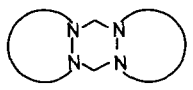
(10)



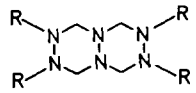
(11)



(12)



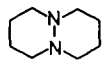
(13)



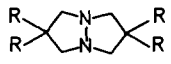
(14)

of different conformational problems could be solved. In this review only a few typical examples will be considered.

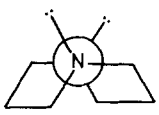
For cyclic *(8)* and bicyclic hydrazines *(9)*, ΔIP values up to 2.4 eV have been observed[40,41,43,45,47,48], indicating large deviations from 90°: 1,6-diazabicyclo[4.4.0]decane *(15)* and the central hydrazine fragment of 1,3,4,6,8,9-hexaazabicyclo[4.4.0]decane *(14)*, R = H, show the largest splittings of n orbitals with $\Delta\varepsilon = -2.35$ and -2.40 eV respectively[48], corresponding to their inversion symmetry ($\phi = 180°$), which is also indicated by their vibrational spectra[52]. Similarly large values can only be found for *syn*-fixed hydrazines ($\phi \approx 0°$).



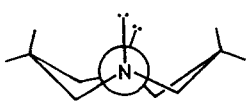
(15)



(16), R = H
(17), R = CH_3



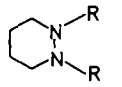
(16)



(17)

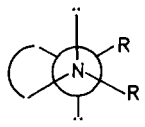
For the 1,5-diazabicyclo[3.3.0]octanes *(16)* and *(17)* ΔIP values of 1.57 and 2.21 eV respectively were measured[40,48]. The *syn* conformation of both compounds was revealed by NMR studies[53]; for *(16)* a structural analysis by gas phase electron diffraction yielded $\phi = 38°$[54]. According to the larger ΔIP values, *(17)* should therefore possess a torsional angle of approximately 0°, which obviously is enforced by the respulsion of the *endo* methyl groups. From eq. (5), $\Delta\varepsilon = 2.05$ eV results for $\phi = 0°$. That this value is exceeded may be due to a nearly coplanar arrangement of the bonds at the nitrogens in *(17)*, which leads to a larger overlap between n_1 and n_2 than sp^3 hybridization. In addition, stronger n/σ interactions are also to be expected at $\phi = 0°$.

Cyclic compounds of type *(8)* have been studied extensively[40,41,43,45,47,48]. Apart from the folding of the ring, particular interest attaches to the arrangement of substituents, the influence of double bonds and the possible existence of conformational mixtures. Moreover, extensive NMR data are available for these compounds. Hexahydropyridazines *(18)* have recently been reviewed by *Nelsen*[55].

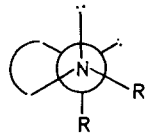


(18)

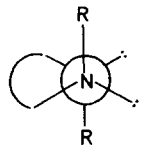
Three conformations (EE, EA, and AA) always have to be considered for compounds of type *(8)*[56]. While the EE form with diequatorial substituents is easily identified from the



EE
$\Phi \approx 180°$



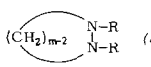
EA
$\Phi \approx 60°$



AA
$\Phi \approx 60°$

large splitting of the n ionization bands, any distinction between the other two forms is difficult due to the similarity of the values of ϕ especially for six-membered rings. Thus PE and NMR spectroscopy are seen to be complementary in these studies: the latter method clearly reveals the EA form, but cannot distinguish between the EE and AA forms. Some results are listed in Table 1.

Table 1. Conformations of cyclic hydrazines of type *(8)*.



(8)

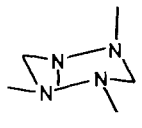
m	R	$\Delta\varepsilon$ [eV]		EE	EA	AA	Ref.
3	CH_3	−0.59			100% *trans*		[48]
4	CH_3	−2.12		100%			[45, 48]
	i-C_3H_7	−2.02,	0.6	much		little	[48]
5	H	0.44,	−1.45	little		much	[40, 48]
	CH_3	−2.22,	0.70	much		little	[40, 48]
	C_2H_5	0.88				100%	[40]
	i-C_3H_7	0.99				100%	[40]
6	H	0.70				100%	[40]
	CH_3	−2.32,	0.77	much	little [a]		[40, 48]
	C_2H_5	0.67			100% [a]		[43]
7	CH_3	0.54			100% [a]		[43]

[a] Decision between EA and AA is not possible on the basis of the spectra (see text).

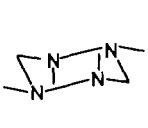
A very impressive example of the efficiency of PE spectroscopic conformational analysis is provided by 1,2,4,5-tetramethylhexahydro-1,2,4,5-tetrazine *(11)*, R = CH_3[48]. NMR studies by *Anderson* and *Roberts*[57] indicated a conformation



(11a)



(11b)



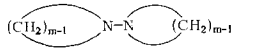
(11c)

with two axial and two equatorial methyl groups. A distinction between the three possibilities *(11a)—(11c)* is immediately possible on the basis of the PE spectrum: The four n-ionization bands of nearly equal intensity could be assigned in pairs to the diequatorial and the diaxial *N,N'*-dimethylhydrazine fragment with $\Delta\varepsilon = -2.47$ eV ($\phi \approx 180°$) and 0.55 eV ($\phi = 70°$), respectively[48].

A detailed analysis of the PE spectra of *(11)* as well as of bi- and tricyclic derivatives with annelated five- and six-membered rings (*(12)* and *(13)*) also considers 1,3- and 1,4-interactions of n orbitals[50]. While the bicyclic compounds *(12)*, like *(11)*, prefer diequatorial-diaxial forms, the tricyclic compounds preferentially adopt tetraequatorial conformations[50,51].

The *N,N'*-connected bi(cycloamines) of type *(10)* exhibit an interesting conformational change with increasing ring size (Table 2)[40,43,45,48,49].

Table 2. Population of the *anti*- and *gauche* conformation of *N,N'*-bi(cycloamines) of type *(10)*.



(10)

m	*anti* [%]	*gauche* [%]	ϕ *(gauche)*
3	100		
4	40	60	64°
5	50	50	99°
6		100	94°

According to vibrational spectroscopy and gas phase electron diffraction[58], the smallest compound, 1,1'-biaziridine ($m = 3$), exhibits an *anti* form with inversion symmetry and thus differs from the isoelectronic bicyclopropyl, which forms a mixture of *gauche*- and *anti* form[59]. For $m \geqq 6$ these compounds exist in a *gauche* form analogous to those of open-chain hydrazines *(7)*.

The *anti*- and *gauche* forms of the four-membered and the five-membered ring compound apparently have similar stabilities and therefore exist as mixtures. This behavior can be understood by considering the repulsion of the α-methylene hydrogens between the rings in the gauche form, which is alleviated by the greater flexibility (folding) of the rings only for $m \geqq 6$.

3.2.2. Hydrazobenzenes

The success of the conformational analysis of hydrazines by PE spectroscopy also stimulated the analysis of hydrazobenzenes *(19)*[60]. Conjugation between n- and π-electrons

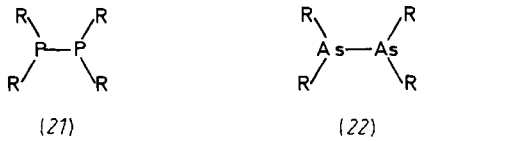


(19) *(20)*

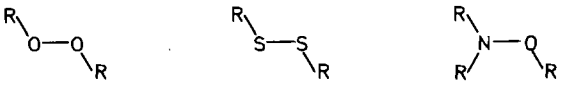
requires that the orientation of the phenyl groups be taken into account as well. A comparison of the spectra of *(19)* with those of the corresponding anilines *(20)* as well as MINDO/2 calculations and studies of molecular models revealed a systematic correlation of the splittings of the first two and the fourth and fifth ionization bands with the dihedral angle ϕ. It was found that the preferred conformation of hydrazobenzenes in the gas phase has the phenyl groups in *anti* positions, unless the geometry of a cyclic system forces the molecule into another conformation.

3.2.3. Other Compounds with Vicinal Lone Pairs

Apart from hydrazines *(7)*, other compounds with vicinal lone pairs like diphosphanes *(21)*[61-65], diarsanes *(22)*[61], peroxides *(23)*[66-70], disulfides *(24)*[71-74], and hydroxylamines *(25)*[75] have also been studied; due mainly to the smaller structural variety of these compounds, however, not nearly so many examples are known. In the case of *(23)* and *(24)*, the situation is complicated by the two electron lone pairs of



(21) *(22)*



(23) *(24)* *(25)*

each oxygen or sulfur atom and for *(25)* by the nonequivalence of the interacting n orbitals.

Studies on open-chain and cyclic peroxides as well as on ozonides suggest a relation analogous to eq. (5) between the splitting of the first two n ionization bands and the twisting with respect to the O—O bond[70]. In disulfides too, the two highest occupied MOs apparently show a sufficiently systematic dependence on the torsional angle to permit their conformational analysis[71-74].

In the case of hydroxylamines, the position of *N*-substituents of isoxazolidines *(26)* and tetrahydro-1,2-oxazines *(27)* could be determined from their PE spectra[75].



(26) *(27)*

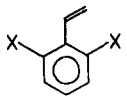
3.3. Systems with π/π Interactions

3.3.1. Dienes and Styrenes

Historically, conformation-dependent orbital interactions were first investigated for biphenyls (see Section 3.1).

The simplest compounds with π/π interactions are 1,3-dienes which generally have a coplanar arrangement of double bonds[76]. For planar systems such as 1,3-butadiene[77] or 1,3-cyclohexadiene[26,78] the difference between the two π-ionization bands is approximately $\Delta IP_{1,2} = 2.5$ eV, independent of the *s-cis* or *s-trans* conformation; for 1,2-dimethylenecyclobutane *(2)* and related compounds, 2,3-substitution and particularly secondary through-space interactions with π_{CH_2} orbitals reduce the value to $\Delta IP_{1,2} = 1.9$ eV[24]. 1,2-Dimethylenecyclohexane *(4)*, on the other hand, prefers a chair conformation with a dihedral angle of $\phi \approx 55°$[79] (see Section 2.2.3).

The interactions between a phenyl and a vinyl group in the styrene derivatives *(28)* were discussed in detail by *Maier* and *Turner*[81]; an approximately linear correlation exists be-

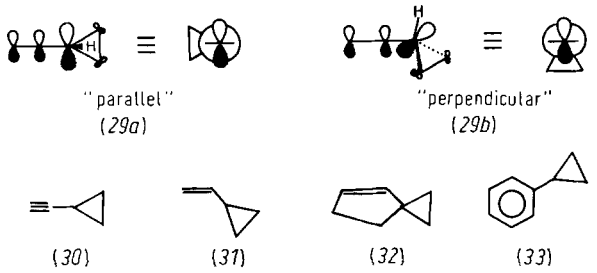


(28)

tween $\cos\phi$ (ϕ = angle of torsion) and the size (calculated e.g. from van der Waals radii) of the substituents X in the *o,o'*-positions, which prevent the coplanar arrangement of the vinyl and phenyl groups.

3.3.2. Cyclopropyl Compounds

The ability of the cyclopropane ring to undergo conjugative interaction with neighboring π centers justifies the treatment of vinyl- *(31)* and phenylcyclopropane *(33)* as systems with π/π interactions. For the vinylcyclopropyl system a parallel *(29a)* and a perpendicular conformation *(29b)* are characterized by maximal and minimal interaction, respec-



tively[82]. The two arrangements which correspond to both these conformations can be observed simultaneously in the spectrum of ethynylcyclopropane *(30)*[83]; $\Delta IP = 2.60$ eV for the parallel arrangement corresponds to the value observed for butadiene, whereas $\Delta IP = 1.50$ eV is found for the perpendicular arrangement. For vinylcyclopropane *(31)* and for the sterically fixed derivative spiro[2.4]hept-4-ene *(32)*, values of $\Delta IP = 2.55$ eV and $\Delta IP = 2.57$ eV have been obtained[84]; for *(31)* a second conformer was not observed at room temperature, and in the case of phenylcyclopropane *(33)* no bands of a second conformer could be detected even at higher temperatures.

The larger number of interacting orbitals makes matters more complicated for two neighboring cyclopropane rings. However, in the case of sterically fixed bicyclopropyl deriva-

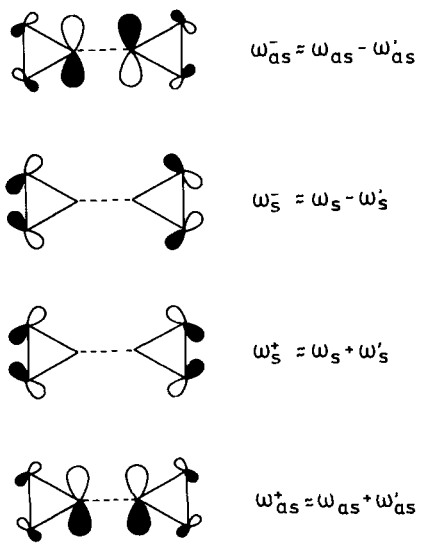


Fig. 8. Walsh orbitals of the bicyclopropyl system *(35)*.

(34)





(35)

tives such as *(34)* the first four PE bands could be assigned to the combinations ω_{as}^{-}, ω_{s}^{-}, ω_{s}^{+}, and ω_{as}^{+} of Walsh orbitals shown in Figure 8[85]. For bicyclopropyl *(35)* in the gas phase a *trans* ($\phi = 90°$) and a *gauche* conformer ($\phi = 30$–$40°$) were found in the ratio 40:60[59], so that in the region between 9 and 11 eV a total of eight PE bands is to be expected, corresponding to ionizations from Walsh orbitals. This marks the limits of conformational analysis by PE spectroscopy: the spectra become too complicated. Nevertheless, a theoretical spectrum based on MINDO/2 results for a mixture of conformers in the above mentioned ratio and assuming Lorentzian curves with a half-width of 0.5 eV is in very good agreement with the observed spectrum (Fig. 9)[86].

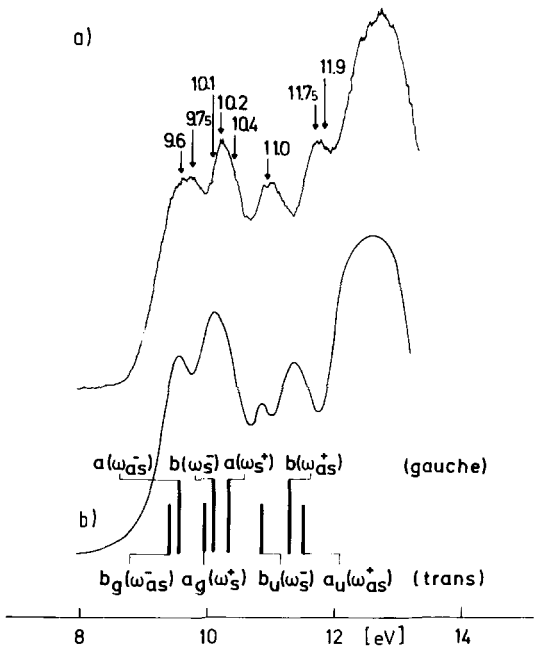
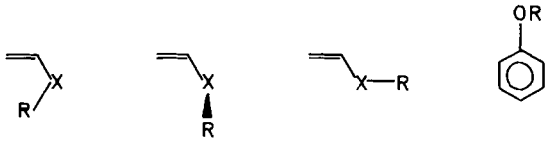


Fig. 9. PE spectrum of bicyclopropyl *(35)*; (a) experimental and (b) calculated for a 40:60 *gauche/trans* ratio assuming Lorentzian curves.

3.4. Systems with n/π Interactions

The principal systems with n/π interactions are vinyl ethers *(36)*, X = O, and vinyl sulfides *(36)*, X = S, as well as the corresponding aryl compounds. The conformations of these compounds have been studied intensively by numerous methods, affording differing results. Thus all the methods indicate that alkyl vinyl ethers and sulfides can exist in a second conformation in addition to the stable *syn* conformation *(36a)*. In the case of the alkyl vinyl ethers, however, there is some doubt whether this is a non-planar gauche conformation, as was concluded from gas phase electron diffraction[87,88] and microwave measurements[89], or a planar *anti* form, as was inferred from the IR spectrum[90], whereas for the alkyl vinyl sulfides different electron diffraction studies[88,91] gave contradictory results for the ratio of the *syn-(36a)* and *anti* form *(36c)* and therefore for the energy difference of these two conformations.

For aryl ethers *(37)*, IR[90,92] and microwave spectra[93] reveal only a planar form, whereas electron diffraction studies[94] and measurements of dipole moments and Kerr constants[95] were interpreted in terms of contributions from nonplanar conformers.

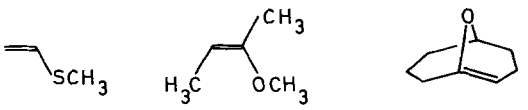


(36a) *(36b)* *(36c)* *(37)*

Information on equilibria between different conformers are obtained by variable temperature PE spectroscopy, as was first shown by *Ames* and *Turner*[62] as well as by *Schweig et al.*[96]. The following examples show that this method is particularly suitable for the investigation of the compounds in question and for deciding in a very simple way between the contradictory results of other investigations.

3.4.1. Alkyl Vinyl Ethers and Alkyl Vinyl Sulfides

The PE spectrum of methyl vinyl sulfide *(38)* has been investigated in the temperature range of 20—600 °C by *Schweig et al.*[95] and has been interpreted on the basis of a temperature-



(38) *(39)* *(40)*

dependent equilibrium between a *syn*- and a *gauche* conformer; the energy difference between the two is estimated as 9.6 ± 0.8 kJ/mol, corresponding to a ratio of 94:6 of *syn*- to *gauche* conformer at room temperature.

Sterically hindered and unhindered alkyl vinyl ethers behave differently[15]: at higher temperatures (*Z*)-2-methoxy-2-butene *(39)* gave two new bands at 9.6 and 10.1 eV (Fig. 10) which have been assigned to a nonplanar *gauche* conformation *(36b)* just like the band at 10.4 eV in the case of isopropyl vinyl ether (*(36)*, X = O, R = *i*-C_3H_7). For methyl vinyl ether *(1)*, on the other hand, no new bands appear between 10 and 12 eV, but from changes in the shape of the second band it was concluded that a new ionization appeared at 12.35 eV, corresponding to a larger splitting ΔIP for the less

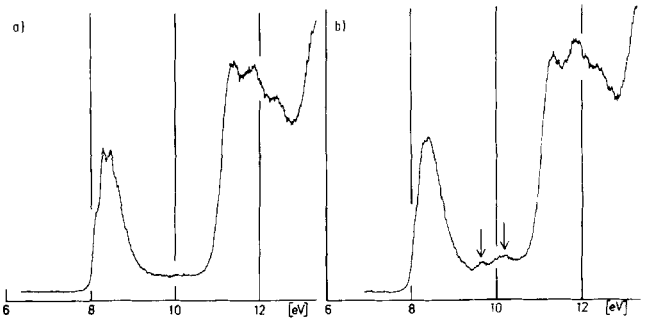


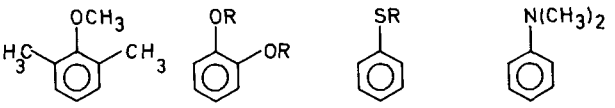
Fig. 10. PE spectrum of (Z)-2-methoxy-2-butene *(39)* at (a) 293 and (b) 508 K; the additional bands of the *gauche* conformation appearing at higher temperatures are marked by arrows.

stable conformer. In connection with the orbital correlation diagram of Figure 2, this shows that in sterically unhindered alkyl vinyl ethers the *syn* conformation predominates over the *anti* conformation, which is approximately 9 ± 3 kJ/mol less stable, whereas in sterically hindered ethers the most stable form is the *anti* conformation, with a nonplanar *gauche* form being 12 ± 1 kJ/mol less stable[15]. These results can be explained quite naturally by assuming strong steric repulsions to occur in the *syn* conformation if the alkyl group is particularly bulky or if the vinyl group carries substituents.

In the case of 9-oxabicyclo[3.3.1]non-1-ene *(40)* and the corresponding sulfur compound *Batich, Heilbronner, et al.*[97] deduced a deviation from coplanarity of the vinyl ether or vinyl sulfide system, respectively, of approximately 70–75° or 75–80° by carefully applying the LCBO model and assuming the angular dependence of the interaction term to be of the form $B = B_0 \cos\phi$.

3.4.2. Alkyl Aryl Ethers and Alkyl Aryl Sulfides

The PE spectra of alkyl aryl ethers *(37)* suggest that sterically hindered compounds such as 2,6-dimethylanisole *(41)*[98] or *tert*-butyl phenyl ether *(37)*, R = *t*-Bu, occur in a nonplanar conformation which is expected to show up as a second, less stable form in the case of sterically nonhindered compounds like anisole *(37)*, R = CH_3. Qualitative considerations of orbital interactions[29] and quantum chemical calculations[99] strongly suggest that, in contrast to the results for alkyl vinyl ethers, the 90° twisted form also corresponds to a potential energy minimum. That the alkyl aryl ethers do indeed assume either a planar or a perpendicular conformation, so that the dihedral angle cannot assume arbitrary values depending on the size of the alkyl group, is seen from a plot of the ionization potential $IP(n_O)$ corresponding to the oxygen lone pair against the ionization potential of the corresponding alkyl iodides: all points lie on a straight line except that for the *tert*-butyl derivative, *i.e.* only the *tert*-butyl ether is sterically hindered and assumes a perpendicular conformation; in all other cases the variation of $IP(n_O)$ is due solely to the inductive effect of the alkyl group[29].



(41) *(42)* *(43)* *(44)*

While one methyl group in position 2 does not alter the conformation of alkyl aryl ethers, PE measurements show that in the gas phase *o*-dimethoxybenzene *(42)* exists predominantly in a nonplanar conformation, whereas in the crystalline state most *o*-dimethoxybenzenes are planar[100]. For the alkyl aryl sulfides, on the other hand, PE measurements always reveal a nonplanar form in addition to the planar conformation. The importance of this nonplanar form increases with increasing size of the alkyl group[98]. In the case of *N*,*N*-dimethylaniline *(44)* just one methyl group in the *o*-position is sufficient for a twisted conformation to predominate, whereas for *N*-methylaniline both *o*-positions have to be substituted in order to force the molecule into such a conformation[101].

4. Scope of the Method

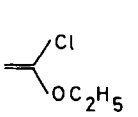
4.1. Assignment of PE Spectra

PE spectroscopy may be applied successfully to conformational problems only if the spectrum is sufficiently simple in the region of interest, for cogent conclusions about the magnitude of orbital interactions and hence about the conformation of a molecule may be obtained from the spectrum only if it is possible to unequivocally assign ionization bands to the orbitals in question. Bicyclopropyl *(35)* has been mentioned as an example of a compound whose PE spectrum is so complex as to reach the limits of the method (Section 3.3.2).

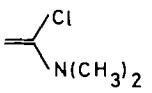
A reliable interpretation of the PE spectrum will usually be possible even in difficult cases by quantum chemical calculations of various degrees of sophistication; moreover progress in experimental techniques may provide new criteria for assignment. Thus, in the case of tetramethyldiphosphane *(21)*, $R = CH_3$, which is known to be a mixture of two conformers, the band at 8.75 eV was originally assigned to the two n orbitals of the energy-rich conformer corresponding to minimal interaction of the n orbitals in a perpendicular conformation ($\phi = 90°$). Measurements at higher temperatures as well as the angular dependence of the PE spectrum and its simulation by Gaussian curves showed that it is not the second but the first band which is due to two different ionizations[65]: it stems from the n_- orbitals of the two conformers, so that $\Delta IP = 0.6$ eV is obtained for the energy-rich conformation corresponding to a *gauche* form with $\phi = 60°$.

4.2. Secondary Orbital Interactions

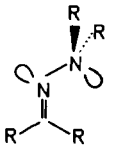
Secondary orbital interactions can also make conformational analysis by PE spectroscopy difficult or even impossible. Thus an attempt to extend the results obtained for the enol ethers *(36)* to the α-chloro derivatives *(45)* and *(46)* was unsuccessful; the experimental ΔIP values are not related to the data of the stable conformers of the unsubstituted compounds. Simple calculations show that ΔIP becomes not only much smaller but also nearly conformationally independent as a result of possible interactions between the π_{CC} as well as the n_O orbitals and the lone-pair orbital of the chlorine[102].



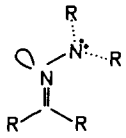
(45)



(46)



(47a)



(47b)

Similar difficulties are observed for hydrazones, for which two stable conformations *(47a)* and *(47b)* are to be expected with the lone pair of the amino nitrogen interacting either with the lone pair of the imino nitrogen or with the π electrons of the C=N bond. As a consequence of these two possible interactions, the energy difference for the two highest orbitals is almost independent of the conformation; only the energy of the third orbital, with an ionization energy expected to lie in a region where unambiguous assignments become difficult, exhibits a marked dependence on the dihedral angle[103].

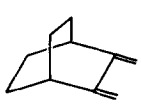
4.3. Other Geometric Changes

Finally it should be noted that other geometric changes may also influence the orbital energies and thus counterfeit changes in the dihedral angle. Thus, on assuming a planar π system for dimethylenenorbornadiene *(48)*, dihedral angles $\phi = 10°$ and $\phi = 20°$, respectively, were derived for dimethylenebicyclooctane *(49)* and the corresponding nonane *(50)* from the relation $\Delta IP_{1,2} = 2\beta_0 \cos\phi$[27]; however, all attempts to prove the nonplanarity of these π systems by other methods failed. Finally, force field calculations suggested that the π systems of all three compounds *(48)*—*(50)* are coplanar, but that the overall geometry of the butadiene fragment is determined by the bicyclic part of the molecule[80].

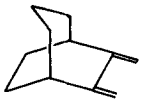
The dependence of the π orbital energies on the geometry of the butadiene fragment, which was demonstrated by *ab-*



(48)



(49)



(50)

initio calculations[24], as well as the linear relation between $\Delta IP_{1,2}$ and the bond angles determined by the force field calculations, suggest that the splitting of the first two ionization potentials of *(49)* and *(50)* is smaller than that of *(48)* not because of a deviation of the π system from coplanarity, but rather because of changes in CCC bond angles[80].

5. Summary and Outlook

In this review only compounds with neighboring n and π electrons were treated. However, interactions between more distant orbitals (*e.g.* 1,3- and 1,4-interactions) can of course also be conformationally dependent. In such cases we cannot expect a simple relation like eq. (2) and (3) to exist between conformational angle and ionization potentials, since through-bond interactions involving suitable "relay orbitals" always have to be taken into account in addition to the direct through-space mechanism. Studies on di- and trioxanes as well as the corresponding thianes by *Sweigart* and *Turner*[104] and those on cyclic 1,3- and 1,4-diamines by *Nelsen* and *Buschek*[105] can be regarded as pilot investigations in this field. Since a distinction between only few conformations is often all that is required for non-aromatic heterocycles, PE spectroscopy is expected to provide valuable information in these cases too.

Summarizing, we should like to state that PE spectroscopy has proved to be a very simple and fast method of conformational analysis, particularly in connection with MO calculations or qualitative MO considerations, and that further interesting applications of this method are to be expected in the future.

In all applications, however, it should always be examined whether and to what extent secondary orbital interactions may affect an expected simple relation between dihedral angle and ionization potentials, and whether geometric changes other than rotations around single bonds have to be considered.

Our thanks are due to our co-workers quoted in the references to our own contributions. We are greatly indebted to our esteemed teacher Professor Lüttke for kindling our interest in problems of molecular structure. This work was supported by the Deutsche Forschungsgemeinschaft, the Landesamt für Forschung in Nordrhein-Westfalen, and the Fonds der Chemischen Industrie.

Received: August 28, 1979 [A 292 IE]
German version: Angew. Chem. *91*, 885 (1979)

[1] *D. H. R. Barton, R. C. Cookson,* Q. Rev. Chem. Soc. *10*, 44 (1956).
[2] *H. H. Lau,* Angew. Chem. *73*, 423 (1961); *D. H. R. Barton,* Angew. Chem. *82*, 827 (1970).
[3] *E. L. Eliel, N. L. Allinger, S. J. Angyal, G. A. Morrison:* Conformational Analysis, Interscience, New York 1965; *M. Hanack:* Conformation Theory. Academic Press, New York 1965; *J. McKenna:* Conformational Analysis of Organic Compounds. The Royal Institute of Chemistry, London 1966; *G. Chiurdoglu:* Conformational Analysis: Scope and Present Limitations. Academic Press, New York 1971; *W. J. Orville-Thomas:* Internal Rotation in Molecules, John Wiley & Sons, London 1974; *J. Dale:* Stereochemie und Konformationsanalyse, Verlag Chemie, Weinheim 1978; Stereochemistry and Conformational Analysis, Universitetsforlaget, Oslo 1975; *D. G. Lister, J. N. Macdonald, N. L. Owen:* Internal Rotation and Inversion. Academic Press, London 1978.
[4] *O. B. Ramsay,* Chem. Ztg. *97*, 573 (1973); *E. L. Eliel, ibid. 97*, 582 (1973); J. Chem. Educ. *52*, 762 (1975).
[5] *A. Golebiewski, A. Parczewski,* Chem. Rev. *74*, 519 (1974); *B. Pullman:* Quantum Mechanics of Molecular Conformations. Wiley, London 1976.
[6] Cf. *H. Bock, B. G. Ramsey,* Angew. Chem. *85*, 773 (1973); Angew. Chem. Int. Ed. Engl. *12*, 734 (1973).
[7] *T. Koopman,* Physica (Utrecht) *1*, 104 (1934).
[8] *R. Hoffmann,* Acc. Chem. Res. *4*, 1 (1971).
[9] *J. P. Maier, D. W. Turner,* Dicuss. Faraday Soc. *54*, 149 (1972).
[10] As *Koopmans'* theorem is valid only within the SCF approximation and therefore can yield only approximate values for ionization potentials it is also referred to as *Koopmans'* approximation.
[11] *K. Wittel, S. P. McGlynn,* Chem. Rev. *77*, 745 (1977).
[12] *E. Heilbronner* in *R. Daudel, B. Pullman:* The World of Quantum Chemistry. Reidel, Dordrecht 1974, p. 211.
[13] Cf., *e.g. W. v. Niessen, W. P. Kraemer, G. H. F. Diercksen,* Chem. Phys. *41*, 113 (1979).
[14] *F. Brogli, P. A. Clark, E. Heilbronner, M. Neuenschwander,* Angew. Chem. *85*, 414 (1973); Angew. Chem. Int. Ed. Engl. *12*, 422 (1973).
[15] *H. Friege, M. Klessinger,* J. Chem. Res. (S) *1977*, 208.
[16] *P. Rademacher,* Chem. Ber. *108*, 1548 (1975).
[17] *M. Klessinger,* Theor. Chim. Acta *49*, 77 (1978).
[18] *R. McWeeny,* Rev. Mod. Phys. *32*, 335 (1960); *M. Klessinger, R. McWeeny,* J. Chem. Phys. *42*, 3343 (1965).
[19] *A. C. Hurley, J. E. Lennard-Jones, J. A. Pople,* Proc. R. Soc. *A 220*, 446 (1953). The orthogonality makes possible the subdivision of the system into fragments; the separation of inductive and conjugative effects used here is therefore based on the strong orthogonality requirement.
[20] *E. Gunkel, M. Klessinger,* Tetrahedron *34*, 3591 (1978).
[21] *M. Klessinger, H. Friege,* to be published.
[22] *G. G. Hall,* Proc. R. Soc. (London) *A 205*, 541 (1951).
[23] Cf., *e.g., E. Heilbronner, J. P. Maier* in *R. Brundle, A. P. Baker:* Electron Spectroscopy. Vol. 1. Academic Press, London 1977, p. 227.
[24] *P. Hemmersbach, M. Klessinger, P. Bruckmann,* J. Am. Chem. Soc. *100*, 6344 (1978).
[25] *Th. Sombeck,* Staatsexamensarbeit, Universität Münster 1976.
[26] *P. Bischof, E. Heilbronner,* Helv. Chim. Acta *53*, 1677 (1970).
[27] *P. Asmus, M. Klessinger,* Tetrahedron *30*, 2477 (1974).
[28] *P. Asmus,* Diplomarbeit, Universität Münster 1972.
[29] *H. Friege, M. Klessinger,* Chem. Ber. *112*, 1614 (1979).
[30] *G. Hentrich, E. Gunkel, M. Klessinger,* J. Mol. Struct. *21*, 231 (1974).
[31] See, *e.g., E. L. Eliel:* Stereochemie der Kohlenstoffverbindungen. Verlag Chemie, Weinheim 1966.
[32] *P. Meunier, M. Coustale, C. Guimon, G. Pfister-Guillouzo,* J. Mol. Struct. *36*, 233 (1977); *P. Meunier, G. Pfister-Guillouzo,* Can. J. Chem. *55*, 2867 (1977).
[33] *W. Flitsch, H. Peeters, W. Schulten, P. Rademacher,* Tetrahedron *34*, 2301 (1978).
[34] For a review, see *Y. Shovo* in *S. Patai:* The Chemistry of the Hydrazo, Azo and Azoxy Groups. Wiley, London 1975, p. 1017.
[35] *S. Wolfe,* Acc. Chem. Res. *5*, 102 (1972), and references cited therein.
[36] *L. Radom, W. J. Hehre, J. A. Pople,* J. Am. Chem. Soc. *94*, 2371 (1972).
[37] *A. Veillard* in *B. Pullman:* Quantum Mechanics of Molecular Conformations. Wiley, London 1976, p. 1.
[38] *N. D. Epiotis, W. R. Cherry, S. Shaik, R. L. Yates, F. Bernardi,* Top. Curr. Chem. *70*, 1 (1977).
[39] *L. S. Bartell, H. K. Higginbotham,* Inorg. Chem. *4*, 1346 (1965); *C. Glidewell, D. W. H. Rankin, A. G. Robiette, G. M. Sheldrick,* J. Chem. Soc. *A 1970*, 318.
[40] *S. F. Nelsen, J. M. Buschek,* J. Am. Chem. Soc. *95*, 2011 (1973); *96*, 6982, 6987 (1974).
[41] *S. F. Nelsen, J. M. Buschek, P. J. Hintz,* J. Am. Chem. Soc. *95*, 2013 (1973).
[42] *S. F. Nelsen, J. M. Buschek,* J. Am. Chem. Soc. *96*, 2392 (1974).
[43] *S. F. Nelsen, V. Peacock, G. R. Weisman,* J. Am. Chem. Soc. *98*, 5269 (1976).
[44] *S. F. Nelsen, V. E. Peacock, C. R. Kessel,* J. Am. Chem. Soc. *100*, 7017 (1978).
[45] *S. F. Nelsen, V. E. Peacock, G. R. Weisman, M. E. Landis, J. A. Spencer,* J. Am. Chem. Soc. *100*, 2806 (1978).
[46] *P. Rademacher,* Angew. Chem. *85*, 410 (1973); Angew. Chem. Int. Ed. Engl. *12*, 408 (1973).
[47] *P. Rademacher,* Tetrahedron Lett. *1974*, 83.
[48] *P. Rademacher, H. Koopmann,* Chem. Ber. *108*, 1557 (1975).
[49] *K. Kirste, W. Lüttke, P. Rademacher,* Angew. Chem. *90*, 726 (1978); Angew. Chem. Int. Ed. Engl. *17*, 680 (1978).
[50] *P. Rademacher, H. Breier, R. Poppek,* Chem. Ber. *112*, 853 (1979).
[51] *A. R. Katritzky, V. J. Baker, F. M. S. Brito-Palma, R. C. Patel, G. Pfister-Guillouzo, C. Guimon,* J. Chem. Soc. Perkin Trans. II *1979*, in press.
[52] *H. Koopmann, P. Rademacher,* Spectrochim. Acta *A 32*, 157 (1976).
[53] *J. M. Lehn,* Fortschr. Chem. Forsch. *10*, 311 (1970).
[54] *P. Rademacher,* J. Mol. Struct. *28*, 97 (1975).
[55] *S. F. Nelsen,* Acc. Chem. Res. *11*, 14 (1978).
[56] Of course ϕ is also affected by the size and folding of the ring.
[57] *J. E. Anderson, J. D. Roberts,* J. Am. Chem. Soc. *90*, 4186 (1968).
[58] *P. Rademacher, W. Lüttke,* Angew. Chem. *82*, 258 (1970); Angew. Chem. Int. Ed. Engl. *9*, 245 (1970); *P. Rademacher,* Spectrochim. Acta *A 28*, 987 (1972); Acta Chem. Scand. *26*, 1981 (1972).
[59] *O. Bastiansen, A. de Meijere,* Angew. Chem. *78*, 142 (1966); Angew. Chem. Int. Ed. Engl. *5*, 124 (1966).
[60] *P. Rademacher, V.-M. Bass, M. Wildemann, H. Weger,* Chem. Ber. *110*, 1939 (1979).
[61] *A. H. Cowley, M. J. S. Dewar, D. W. Goodman, M. C. Padolina,* J. Am. Chem. Soc. *96*, 2648 (1974).
[62] *D. L. Ames, D. W. Turner,* J. Chem. Soc. Chem. Commun. *1975*, 179.
[63] *S. Elbel, H. tom Diek, G. Becker, W. Ensslin,* Inorg. Chem. *15*, 1235 (1976).
[64] *H. Goetz, G. Frenking, F. Marschner,* Phosphorus Sulfur *4*, 309 (1978).
[65] *A. Schweig, N. Thon, H. Vermeer,* J. Am. Chem. Soc. *101*, 80 (1979).
[66] *C. Batich, W. Adam,* Tetrahedron Lett. *1974*, 1467.
[67] *K. Kimura, K. Osafune,* Bull. Chem. Soc. Jpn. *48*, 2421 (1975).
[68] *R. S. Brown,* Can. J. Chem. *53*, 3439 (1975).
[69] *D. J. Coughlin, R. S. Brown, R. G. Salomon,* J. Am. Chem. Soc. *101*, 1533 (1979).
[70] *P. Rademacher, W. Elling,* Justus Liebigs Ann. Chem., in press; *W. Elling,* Diplomarbeit, Universität Münster 1976.
[71] *G. Wagner, H. Bock,* Chem. Ber. *107*, 68 (1974).
[72] *A. D. Baker, M. Brisk, M. Gellender,* J. Electron Spectrosc. Relat. Phenom. *3*, 227 (1974).
[73] *M. F. Guimon, C. Guimon, G. Pfister-Guillouzo,* Tetrahedron Lett. *1975*, 441.
[74] *M. F. Guimon, C. Guimon, F. Metras, G. Pfister-Guillouzo,* J. Am. Chem. Soc. *98*, 2078 (1976).
[75] *P. Rademacher, B. Freckmann,* Tetrahedron Lett. *1978*, 841; *B. Freckmann,* Diplomarbeit, Universität Münster 1976.
[76] Cf., however, *C. R. Brundle, M. B. Robin,* J. Am. Chem. Soc. *92*, 5550 (1970).
[77] *M. Beez, G. Bieri, H. Bock, E. Heilbronner,* Helv. Chim. Acta *56*, 1028 (1973).
[78] *P. Bischof, E. Heilbronner,* Helv. Chim. Acta *53*, 1677 (1970); for cyclic dienes and trienes, cf. *Ch. Batich, P. Bischof, E. Heilbronner,* J. Electron Spectrosc. Relat. Phenom. *1*, 333 (1972/73).
[79] Force field calculations yielded 53° [80].
[80] *H.-U. Pfeffer, M. Klessinger,* Chem. Ber. *112*, 890 (1979).
[81] *J. P. Maier, D. W. Turner,* J. Chem. Soc. Faraday Trans. II *69*, 196 (1973).
[82] *R. Hoffmann, R. B. Davidson,* J. Am. Chem. Soc. *93*, 5699 (1971).
[83] *P. Bruckmann, M. Klessinger,* J. Electron Spectrosc. Relat. Phenom. *2*, 341 (1973).
[84] *P. Bruckmann, M. Klessinger,* Chem. Ber. *107*, 1108 (1974).
[85] *P. Asmus, M. Klessinger,* Justus Liebigs Ann. Chem. *1975*, 2169.
[86] *P. Asmus, M. Klessinger,* Angew. Chem. *88*, 343 (1976); Angew. Chem. Int. Ed. Engl. *15*, 310 (1976).
[87] *N. L. Owen, H. M. Seip,* Chem. Phys. Lett. *5*, 162 (1970).
[88] *S. Samdal, H. M. Seip,* J. Mol. Struct. *28*, 193 (1975).
[89] *P. Cahill, L. P. Gold, N. L. Owen,* J. Chem. Phys. *48*, 1620 (1968).
[90] *A. R. Katritzky, R. F. Pinzelli, R. D. Topsom,* Tetrahedron *28*, 3441 (1972).
[91] *J. L. Derissen, J. M. J. M. Bijen,* J. Mol. Struct. *16*, 289 (1973).

[92] T. B. Grindley, A. R. Katritzky, R. D. Topsom, J. Chem. Soc. Perkin Trans. II 1974, 289.
[93] N. L. Owen, R. E. Hester, Spectrochim. Acta A 25, 343 (1969).
[94] H. M. Seip, R. Seip, Acta Chem. Scand. 27, 4024 (1973).
[95] M. J. Aroney, R. J. W. Lefèvre, R. K. Pierens, M. C. N. The, J. Chem. Soc. B 1969, 666.
[96] C. Müller, W. Schäfer, A. Schweig, N. Thom, H. Vermeer, J. Am. Chem. Soc. 98, 5440 (1976).
[97] Ch. Batich, E. Heilbronner, C. B. Quinn, J. R. Wisemann, Helv. Chim. Acta 59, 512 (1976).
[98] P. S. Dewar, E. Ernstbrunner, J. P. Gilmore, M. Godfrey, J. M. Mellor, Tetrahedron 30, 2455 (1974).
[99] A. Zywietz, Diplomarbeit, Universität Münster 1979.
[100] C. M. Anderson III, P. A. Kollman, L. N. Domelsmith, K. N. Houk, J. Am. Chem. Soc. 101, 2344 (1979), and references cited therein.
[101] J. P. Maier, D. W. Turner, J. Chem. Soc. Faraday Trans. II 69, 521 (1973).
[102] P. Bovy, L. Ghosez, M. Klessinger, H. Friege, unpublished.
[103] P. Rademacher, H.-U. Pfeffer, D. Enders, H. Eichenauer, P. Weuster, J. Chem. Res. (S) 1979, 222; (M) 2501.
[104] D. A. Sweigart, D. W. Turner, J. Am. Chem. Soc. 94, 5599 (1972).
[105] S. F. Nelsen, J. M. Buschek, J. Am. Chem. Soc. 96, 7930 (1974).

Catalytic Reactions with Hydrosilane and Carbon Monoxide

New synthetic methods (30)

By Shinji Murai and Noboru Sonoda[*]

The reagent hydrosilane/carbon monoxide opens up new possibilities for organic synthesis. Four cases will be discussed: 1. The reaction of olefins with hydrosilane (trialkylsilane) and carbon monoxide in the presence of Co, Ru, and Rh complexes leads to enol silyl ethers having one more carbon atom than the olefins. 2. Cyclic ethers undergo carbonylative ring opening to ω-siloxyaldehydes when reacted with hydrosilane and carbon monoxide in the presence of $Co_2(CO)_8$ as catalyst. 3. Aldehydes are catalytically converted into the next higher α-siloxyaldehydes or 1,2-bis(siloxy)alkenes depending on the reaction conditions used. 4. The reaction of alkyl acetates proceeds in various ways depending on the nature of the alkyl group; enol silyl ethers or alkenes are obtained.—Mechanisms for these $Co_2(CO)_8$ catalyzed reactions using hydrosilane and carbon monoxide are discussed in which $HCo(CO)_n$ or $R_3SiCo(CO)_nL$ function as catalytically active agents. With these species there are four types of catalytic cycles.—The synthetic possibilities of these catalytic reactions have still not been fully explored.

1. Introduction

The hydroformylation of olefins with molecular hydrogen and carbon monoxide to produce aldehydes has been extensively studied for almost forty years; the interest attached to homogeneous catalysis and the growing industrial importance of such reactions are continually stimulating new investigations.

A naive idea occurred to us about four years ago: what happens if a hydrosilane ($HSiR_3$) is employed in place of molecular hydrogen in the hydroformylation? The idea was based on the known similarity in reactivity between molecular hydrogen and hydrosilanes toward transition metal complexes (cf. Section 2.1). A few months later, clean but rather puzzling reactions were found. For example, the $Co_2(CO)_8$ catalyzed reaction of cyclohexene with a hydrosilane and carbon monoxide gave a silyl ether of cyclohexanecarbaldehyde-enol *(vide infra)*. This finding led to the discovery of a series of new catalyzed reactions using hydrosilane and carbon monoxide, opening up a new field embracing organosilicon chemistry, homogeneous catalysis, and synthetic organic chemistry.

Not only olefins but also various oxygenated compounds such as cyclic ethers and carbonyl compounds have been found to react with hydrosilane and carbon monoxide in the presence of group VIII transition metal complexes. In most cases $Co_2(CO)_8$ has been used as catalyst. Both olefins and oxygenated compounds incorporate carbon monoxide and the silyl moiety to give stable *O*-silylated derivatives of usually unstable or otherwise inaccessible hydroxy compounds such as enols, hydroxy aldehydes, or ene-diols.

In this article we present a survey of these new catalytic reactions, almost all of which were discovered in our laboratory. Emphasis will be laid on the basic features of the reactions and hence on the possible role of the catalytic agents. We shall also focus attention on the unsolved problems in this area, for these reactions are still in an early stage of development.

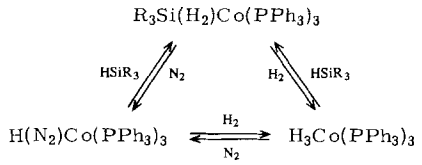
2. Catalytic Reactions of Olefins with Hydrosilane and Carbon Monoxide

2.1. Similarity in Reactivity of Hydrosilanes and Molecular Hydrogen toward Transition Metal Complexes

It is interesting to note that reactions of hydrosilanes ($HSiR_3$) with transition metal complexes parallel those of

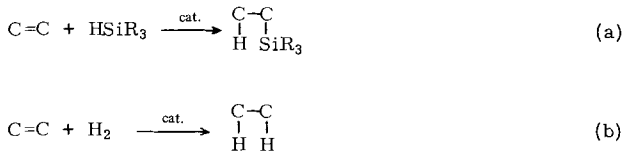
[*] Prof. Dr. S. Murai, Prof. Dr. N. Sonoda
Department of Petroleum Chemistry, Faculty of Engineering
Osaka University, Suita, Osaka 565 (Japan)

molecular hydrogen. Both hydrosilanes[1] and molecular hydrogen[2] undergo oxidative addition[3] to group VIII metal



Scheme 1. Similarity of hydrosilane and molecular hydrogen. R = OEt.

complexes. The reactions[4] shown in Scheme 1 may serve as illustrative examples of the similar behavior of hydrosilanes and molecular hydrogen. Catalytic hydrosilylation[1,5], *i.e.* the addition of hydrosilanes to unsaturated compounds with

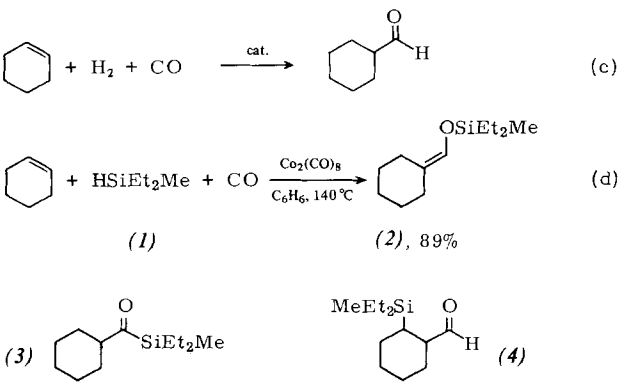


the aid of transition metal complexes [eq. (a)], is formally analogous to catalytic hydrogenation [eq. (b)][2]. Mechanistically, these two reactions seem to be very closely related[1,2].

Various attempts have been made at the insertion of carbon monoxide into the Si—H bond[6] or into silicon-transition metal bonds[7], but all have proven unsuccessful. This parallels the fact that no definite example of carbonyl insertion into a hydrogen-transition metal bond has been recorded[8], although this reaction to give formylmetal complexes is suggested to be important as the initial step in the Fischer-Tropsch synthesis[8a] or in the Union Carbide ethylene glycol synthesis[9]. In this context, the copper(II) catalyzed insertion of cyclohexyl isocyanide, which is isoelectronic to carbon monoxide, into the Si—H bond of triethylsilane[10] is very intriguing. Carbon monoxide, however, does not react with the silane under the same conditions[11].

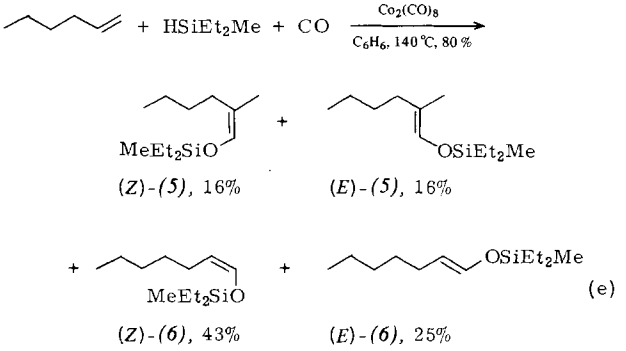
2.2. Reaction of Olefins with Hydrosilanes and Carbon Monoxide Catalyzed by $Co_2(CO)_8$

The well known Roelen reaction (so-called hydroformylation or oxo reaction)[12] involves addition of hydrogen and carbon monoxide to olefins [eq. (c)]. The similarity between hydrosilanes and molecular hydrogen in transition metal reactions urged us to study the reaction of olefins with hydrosilanes and carbon monoxide in the presence of various

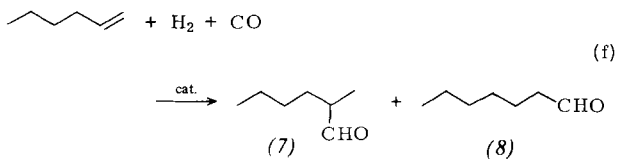


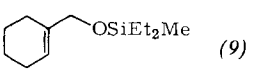
transition metal complexes[14–16]. The important works of *Colleuille*[17], as well as those of *Chalk* and *Harrod*[6,18], will be referred to at the end of this section.

As shown in eq. (d), the reaction of diethyl(methyl)silane *(1)* and carbon monoxide in the presence of a catalytic amount of $Co_2(CO)_8$ gives [diethyl(methyl)siloxymethylene]cyclohexane *(2)*, an enol silyl ether, as sole product and no trace of the acylsilane *(3)* or the β-silyl aldehyde *(4)*, as would be expected as products by direct formal analogy with the Roelen reaction[11,14,15]. Similarly, the (siloxymethylene)cycloalkanes of type *(2)* were obtained from cyclopentene (48%), cycloheptene (74%), and cyclooctene (69%)[14,15]. The reaction conditions were: catalyst 0.2—0.4 mmol, olefin 30—200 mmol, $HSiEt_2Me$ *(1)* 10 mmol, initial pressure of CO 50—80 bar at 25 °C, reaction temperature 140 °C, 20 h. Since two reaction sites are available in a terminal olefin, four isomers of siloxymethylene derivatives (regio- and stereoisomers) are expected in this case. All these isomers have been obtained (80%) and characterized in the $Co_2(CO)_8$ catalyzed reaction of 1-hexene[11,16] [eq. (e)].



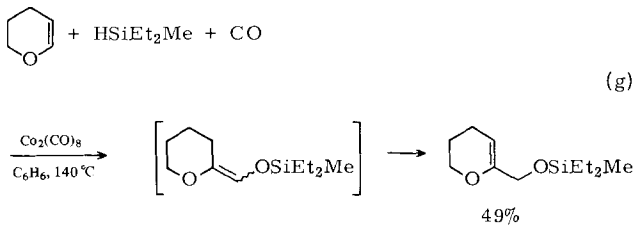
The regioisomers *(5)* and *(6)* may correspond to those [*(7)* and *(8)*] obtained by the Roelen reaction[12] [eq. (f)]. Methyl acrylate, a terminal olefin having an electron withdrawing group, also gave a mixture of four isomeric enol silyl ethers[11]. When the reaction was carried out at higher temperatures or with higher concentrations of catalyst, migration of the double bond in the product took place. The reaction of cyclohexene at 200 °C gave 1-(siloxymethyl)cyclohexene *(9)* in addition to *(2)* in a ratio 1:5[15].





When migration of the double bond gives the more stable isomer, complete isomerization is observed as in eq. (g)[11].

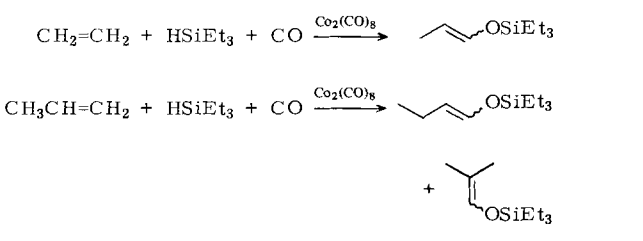
So far, we have examined only a few types of olefins. Besides olefins, there still remain dienes and acetylenes to be studied. The effective range of transition metal complexes as catalysts has been studied and will be discussed in Section



(g)

2.3. While the reactivity of the H—H bond in H_2 obviously cannot be changed, that of the Si—H bond can be varied by changing the substituents on the silicon atom. This is one of the interesting aspects of the reactions using hydrosilanes. The reactivity of the hydrosilanes ($HSiR^1R^2R^3$ where R^n = H, alkyl, aryl, alkoxy, halogen *etc.*) in hydrosilylation depends upon the substituents[1,5]. A brief examination of the reactivity of hydrosilanes has been made for the $Co_2(CO)_8$ catalyzed reaction of cyclohexene [eq. (d)][15]. In this particular case the trialkylsilanes (alkyl = Me and/or Et) appear to be the reaction partners of choice. Although hydrosilanes having alkoxy or chloro groups proved to be very reactive, the reactions were complex and gave mixtures of many products whose structures have not yet been clarified. Diethyl(methyl)silane *(1)* was used exclusively in the present study because it is easy to handle (b.p. 76 °C, very stable towards water and oxygen). Moreover, the NMR spectrum of a compound containing an Et_2MeSi group(s) shows nice sharp singlet(s) due to the methyl group(s). This is of great experimental utility, because it enables the purity of a product or the number of the products formed to be ascertained immediately.

Pioneering work on the $Co_2(CO)_8$ catalyzed reactions of olefins with hydrosilanes and carbon monoxide has also been carried out independently by *Colleuille* and his results have appeared in the patent literature[17]; we first became aware of this only very recently. Although details for the characterization of products are not given, as is usual in patents, it has been clearly demonstrated that the corresponding enol triethylsilyl ethers were obtained from ethylene (44%), propene (70%), 1-butene (27%), isobutene (44%), cyclohexene (87%), and norbornene (65%) on using $HSiEt_3$ and CO. With exception of the reaction with propene, however, in all the cases mentioned considerable amounts of unidentified by-products (1 to 0.15:1) were obtained which could not be separated from the enol silyl ethers by fractional distillation. These by-products are likely to be double bond-isomers similar to *(9)* and/or hexaethyldisiloxane. No comment is made about the presence of stereoisomers, as in the reaction of 1-hexene [eq. (e)]. *Chalk* and *Harrod* have also reported the $Co_2(CO)_8$ catalyzed reaction of ethylene with $HSiEt_3$ and CO to give 1-(triethylsiloxy)-1-propene[6,8]. Both groups of workers reported that the reaction of 1-hexene was too complex, which is in contrast to our findings.



2.3. Catalysts

A search for good catalysts for a certain reaction will never be complete since there are numerous possible combinations of metals, ligands, additives, reactants, and reaction conditions. Even for the Roelen reaction[12], which has forty years of history, the research in this field is still in progress. So far, we have examined the catalytic activity of various transition metal complexes only for the reaction of 1-hexene according to eq. (e).

For this particular reaction the following complexes show little or no catalytic activity[11]: $CuCl_2$, Cu_2Cl_2, $W(CO)_6$, $Mn_2(CO)_{10}$, $Fe(CO)_5$, $Fe_2(CO)_9$, $Fe(CO)_4PPh_3$, $RuCl_2(PPh_3)_3$, Rh_2O_3, $IrCl(CO)(PPh_3)_2$, $Ni(CO)_4$, $Ni(CO)_2(PPh_3)_2$, $Ni(acac)_2$, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, Pd-black, H_2PtCl_6, Pt-black. The effective complexes found are listed in Table 1[11,16].

Table 1. Reaction of 1-hexene with $HSiEt_2Me$ and CO to give the linear isomer *(6)* and the branched isomer *(5)* [a].

Catalyst (mmol)	Yield *(5)* + *(6)* [%]	Rel. Yield *(6)* [%] [*(6)*/(*(5)* + *(6)*)] × 100
$Ru_3(CO)_{12}$ (0.4)	40	89
$Co_2(CO)_8$ (0.4)	57	68 (55) [b]
$Co_2(CO)_8$ (0.4) [c]	80	68
$Co_2(CO)_8$ (0.4) + Ph_3P (1.0)	77	83 (90) [b]
$Co_2(CO)_8$ (0.4) + *n*-Bu_3P (1.0)	18	92 (62) [b]
$RhCl(PPh_3)_3$ (0.4)	41	82
$RhCl(PPh_3)_3$ (0.4) + Et_3N (1.0)	88	79

[a] Reaction conditions: 1-hexene (30 mmol), $HSiEt_2Me$ (10 mmol), CO (50 bar, initial pressure at 25 °C), catalyst (as given), solvent (benzene, 20 ml), 140 °C, 20 h. [b] For comparison: Relative yield of linear isomer in the Roelen reaction [19] [eq. (f)] in (%), [*(8)*/(*(7)* + *(8)*)] × 100. [c] 200 mmol 1-hexene.

These effective complexes for the reaction of 1-hexene were also tested in the reaction of cyclohexene [eq. (e)]; the results are shown in Table 2. Interestingly, whereas $Co_2(CO)_8$ was more effective for cyclohexene, $Ru_3(CO)_{12}$ and $RhCl(PPh_3)_3$ were more effective in the case of 1-hexene. Further investigations in this area should open up the possibility of selective reaction of different double bonds in one molecule.

Table 2. Reaction of cyclohexene with $HSiEt_2Me$ and CO [a].

Catalyst (mmol)	Yield of *(2)* [%]
$Ru_3(CO)_{12}$ (0.2)	1.4
$Co_2(CO)_8$ (0.2)	71
$Co_2(CO)_8$ (0.4) [b]	89
$RhCl(PPh_3)_3$ (0.2)	0.5
$RhCl(PPh_3)_3$ (0.2) + Et_3N (1.0)	30

[a] Reaction conditions: cyclohexene (30 mmol), $HSiEt_2Me$ (10 mmol), CO (80 bar, initial pressure at 25 °C), catalyst (as given), solvent (benzene, 20 ml), 140 °C, 20 h. [b] Cyclohexene (200 mmol), CO (50 bar, initial pressure at 25 °C).

Since the present reaction requires the activation of both hydrosilane and carbon monoxide, it seems of interest to compare these results with those of hydrosilylation[1,5] and the Roelen reaction[12]. The effective catalysts found for the reaction of 1-hexene with $HSiEt_2Me$ and CO, *i.e.* $Ru_3(CO)_{12}$,

$Co_2(CO)_8$, and $RhCl(PPh_3)_3$, are known to be active in the Roelen reaction. The latter two complexes are also effective in hydrosilylation[1]. However, among the complexes which show little or no activity in the present reaction there are some which are effective catalysts for the Roelen reaction [for example, Rh_2O_3 and $IrCl(CO)(PPh_3)_3$][12] and for hydrosilylation [$PdCl_2(PPh_3)_2$, H_2PtCl_6, *etc.*][1]. A tentative conclusion that could be drawn here is that an effective catalyst in the present reaction may also be effective as a catalyst in both the Roelen reaction and in hydrosilylation[20]. However, more extensive studies are obviously necessary in this field.

It is noteworthy that the change in regioselectivity of the reaction of 1-hexene [eq. (e), Table 1], is similar to that observed in the Roelen reaction [eq. (f)] when using $Co_2(CO)_8$/PR_3 as catalyst[16]. This implies that the interaction of 1-hexene with $HCo(CO)_3$ is also important as initial step in the reaction using hydrosilane and carbon monoxide (cf. Section 2.5).

2.4. Reaction Conditions

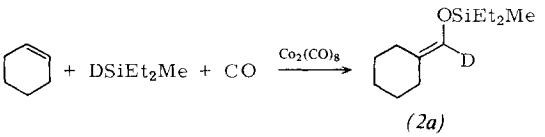
The effects of a change in reaction conditions have been examined for the $Co_2(CO)_8$ catalyzed reaction of 1-hexene with $HSiEt_2Me$ and CO [eq. (e)]. The reaction conditions described in footnote [a] of Table 1 have been regarded as the standard conditions. Under these standard conditions *(5)* and *(6)* were obtained in a combined yield of 57%. Some of the more important results[11] will be summarized below.

The combined yield of *(5)* and *(6)* markedly increases on using a higher molar ratio of 1-hexene to hydrosilane: The yields were 7, 57, and 80% at olefin/hydrosilane ratios of 1:1, 3:1 and 20:1, respectively. Good yields were obtained with $Co_2(CO)_8$:hydrosilane in the molar ratio 1:25. The use of smaller amounts of catalyst gave lower yields, while the use of a higher catalyst: hydrosilane ratio (1:10) resulted in the formation of a hydrosilylation product (n-$C_6H_{13}SiEt_2Me$) at the expense of the enol silyl ethers *(5)* and *(6)*. The effect of CO pressure was examined in the range between 3 and 150 bar (initial pressure at 25 °C). The yield increased from 14% at 3 bar to 68% at 80 bar and remained almost unchanged at higher pressures. The best results for the reaction of 1-hexene were obtained at a reaction temperature of 140 °C. The yields of the enol silyl ethers decreased with decreasing temperature, and no reaction took place below 80 °C. At 200 °C, migration of the double bond in the products took place to some extent. The distribution of the four isomers [(*Z*)- and (*E*)-*(5)* (branched), (*Z*)- and (*E*)-*(6)* (linear)], and hence the proportion of linear isomers, did not change significantly under the various reaction conditions described above. Nor did changes in the reaction time have any influence on the distribution. The reactions were almost complete within 7 h under the standard conditions.

2.5. Mechanistic Aspects

The mechanism of the catalyzed reaction of olefins with hydrosilane and carbon monoxide is one of the most intriguing problems. An understanding of the mechanism is, however, essential for further development of new reactions. On the basis of the arguments outlined below, we propose here the mechanism given in Scheme 2 for the $Co_2(CO)_8$ catalyzed reaction of cyclohexene with $DSiEt_2Me$ and CO.

While it is obvious that the carbon and oxygen atoms of carbon monoxide are incorporated into the oxymethylene group of the product, the enol silyl ethers, it is much more difficult to establish which hydrogen atom in the product stems from the hydrosilane used in the reaction. To clarify



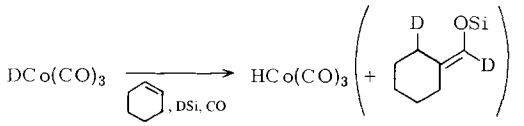
(2a)

this problem we carried out the reaction of cyclohexene with $DSiEt_2Me$ and CO using $Co_2(CO)_8$ as a catalyst[11]: the deuterium was found predominantly (91%) in the vinylic position of the product *(2a)*.

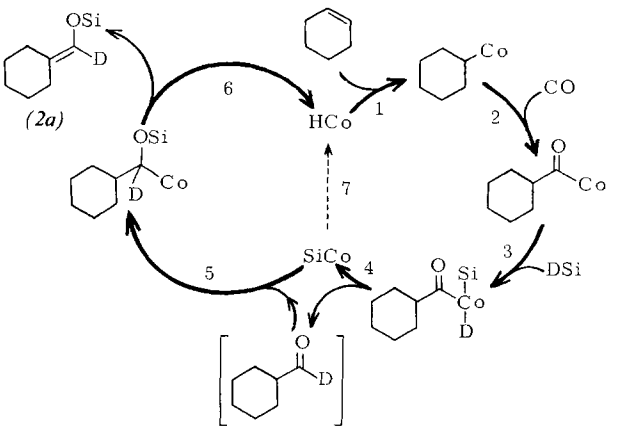
Initiation:

$$Co_2(CO)_8 + DSiEt_2Me \longrightarrow DCo(CO)_4 + MeEt_2SiCo(CO)_4$$

The first catalytic cycle:



Succeeding catalytic cycles:



Scheme 2. $Co_2(CO)_8$ catalyzed reaction of cyclohexene with $DSiEt_2Me$ and CO. (The step *(7)* is not involved in the catalytic cycle; see text.) Abbreviations: SiCo *etc.* = $MeEt_2SiCo(CO)_n$, *etc.*, $n = 3$ or 4.

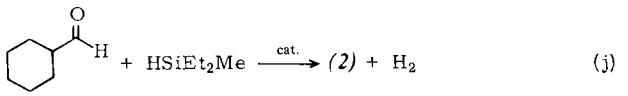
The course of the deuterium incorporation may be best explained in terms of the catalytic cycle shown in Scheme 2. For simplicity, the alkyl groups on the silicon and the CO ligands on the cobalt have been omitted. The most important reactions of hydrosilanes with $Co_2(CO)_8$ have been studied by *Chalk* and *Harrod*[6] and later by *Baay* and *MacDiarmid*[21]. The reaction of $HSiR_3$ with $Co_2(CO)_8$ takes place smoothly even at room temperature to give $HCo(CO)_4$ and $R_3SiCo(CO)_4$ [eq. (h)]. In the presence of excess amounts of the hydrosilane, the former reacts with the silane with evolution of molecular hydrogen [eq. (i)]. The catalytic cycle may

$$HSiR_3 + Co_2(CO)_8 \rightarrow HCo(CO)_4 + R_3SiCo(CO)_4 \quad (h)$$

$$HSiR_3 + HCo(CO)_4 \rightarrow R_3SiCo(CO)_4 + H_2 \quad (i)$$

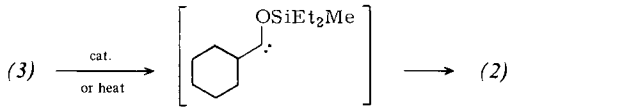
start by the insertion of olefin into the H—Co bond (Step 1). This is in agreement with the observed similarity of the product linearities with those in the Roelen reaction (Section 2.3) and with the fact that better yields of the product have been obtained at higher concentrations of olefin (Section 2.4), suggesting competition between insertion (Step 1) and hydrogen evolution [eq. (i)]. Although the reaction with $DSiEt_2Me$ proceeds primarily *via* $DCo(CO)_4$, this catalytically active species may be converted into $HCo(CO)_3$ in the first catalytic cycle (Scheme 2). In the second and all succeeding catalytic cycles the reaction of the olefin is catalyzed by $HCo(CO)_3$ (Step 1) which is repeatedly regenerated by β-elimination in the product-forming step (Step 6). Thus, the deuterium taken up in the oxidative addition (Step 3) moves to the acyl position of the intermediate aldehyde in the reductive elimination step (Step 4), and finally appears at the vinylic position of the enol silyl ether *(2a)* (Step 6). The possible intermediacy of an aldehyde will be discussed later.

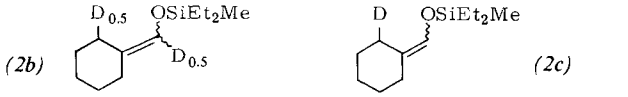
This deuterium labeling experiment clearly rules out the following two alternative mechanisms. The first one involves intervention of molecular hydrogen and is represented by two successive reactions [eq. (c) and (j)]. At first glance, it might be surmised that the present reaction involves the well



(j)

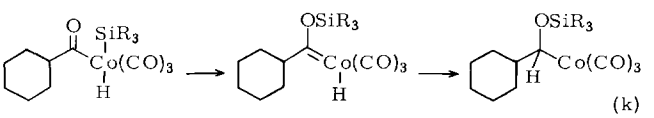
known Roelen reaction[12] [eq. (c)] utilizing molecular hydrogen which could be generated *in situ* by dehydrogenative silylation[5] [eq. (j)] of the aldehyde thus formed. The second alternative mechanism involves initial formation of an acylsilane such as *(3)* as an intermediate, followed by Brook rearrangement[22] to give *(2)*. This mechanism has been proposed by *Chalk* and *Harrod* to account for their observations[18].





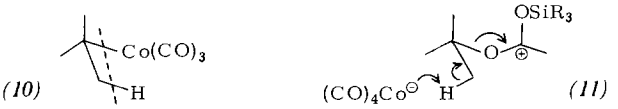
According to the first or the second alternative mechanism the reaction using $DSiEt_2Me$ should afford *(2b)* or *(2c)*, respectively[23]. However, the formation of *(2a) (vide supra)* is observed.

In the proposed mechanism (Scheme 2), the C—Co bond is first cleaved in the reductive elimination step (Step 4)—giving an aldehyde—and is then reformed again in the subsequent step (Step 5). Whether an aldehyde is first formed as an intermediate or not may be an important question[24], for a more direct path *via* a carbene-metal complex, in which the C—Co bond remains unbroken—with no aldehyde being produced [eq. (k)][25]—is also conceivable.

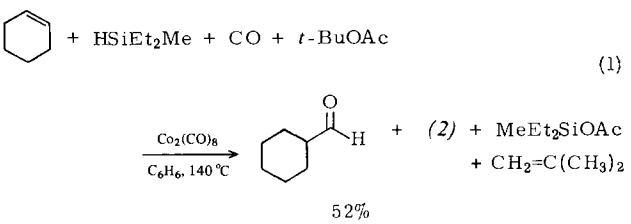


(k)

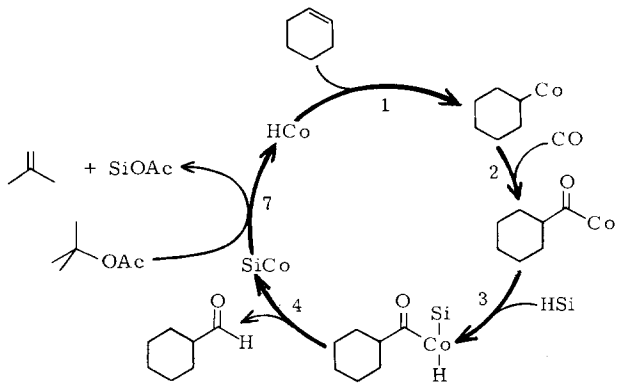
In order to decide which mechanism is operating, one could attempt to isolate the aldehyde. Examination of Scheme 2 suggests that introduction of an efficient by-path (Step 7) to convert the silyl(carbonyl)cobalt compound (SiCo in the Scheme) into $HCo(CO)_3$ (HCo in the Scheme) would leave the aldehyde intact without breaking the catalytic cycle. It occurred to us that *tert*-butyl acetate would be suitable for this purpose. The conversion could be expected to proceed *via (10)* or *(11)* (see Section 3.4).



Indeed, cyclohexanecarboxaldehyde was obtained in 52% yield when the $Co_2(CO)_8$ catalyzed reaction of cyclohexene (90 mmol) with $HSiEt_2Me$ (10 mmol) and CO (50 bar) was carried out in the presence of *tert*-butyl acetate (30 mmol) in benzene at 140 °C for 20 h[11]. The enol silyl ether *(2)* (20%), diethyl(methyl)silyl acetate, and isobutene were also formed [eq. (l)]. For this reaction we suggest the catalytic cycle



shown in Scheme 3, and that an aldehyde is formed as intermediate in the reaction (d); but further verification of Scheme 3 is required, since the possible intervention of the carbene complex [eq. (k)] is still not out of the question.



Scheme 3. Formation of an aldehyde from cyclohexene. (The numbering of the steps and abbreviations correspond to those in Scheme 2.)

It should be noted that the formation of an aldehyde according to eq. (l) is a new type of hydroformylation of an olefin and differs from the Roelen[12] or Reppe reactions[13]. It is hoped that still better trapping agents than *tert*-butyl acetate will be found.

There are still many unsettled questions regarding the mechanism. Above all, a detailed knowledge of the numerous steps involved and of the structures of the catalytically

effective intermediates is still lacking. A further interesting question is whether the mechanism suggested above is also valid or not for reactions with other catalysts, such as Rh and Ru complexes.

3. $Co_2(CO)_8$ Catalyzed Reactions of Oxygenated Compounds with Hydrosilane and Carbon monoxide

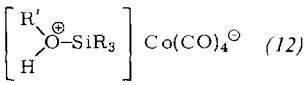
3.1. Reactivity of Silyl(carbonyl)cobalt Compounds

Reaction of a hydrosilane with $Co_2(CO)_8$ gives $HCo(CO)_4$ and $R_3SiCo(CO)_4$, [eq. (h)]. As we have already seen, $HCo(CO)_4$ is important in the catalyzed reaction of olefins. It has now been found that there are other reactions of hydrosilane and carbon monoxide in which $R_3SiCo(CO)_4$ seems to play the key role as catalyst. In these reactions, the catalytic cycles evidently begin with interaction between the substrates and $R_3SiCo(CO)_4$ and terminate with the regeneration of this compound. The substrates may be oxygenated organic compounds such as cyclic ethers, aldehydes, and esters. These compounds incorporate carbon monoxide and form siloxyaldehydes or enol silyl ethers having one or two more carbon atom(s). So far, we have studied these reactions only with $Co_2(CO)_8$ as catalyst (or catalyst precursor). Before discussing such reactions, it may be appropriate to take a brief look at the characteristic reactivity of $R_3SiCo(CO)_4$[27].

Trialkylsilyl(tetracarbonyl)cobalt, $R_3SiCo(CO)_4$, may be obtained by the reaction of hydrosilane with $Co_2(CO)_8$ as shown in eqs (h) and (i) and can be isolated by distillation or by crystallization when desired[6,21,28,29]. The most important property of these silyl(carbonyl)cobalt compounds is perhaps that they are very susceptible toward nucleophilic attack at the silicon atom even by weak bases such as alcohols [eq. (m)][21,29]. Since the stereochemistry of this reaction involves

$$R'OH + R_3SiCo(CO)_4 \rightarrow R'OSiR_3 + HCo(CO)_4 \qquad (m)$$

inversion at the silicon atom[29] the reaction most likely proceeds *via* the intermediate *(12)*[30]. Aprotic bases such as ter-



(12)

tiary amines or phosphanes react similarly[27]. For example, the reaction of trimethylsilyl(tetracarbonyl)cobalt with trimethylphosphane gives a silylphosphonium salt [eq. (n)] and not a phosphanecobalt complex obtainable by ligand exchange[31]. Strong bases such as MeLi and MeMgBr substi-

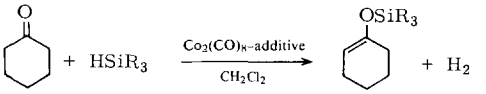
$$Me_3P + Me_3SiCo(CO)_4 \rightarrow [Me_3P{-}SiMe_3]^+[Co(CO)_4]^- \qquad (n)$$

tute triphenylsilyl(tetracarbonyl)cobalt[32] at the silicon atom, while PhLi attacks at the carbonyl ligand[33].

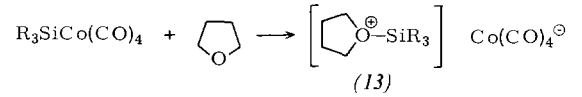
$Co_2(CO)_8$ is known to catalyze the silylation of alcohols, carboxylic acids, and amides[30]. In these silylations, the ac-

$$EtOH + HSiEt_3 \xrightarrow{\text{cat. } Co_2(CO)_8} EtOSiEt_3 + H_2$$

tive catalyst must be $Et_3SiCo(CO)_4$, which is generated by the reaction (h); it silylates the alcohol according to eq. (m), and is regenerated in the subsequent reaction (i) with evolution of molecular hydrogen. Recently, *Sakurai, Miyoshi,* and *Nakadaira* have found that the dehydrogenative silylation of ketones with hydrosilanes is effectively catalyzed by a $Co_2(CO)_8$-additive (additive: amines, phosphanes *etc.*)[34]. Again, silyl(carbonyl)cobalt must play an important role in



this useful reaction. *Chalk* has reported that $Co_2(CO)_8$ in the presence of a twofold or greater excess of $HSiEt_3$ catalyzes the cationic polymerization of tetrahydrofuran, an oxetane, and propylene oxide[30]. A silyloxonium ion of type *(13)* has been postulated[30] as intermediate.

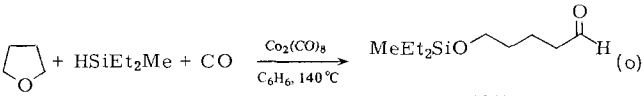


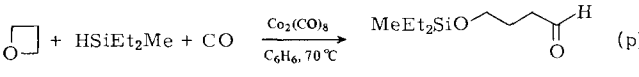
(13)

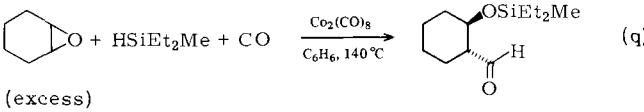
These examples imply that the central silicon atom in $R_3SiCo(CO)_4$ is strongly acidic and strongly electrophilic.

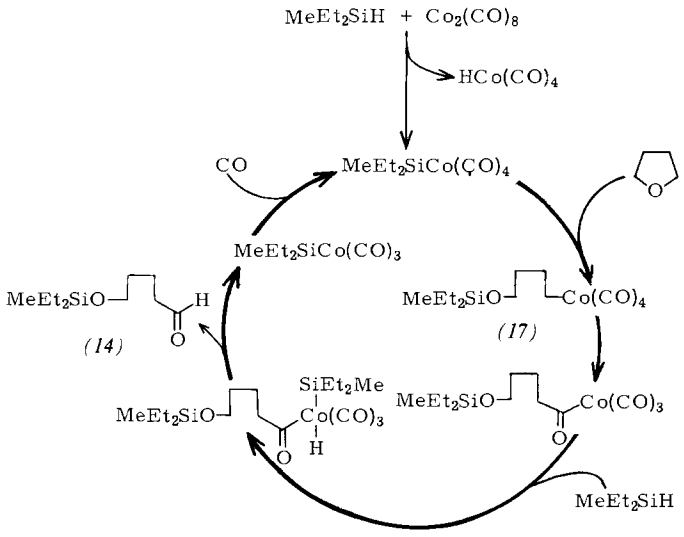
3.2. Catalytic Reactions of Cyclic Ethers with Hydrosilane and Carbon Monoxide

The reaction of cyclic ethers (tetrahydrofuran, oxetane, and 1,2-epoxycyclohexane) with $HSiEt_2Me$ and CO using $Co_2(CO)_8$ as catalyst has been found to give ω-[diethyl(methyl)siloxy]aldehydes[35]. The reaction conditions were: cyclic ether (3—5 equiv.), $HSiEt_2Me$ (1 equiv.), CO with initial pressure of 60 bar at 25 °C, $Co_2(CO)_8$ (0.02 equiv.), in benzene at 70—140 °C for 20 h. For the synthesis of the ω-siloxyaldehydes *(14)* to *(16)* excess amounts of cyclic ether are essential (see Section 3.3). The reaction appears to be limited to three-, four-, and five-membered cyclic ethers. Neither tetrahydropyran nor diethyl ether reacted under these conditions. Interestingly, diethyl ether could even be used as a solvent in the reaction of tetrahydrofuran. The enhanced reactivity of tetrahydrofuran toward $R_3SiCo(CO)_4$ has been known for some time[30,36].





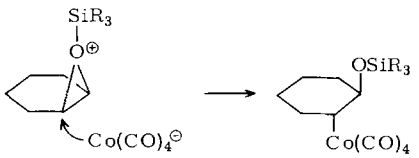




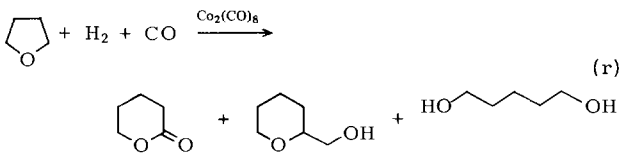
Scheme 4. $Co_2(CO)_8$ catalyzed reaction of THF with $HSiEt_2Me$ and CO.

Although a detailed reaction mechanism has not as yet been formulated, the catalytic cycle shown in Scheme 4 would appear to account for the present carbonylative ring opening. Two important aspects of this mechanism are: firstly, $R_3SiCo(CO)_4$, and not $HCo(CO)_4$, undergoes initial interaction with the cyclic ether, and is later regenerated; secondly, the well known high affinity of the organosilyl group for the oxygen atom[37] could be regarded as the important driving force for formation of the intermediate having a C—Co bond like *(17)*. In other words, Scheme 4 illustrates a new method for the formation of a carbon-transition metal bond; the carbonyl insertion is made possible by using the strong affinity of silicon for oxygen.

The ring-opening of tetrahydrofuran to the alkylcobalt complex *(17)* could proceed *via* the oxonium ion *(13)*. In this context, the configuration of the product *(16)* from 1,2-epoxycyclohexane is very interesting. The *trans* configuration of *(16)* could be understood by assuming an S_N2-type ring-opening of the oxonium ion intermediate.



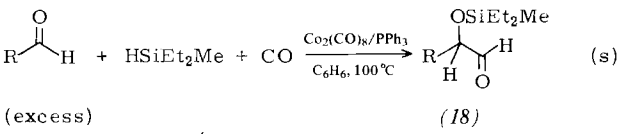
In contrast to reaction (o), the Roelen reaction[12] of tetrahydrofuran with $Co_2(CO)_8$ as a catalyst gives several products [eq. (r)][38].



3.3. Catalytic Reactions of Aldehydes with Hydrosilane and Carbon Monoxide

We have tested whether the above described new entry to intermediates having a C—Co bond is also applicable to aldehydes, and have revealed unique catalytic reactions in which interaction of the carbonyl group of an aldehyde with $R_3SiCo(CO)_4$ seems to be the key step.

Reaction of 3 equivalents of aldehyde with 1 equiv. of $HSiEt_2Me$ and CO (50 bar) in the presence of 0.04 equiv. of $Co_2(CO)_8PPh_3$ (1:1) in benzene at 100 °C for 20 h, afforded the α-siloxyaldehydes *(18)* having one more carbon atom [eq. (s)][39]. The yields of *(18)* were 49% (R = *n*-C_3H_7), 50% (R = *n*-C_6H_{13}), and 54% (R = cyclohexyl). Although it is not

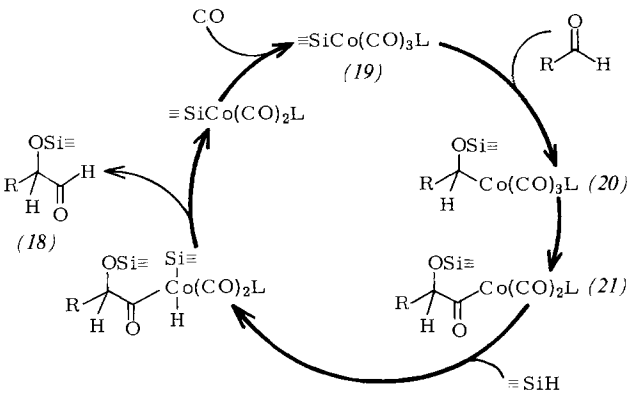


(s)

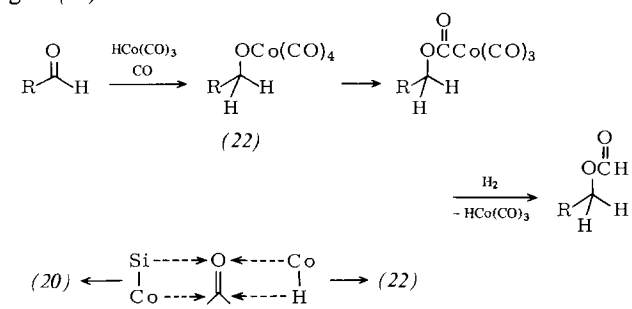
always necessary to use PPh_3 as a co-catalyst, it was found effective in suppressing the simple hydrosilylation of aldehydes [eq. (t)].

$$RCHO + HSiEt_2Me \xrightarrow{cat.} RCH_2OSiEt_2Me \qquad (t)$$

We suggest the catalytic cycle shown in Scheme 5 for the reaction (s). Here also, the active catalyst is a silyl(carbonyl)cobalt compound, $MeEt_2SiCo(CO)_3L$ (L = CO or PPh_3) *(19)*, and this reacts with the aldehyde to give the α-siloxyalkylcobalt *(20)*. The strong affinity between silicon and oxygen forces bond formation between the carbonyl carbon and the cobalt atom. In contrast, under the conditions of the Roelen reaction[12] (H_2 and CO) aldehydes are known to give formates. This implies that the interaction of aldehydes with $HCo(CO)_n$ (*n* = 3 or 4) takes place in the opposite direction to give *(22)*[40].



Scheme 5. $Co_2(CO)_8/PPh_3$ catalyzed conversion of a aldehyde to the next higher α-siloxyaldehyde using $MeEt_2SiH$ and CO. (The substituents on the silicon are not shown.) L = CO or PPh_3.



Insertion of carbon monoxide into the C—Co bond of *(20)* takes place to give the acylcobalt *(21)*. Very recently, inser-

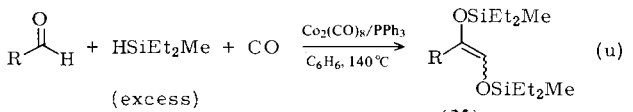
tion of carbon monoxide into an α-siloxyalkylmanganese complex having similar structure to *(20)* has been reported[41]. Such reactions involving α-hydroxyalkylmetal compounds are very important with regard to the mechanism of the Fischer-Tropsch reaction[8a] and the Union Carbide ethylene glycol synthesis[9] in which α-hydroxyalkylmetal compounds [*(23)* and *(24)*, respectively] are thought to play a key role.



(23) *(24)*

Two significant aspects of the reaction (s) may be worth mentioning. Firstly, the reaction (s) represents the first definite example of a catalytic reaction in which carbonylation with carbon monoxide takes place directly at the carbon of a carbonyl group. To our knowledge no reaction of this type, except for a few equivocal ones[42], has so far been reported, probably because no appropriate entry to the required α-hydroxyalkylmetal precursor has been available. Secondly, so far as we know, reaction (s) (Scheme 5) constitutes the first example of the interception of a plausible intermediate of carbonyl hydrosilylation [*e.g.* (t)], viz. of the compound *(20)*.

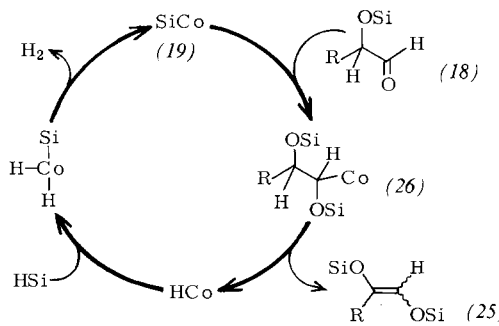
To obtain the α-siloxyaldehydes *(18)* by reaction (s), it is essential to use the starting aldehydes in excess over the hydrosilane; otherwise, the yields of *(18)* decrease. This implies that the catalyst species $R_3SiCo(CO)_3L$ *(19)* can react not only with the starting aldehydes but also with the α-siloxyaldehydes *(18)* that are formed. Thus, the $Co_2(CO)_8/PPh_3$ catalyzed reaction of an aldehyde with an excess of $HSiEt_2Me$ (1:3) and CO gave a different product, the 1,2-bis(siloxy)al-



(u)

(25)

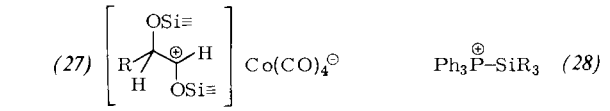
kene *(25)* was obtained instead of *(18)* [eq. (u)][43]. The yields were 67% (R = *n*-C_3H_7), 66% (R = *n*-C_6H_{13}), and 37% (R = cyclohexyl). Apparently, *(25)* may have been obtained as a result of dehydrogenative silylation of the initially formed *(18)*. Scheme 6 shows the simplified catalytic cycle for the conversion of *(18)* into *(25)*; the active catalyst *(19)* is regenerated, similarly as in reaction (i), with evolution of molecular hydrogen. The overall reaction (u) may be regarded as a combi-



Scheme 6. Catalytic conversion of α-siloxyaldehydes *(18)* into 1,2-bis(siloxy)alkenes. (The substituents on the silicon are not shown. For simplicity, the ligands on the cobalt whose number may possibly change during the cycle are also not shown.) Abbreviations: SiCo *etc.* = $MeEt_2SiCo(CO)_nL$ *etc.*; *n* = 3 or 4, L = CO or PPh_3.

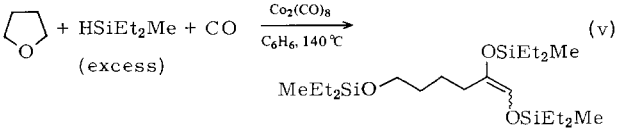
nation of the catalytic cycles given in Schemes 5 and 6. The use of PPh_3 was essential in these cases to suppress reaction (t).

Instead of the mechanisms shown in Schemes 5 and 6 some alternative ones could be suggested in which ionic species such as *(27)* or *(28)* could play a role. These possibilities remain open.



(27) *(28)*

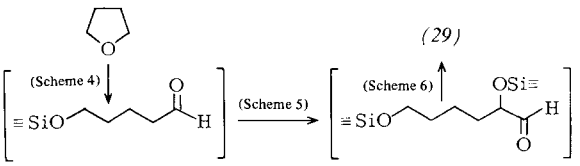
Since the product from tetrahydrofuran is the aldehyde *(14)* [see eq. (o)], it can be expected that the use of excess amounts of $HSiEt_2Me$ will convert it into the corresponding 1,2,6-tris(siloxy)hexene *(29)*. This is indeed the case, as is shown in eq. (v)[43]. In this reaction, it was unnecessary to use



(v)

(29), 89%

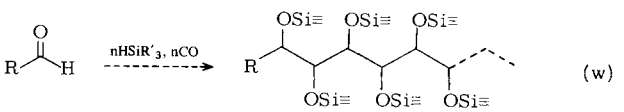
PPh_3 as a co-catalyst since the starting material was not an aldehyde [cf. reactions (s), (t), and (u)]. The course of the reaction (v) may be explained by a sequence of three catalytic cycles corresponding to Schemes 4, 5, and 6. The route from tetrahydrofuran to the product *(29)* is possibly very long, most likely involving more than a dozen steps. By using



(29)

excess amounts of $HSiEt_2Me$, oxetane gave a product similar to *(29)*, but 1,2-epoxycyclohexane unexpectedly afforded *(2)* as the major product[11].

A fascinating possibility could be envisaged on considering this type of C—C bond forming reaction with carbon monoxide. If one could carbonylate the α-siloxyaldehyde *(18)* in the same manner as in eq. (s), one would obtain a higher α,β-bis(siloxy)aldehyde. By repeating this process, one would in principle be able to "copolymerize" hydrosilane and carbon monoxide to persilylated polyhydroxymethylenes *(30)* [eq. (w)][44]. However, various other problems still have to be solved before seriously attempting this "copolymerization".



(w)

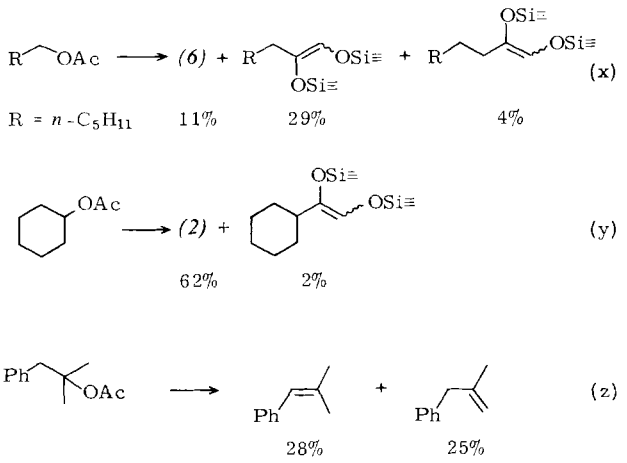
(30)

3.4. Catalyzed Reactions of Alkyl Acetates with Hydrosilane and Carbon Monoxide

There are many promising candidates available as partners for a catalyzed reaction with hydrosilane and carbon

monoxide. The reactions of oxygenated compounds such as esters, acid anhydrides, ketones, enones, acetals, ketals, and orthoesters as well as those of organic halides would be of great interest. So far, only a few substrates have been examined; some preliminary results of experiments with alkyl acetates are described below[11].

Alkyl acetates were allowed to react with $HSiEt_2Me$ (3:1) and CO (50 bar) in the presence of $Co_2(CO)_8$ in benzene at 140 °C for 20 h [eq. (x)—(z)].



Although not shown in eqs. (x)—(z), a silyl acetate $MeEt_2SiOAc$ was obtained in all cases. From the primary alkyl acetate [eq. (x)], only a trace amount of the branched isomers *(5)* was obtained, thus indicating little isomerization of the intermediary *n*-hexyl(carbonyl)cobalt compound under these reaction conditions. Interestingly, up to three molecules of carbon monoxide have been incorporated [eq. (x)]. The reaction of the secondary alkyl acetate [eq. (y)] seems to be promising as a synthetic reaction. In the plausible catalytic cycle of reaction (z), $H(CO)_4Co$ is very likely to arise in the product forming step. This process has already been formulated for step 7 in Schemes 2 and 3. In the present reaction (z), $HCo(CO)_4$ can be converted into a silyl(carbonyl)cobalt compound [eq. (z)].

4. Outlook

There are four types of catalytic cycles or overall catalytic transformations for the reaction with hydrosilane and carbon monoxide. One cycle begins with $HCo(CO)_4$ ("HCo"), another with a silyl(carbonyl)cobalt compound ("SiCo"); both terminate with regeneration of the same initial catalyst species in the product forming step [Scheme 2 for "HCo"; and Schemes 4 and 5 for "SiCo"]. In the other two catalytic cycles or overall catalytic transformations, regeneration of the initial catalyst species occurs after the product is formed [Scheme 3 for "HCo"; and the transformation (u) outlined by Schemes 5 and 6 for "SiCo"]. Availability of the two catalyst species, "HCo" and "SiCo", and hence of the four types of catalytic cycles or catalytic transformations provides a unique opportunity for designing a reaction. Moreover, in planning a new reaction, it will also be of great help to recall the close analogy between the reaction patterns of "SiCo" described in this paper and those of the well studied Me_3SiX, where X is a soft base such as CN, N_3, SR, I *etc.*[37,45].

From the synthetic point of view, the new catalyzed reactions have not as yet been fully explored. It should be noted, however, that the products obtained are *O*-silyl ethers of hydroxy compounds which are otherwise unstable or hardly accessible, *i.e.* enols, enediols, and α- and ω-hydroxyaldehydes. The synthetic utility of enol silyl ethers was first demonstrated by our research group[46] and has now been well established[37,45,47].

We wish to express our sincere gratitude to our able former students: Dr. Y. Seki (now at Kagawa University) for his conceptual and experimental contributions, Messrs. A Hidaka, I. Yamamoto, Y. Agari, S. Makino, and M. Fukutani for their skill and insight, and also to our present students (T. Kato, Y. Hatayama, and N. Chatani). We thank Prof. K. Kawamoto (Kagawa University) for valuable discussions.

Received: April 3, 1979 [A 295 IE]
German version: Angew. Chem. *91*, 896 (1979)

[1] *J. F. Harrod, A. J. Chalk* in *I. Wender, P. Pino:* Organic Synthesis *via* Metal Carbonyls. Vol. 2. Wiley, New York 1977, p. 673 ff.
[2] *R. E. Harmon, S. K. Gupta, D. J. Brown*, Chem. Rev. *73*, 21 (1973).
[3] *J. P. Collman, W. R. Poper*, Adv. Organomet. Chem. *7*, 53 (1968).
[4] *N. J. Archer, R. N. Haszeldine, P. V. Parish*, Chem. Commun. *1971*, 524.
[5] *E. Lukevics, Z. V. Belyakova, M. G. Pomerantseva, M. G. Voronkov*, J. Organomet. Chem. Libr. *5*, 1 (1977).
[6] *A. J. Chalk, J. F. Harrod*, J. Am. Chem. Soc. *89*, 1640 (1967).
[7] *B. J. Aylett, J. M. Campbell*, J. Chem. Soc. *A 1969*, 1910, 1916; Inorg. Nucl. Chem. Lett. *3*, 137 (1976); *F. de Charentenay, J. A. Osborn, G. Wilkinson*, J. Chem. Soc. *A 1968*, 787; *A. P. Hargen, L. McAmis, M. A. Stewart*, J. Organomet. Chem. *66*, 127 (1974).
[8] a) *G. Henrici-Olivé, S. Olivé*, Angew. Chem. *88*, 144 (1976); Angew. Chem. Int. Ed. Engl. *15*, 136 (1976); b) *F. Calderazzo, ibid. 89*, 305 (1977) and *16*, 299 (1977), respectively.
[9] *R. L. Pruett*, Ann. N. Y. Acad. Sci. *295*, 239 (1977).
[10] *T. Saegusa, Y. Ito, S. Kobayashi, K. Hirota*, J. Am. Chem. Soc. *89*, 2240 (1967).
[11] *S. Murai, N. Sonoda*, unpublished results.
[12] a) *O. Roelen*, DRP 849548 (1938); b) For recent reviews, *F. Piancenti, M. Bianchi, P. Pino* in [1], Chapters 1—3; c) In the present paper, we use the term "Roelen reaction" for the catalyzed reactions of organic compounds with H_2 and CO. The term "oxo reaction" is not recommended because many "oxo reactions" do not give oxo (*i.e.* carbonyl) compounds [12b]. The popular term "hydroformylation", introduced by *H. Adkins* and *G. Krsek* [J. Am. Chem. Soc. *71*, 3051 (1949)], may also be confusing since it has, unfortunately, often been used not only to show the type of transformation (the addition of a hydrogen atom and a formyl group) but, improperly, to indicate the reactants (H_2 and CO). In the present paper, the term "hydroformylation" will be used only in the context of its original meaning, *i.e.* to show the type of transformation. Besides hydroformylation by the Roelen reaction (H_2 and CO), hydroformylation has also been observed in the Reppe reaction (H_2O and CO) [13] and in the reaction dealt with here ($HSiR_3$ and CO), see Section 2.5.
[13] *W. Reppe, H. Vetter*, Justus Liebigs Ann. Chem. *582*, 133 (1953); *N. von Kutepow, H. Kindler*, Angew. Chem. *72*, 802 (1960); *H. Kang, C. H. Mauldin, T. Cole, W. Sleger, K. Cann, R. Pettit*, J. Am. Chem. Soc. *99*, 8323 (1977); *R. M. Laine, ibid. 100*, 6451 (1978).
[14] *Y. Seki, A. Hidaka, S. Murai, N. Sonoda*, Angew. Chem. *89*, 196 (1977); Angew. Chem. Int. Ed. Engl. *16*, 174 (1977).
[15] *Y. Seki, A. Hidaka, S. Makino, S. Murai, N. Sonoda*, J. Organomet. Chem. *140*, 361 (1977).
[16] *Y. Seki, S. Murai, A. Hidaka, N. Sonoda*, Angew. Chem. *89*, 919 (1977); Angew. Chem. Int. Ed. Engl. *16*, 881 (1977).
[17] *Y. Colleuille*, Holl. Pat.-Appl. 6513584 (1966); Chem. Abstr. *65*, 8959 (1966); DBP 1248050 (1967); US-Pat. 3450737 (1969).
[18] *A. J. Chalk, J. F. Harrod*, Adv. Organomet. Chem. *6*, 119 (1968).
[19] *E. R. Tucci*, Ind. Eng. Chem. Prod. Res. Dev. *9*, 516 (1970).
[20] The hydrosilylation of olefins using $Ru_3(CO)_{12}$ is in progress.
[21] *Y. L. Baay, A. G. MacDiarmid*, Inorg. Chem. *8*, 986 (1969).
[22] a) *A. R. Bassindale, A. G. Brook, J. Harris*, J. Organomet. Chem. *90*, C6 (1975); b) *A. G. Brook*, Account Chem. Res. *7*, 77 (1974).
[23] Details will be published later.

[24] A control experiment, in which *n*-heptanal did not give the enol silyl ethers *(6)* but afforded n-$C_7H_{15}OSiEt_2Me$ under the standard reaction conditions, led us to suggest that an aldehyde might not be an intermediate [14]. Later, we found that this conversion into the alkoxysilane was complete before the temperature of the reaction vessel reached at 140 °C. When *n*-heptanal was injected under pressure at 140 °C, the enol silyl ethers *(6)* were found among the products [11].

[25] The silyl group migration to give the metal-carbene complex finds its topological analog in the known rearrangement of α-silyl ketones to enol silyl ethers [22b]. Hydrogen migration to a carbene ligand similar to that in eq. (k) has been suggested in some reactions [26].

[26] a) *K. J. Ivin, J. J. Rooney, C. D. Stewart, M. L. H. Green, R. Mahtab,* J. Chem. Soc. Chem. Commun. *1978,* 604; b) *R. B. Calvert, J. R. Shapley,* J. Am. Chem. Soc. *99,* 5225 (1977).

[27] *H. G. Ang, P. T. Lau,* Organomet. Chem. Rev. *A 8,* 235 (1972); *C. S. Cundy, R. M. Kingston, M. F. Lappert,* Adv. Organomet. Chem. *11,* 253 (1973).

[28] *D. L. Morrison, A. P. Hagen,* Inorg. Synth. *13,* 65 (1972).

[29] *L. H. Sommer, J. E. Lyons, H. Fujimoto,* J. Am. Chem. Soc. *91,* 7051 (1969).

[30] *A. J. Chalk,* Chem. Commun. *1970,* 847.

[31] *B. J. Alylett, J. M. Campbell,* J. Chem. Soc. *A 1969,* 1910; *J. M. Burlitsh,* J. Am. Chem. Soc. *91,* 4562 (1969); *J. F. Bald, Jr., A. G. MacDiarmid,* J. Organomet. Chem. *22,* C22 (1970); *H. Schäfer, A. G. MacDiarmid,* Inorg. Chem. *15,* 848 (1976).

[32] *E. Colomer, R. J. P. Corriu,* J. Chem. Soc. Chem. Commun. *1976,* 176.

[33] *E. Colomer, R. J. P. Corriu, J. C. Young,* J. Chem. Soc. Chem. Commun. *1977,* 73.

[34] *H. Sakurai, K. Miyoshi, Y. Nakadaira,* Tetrahedron Lett. *1977,* 2671.

[35] *Y. Seki, S. Murai, I. Yamamoto, N. Sonoda,* Angew. Chem. *89,* 818 (1977); Angew. Chem. Int. Ed. Engl. *16,* 789 (1977).

[36] *W. M. Ingle, G. Preti, A. G. MacDiarmid,* J. Chem. Soc. Chem. Commun. *1973,* 497; *B. K. Nicholson, B. H. Robinson, J. Simpson,* J. Organomet. Chem. *66,* C3 (1974); *B. K. Nicholson, J. Simpson, ibid. 155,* 237 (1978).

[37] *E. W. Colvin,* J. Chem. Soc. Rev. *1977,* 15.

[38] *W. Reppe, H. Kroper, H. J. Pistor, O. Weissbarth,* Justus Liebigs Ann. Chem. *587,* 87 (1953).

[39] *S. Murai, T. Kato, N. Sonoda, Y. Seki, K. Kawamoto,* Angew. Chem. *91,* 421 (1979); Angew. Chem. Int. Ed. Engl. *18,* 393 (1979).

[40] *L. Marko,* Proc. Chem. Soc. *1962,* 67; *L. Marko, P. Szabo,* Chem. Technol. (Berlin) *13,* 482 (1961); Chem. Abstr. *56,* 7102 (1962); *M. Polievka, E. J. Mistrik,* Chem. Zvesti *26,* 149 (1972); Chem. Abstr. *77,* 113388 (1972). See [12b], pp. 12 and 84, and also [48a].

[41] *J. A. Gladyz, J. C. Selover, C. E. Strouse,* J. Am. Chem. Soc. *100,* 6766 (1978); see also [48b].

[42] *T. Yukawa, H. Wakamatsu,* Brit. Pat. 1408857 (1974); *S. K. Bhattacharyya, S. K. Palit, A. D. Das,* Ind. Eng. Chem. Prod. Res. Dev. 9, 92 (1970).

[43] *Y. Seki, S. Murai, N. Sonoda,* Angew. Chem. *90,* 139 (1978); Angew. Chem. Int. Ed. Engl. *17,* 119 (1978).

[44] The possibility of "co-oligomerization" of $HSiR_3$ and CO as an entry to persilylated sugar derivatives was suggested by Prof. *A. Nakamura* at the Summer Organometallic Chemistry Seminor, Yunoyama, Japan, June 1978.

[45] For reviews see: *F. Hudrlik,* J. Organomet. Chem. Library *1,* 127 (1976); *S. S. Washburne,* J. Organomet. Chem. *83,* 155 (1974); c) *E. Cooper,* Chem. Ind. (London) *1978,* 794.

[46] *S. Murai, Y. Kuroki, T. Aya, N. Sonoda, S. Tsutsumi,* J. Chem. Soc. Chem. Commun. *1972,* 741; *S. Murai, Y. Kuroki, K. Hasegawa, S. Tsutsumi, ibid. 1972,* 946. For the latest paper of this series: *I. Ryu, S. Murai, Y. Hatayama, N. Sonoda,* Tetrahedron Lett. *1978,* 3455.

[47] *J. K. Rasmussen,* Synthesis *1977,* 91.

[48] *Note added in proof:* a) The reaction of HCHO with $HCo(CO)_4$ is reported to give $HOCH_2CHO$; *J. A. Roth, M. Orchin,* J. Organement. Chem. *172,* C 27 (1979). b) An α-siloxyalkylmanganese complex was obtained by reaction of C_6H_6CHO with $(CH_3)_3SiMn(CO)_5$; *D. L. Johnson, J. A. Gladyze,* submitted for publication.

Neurophysins: Molecular and Cellular Aspects[**]

By Roger Acher[*]

Neurophysins are linear cystine-rich proteins containing 93—95 amino acid residues which like the neurohypophysial hormones oxytocin and vasopressin are formed in the hypothalamus and travel from there to the hypophysial posterior lobe. A species usually contains two (or three) neurophysins which differ only slightly in chain length and/or sequence. Many observations suggest that both oxytocin and one of the neurophysins as well as vasopressin and the other neurophysin have a common precursor whose long chain is split into neurophysin and hormone. It can be shown on rats having considerable diabetes insipidus that a single gene controls the biosynthesis of the vasopressin and one of the neurophysins.

1. Neurosecretion and Neurohormones: First Investigations

The history of the neurophysins cannot be dissociated from that of neuroendocrinology. In fact, the early efforts of biochemists to purify the "posterior lobe hormones" of the pituitary, the activities of which have been known since the beginning of this century, were paralleled by cytologists' studies aimed at identifying the cells synthesizing these substances and at elucidating the secretory mechanism involved.

It was *Ernst Scharrer*[1] who in 1928, on the basis of his observations in certain hypothalamic neurons of a teleost fish, *Phoxinus laevis* (Fig. 1), for the first time clearly proposed the concept of neurosecretion. At the time, this idea was indeed revolutionary, nerve cells being considered as highly specialized for the conduction of nervous impulses and totally different from regular gland cells. For a long time thereafter, the posterior pituitary was interpreted as an autonomic endo-

[*] Prof. Dr. R. Acher
Laboratoire de Chimie Biologique
Université de Paris VI
96 Boulevard Raspail, F-75006 Paris (France)

[**] This review is dedicated to the memory of Ernst Scharrer, who some fifty years ago discovered neurosecretion.

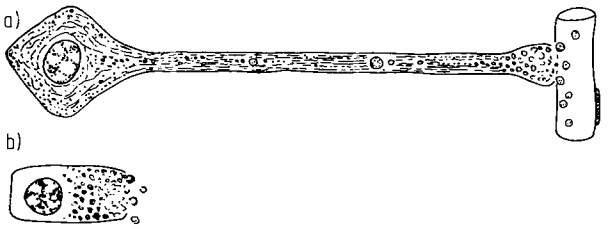


Fig. 1. The neurosecretory cell (a) can be considered as either a nerve cell with the characteristics of a gland cell (b), or a gland cell having acquired the characteristics of a nerve cell. In fact, it is a neuron which has very early undergone a second differentiation. The secretory granules have to be transported along a particularly long pathway from the site of their synthesis (perikaryon) to the site of their release (after [12]).

crine gland, and the synthesis of its hormones was attributed to special glial cells, the pituicytes, present in this lobe[2].

Only after the introduction by *Bargmann*[3] of the chrome hematoxylin phloxin method—originally intended by *Gomori*[4] for the demonstration of the β cells of the islets of Langerhans—was it possible to demonstrate the presence of secretory granules throughout the entire neurosecretory neuron. In 1951, *Bargmann* and *Scharrer*[5] definitely established that the perikarya of the supraoptic and paraventricular nuclei of the hypothalamus of higher vertebrates (corresponding to the preoptic nuclei of fishes and amphibians) synthesize a substance, called neurosecretory material, which is transported by axoplasmic flow to the posterior lobe where it

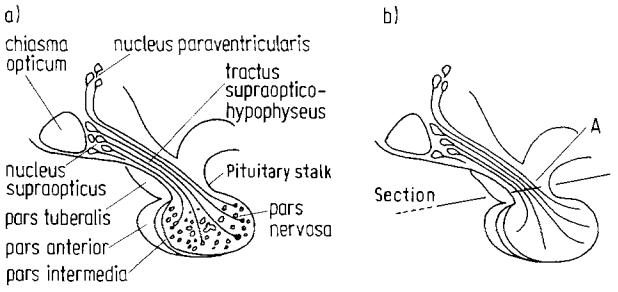


Fig. 2. Effects of severance of the pituitary stalk in the dog. Diagram of hypothalamo-hypophysial system, (a) of normal dog, and (b) of operated dog. The neurosecretory material originating in the supraoptic and paraventricular nuclei "migrates" along the axons and accumulates in the posterior lobe. After stalk sectioning neurosecretory material accumulates at the proximal stump of the axons (in A) (after [12]).

is stored and eventually released (Fig. 2). Thus the concept of a hypothalamic-neurohypophysial secretory system became established, involving a long intracellular route of transport in the course of which the possibility of modification of the initial product cannot be excluded. The fact that the presence of active principles demonstrated in various experiments generally coincided with that of the substance stainable by the Gomori technique led to the conclusion that the neurosecretory material represents either a substance associated with these hormones or the hormones themselves.

In the area of chemical characterization, the first papers by *Abel et al.*[6] between 1920 and 1930, suggested that the oxytocic, pressor and antidiuretic activities of the posterior pituitary belong to a single hormone. Later, two contradictory concepts were defended by different laboratories: the ones maintaining to have isolated a substance of high molecular weight possessing oxytocic as well as pressor activities, the others having succeeded in obtaining substances with either the one or the other activity possessing a very low molecular weight, of the order of 1000. The investigations of *Rosenfeld*[7], based on ultracentrifugation, suggested that the activities are due to one or two proteins with a molecular weight of the order of 20000 to 30000, but that substances of low molecular weight appear after treatment of the extracts with hot 0.25% acetic acid. In 1942, *Van Dyke et al.*[8] extracted frozen glands at low temperature and, after fractional precipitation with sodium chloride, obtained a protein considered to be pure and endowed with oxytocic, galactogogic, pressor and antidiuretic activities in ratios corresponding to those in the posterior lobe. *Van Dyke*[8] dismissed the possibility of the absorption of small active molecules by an inert protein on the basis of several experiments the two principal ones of which were as follows:

Free-boundary electrophoresis does not dissociate the activities from the protein, the unfolding of the protein as a film 8 Å thick leads to inactivation, whereas if the activities belonged to separate peptides, they would have to be always present, be it in the surrounding fluid or associated with the denatured protein. The liberation of active peptides would require cleavages which in the case of extracts are artificial, but which could be physiological at the time of secretion. Nevertheless, *Kamm*[9], followed by *Du Vigneaud*[10], *Fromageot*[11] and their collaborators, in 1953, isolated from acetone-treated glands ("acetone powder") by extraction with hot 0.25% acetic acid two fractions, one with oxytocic and galactogogic, the other with pressor and antidiuretic activities. This then presented the problem of determining the natural form of the hormones, protein or peptides, and of clarifying the relationships between the different active principles.

Moreover, the intracellular localization of the hormones and the endocrine significance of the substance stainable with the Gomori technique remained to be established. The Gomori reaction with chrome hematoxylin is not specific for a given chemical substance, but rather constitutes a staining process; not only can certain other neurosecretory systems, *i.e.* those of invertebrates[12], be demonstrated by this method, but also different endocrine cell types, *e.g.* the β cells of the islets of Langerhans. Thus the chemical nature of the stainable substance cannot be determined in this way. Despite the fact that *Hild* and *Zetler*[13] suggested that one is dealing with a phosphatide soluble in organic solvents and not with hormonal proteins or peptides, the histochemical studies of *Sloper et al.*[14] showed that the "Gomori-positive" granules stain equally well with performic acid/alcian blue, which are specific for cystine and cysteine, and that consequently the material has to be either a protein or a peptide rich in these amino acids. This applies specifically to the neurohypophysial peptide hormones or to the proteins with which they are associated, *i.e.* the neurophysins. It was, therefore, particularly interesting to find that the neurophysins, be they alone or in association with the hormones, stain with the Gomori method[15].

Since the first review on the neurophysins by *Acher* and *Fromageot*[11] several monographs on this subject have been published (see *e.g.* [16, 17]). Furthermore, the proceedings of a symposium on "Neurophysins: carriers of peptide hormones" has appeared as a separate volume[18].

2. The Reversible Neurophysin-Neurohypophysial Hormone Complex

Without denying the existence of small peptides endowed with hormonal activity, the followers of the unitary theory considered them as degradation products formed in the course of purification of the active protein. In fact, the posterior lobe extracts obtained at cold temperature appeared to be devoid of these small molecules. Besides, the possibility of non-covalent binding between a protein and peptides, at the time visualized as purely fortuitous, seemed hardly plausible, since the different protein preparations possessed specific reproducible activities and in ratios corresponding to the glandular content.

Since the active protein could play the role of a common precursor for oxytocin and vasopressin, it seemed to us important to elucidate the mechanism of formation of the peptides from a macromolecule[19,20]. The material obtained, under the conditions of *Van Dyke,* from fresh or acetone dried glands had all the characteristics described, namely: oxytocic and pressor activities of 18 U/mg, a sedimentation constant of 2.6—2.8 S, and a diffusion constant of 8.5×10^{-7} cm^2 s^{-1}, from which it could be concluded that the molecular weight was close to 30000. Based on this value, the estimated activities appeared in the neighborhood of 500 U per μmol, *i.e.* about equal to those of 1 μmol of oxytocin and 1 μmol of vasopressin. It was tempting to assume a stoichiometric relationship between the putative precursor and the active peptides. What then became a primary task was the rigorous verification of the homogeneity of the active protein. In the electrophoresis experiments of *Van Dyke*[8] the protein activities were not separated; this was accomplished by *Irving* and *Du Vigneaud*[21] who used the juice pressed from freshly slaughtered glands that had been immediately frozen and then ground up in the cold in the laboratory. This suggests that, under conditions of apparently weak proteolysis, the pressor principle migrates more quickly towards the cathode than the oxytocic principle.

We first carried out the free-boundary electrophoresis of the Van Dyke protein at low temperature (so as to minimize hydrolysis), and quantitatively determined the activities and the nitrogen content in the three parts of the U-shaped cell. Under conditions where the yields of the active principles and of nitrogen were of the order of 90—95% at the end of the experiment, the pressor activity per mg nitrogen was 5 times higher on the cathode side than on the anode side. The electrophoretic dissociation thus accomplished was then further exploited by subjecting the material to electrodialysis which separated proteins from small peptides. On using an electrodialyzer with three compartments separated by cellophane membranes and a current of only 12—15 mA (so as to avoid heating), it was possible to collect, from the active protein placed in the central compartment, practically all of the oxytocic and pressor activities in the cathode compartment. 90% of the nitrogen was recovered from the original, *i.e.* central compartment, the protein having remained there[19,20]. The only constituents identified in the cathode compartment were oxytocin and vasopressin, thus indicating that the entire activities of the protein complex were due to these peptides associated with the protein by non-covalent bonds. The quantitative dissociation of the active protein into three components was obtained likewise, either by counter-current distribution (Fig. 3) or by treatment with 5% trichloracetic acid,

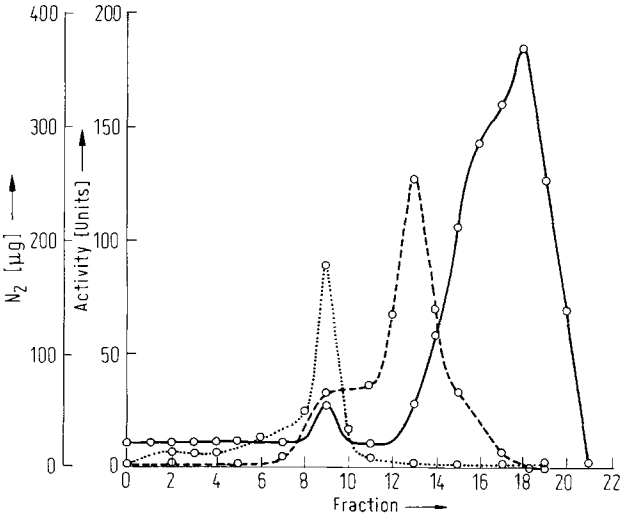


Fig. 3. Separation of the components of the neurophysin-neurohypophysial hormone complex by counter-current distribution in the system *sec*-butanol/0.5% trichloroacetic acid. ···· vasopressin activity, ---- oxytocin activity, —— nitrogen.

which precipitates the protein but leaves the peptides in the supernatant fluid (Fig. 4). This latter method opened the way to the simultaneous purification of the two hormones: the

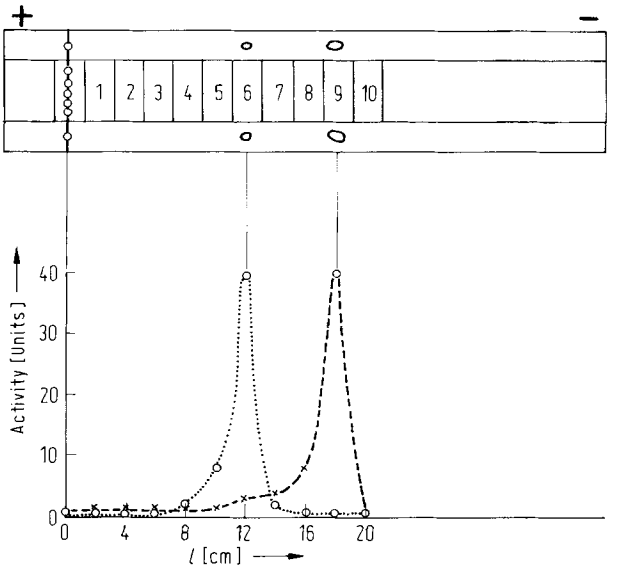


Fig. 4. Identification by paper electrophoresis of oxytocin and arginine vasopressin in the cathodic material obtained after electrodialysis of the supernate resulting from the dissociation of the "active" complex by 5% trichloroacetic acid. Above: electrophoresis strips developed with Bromophenol blue, numbered according to fraction. Below: activity test; ···· oxytocin activity, ---- vasopressin activity. *l* = migration towards cathode (after [20]).

protein-peptide complex was first separated from the extract by fractionated precipitation; after dissociation of the complex with trichloracetic acid, oxytocin and vasopressin were isolated by chromatography on an ion-exchange column[22] (Fig. 5).

We have proposed the term *neurophysin* for the protein which seems to be specifically associated with the hor-

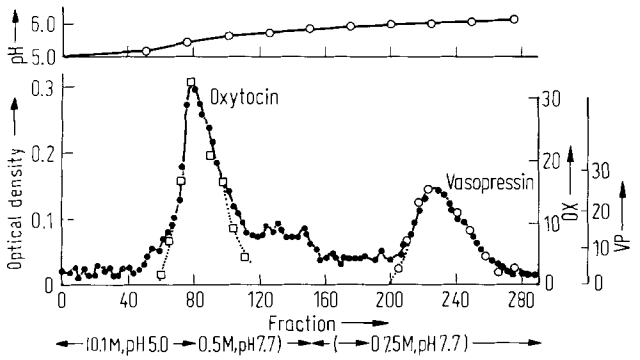


Fig. 5. Simultaneous isolation of oxytocin and arginine vasopressin by gradient chromatography, on Amberlite CG-50, of the supernatant material resulting from the dissociation of bovine "active" complex by 5% trichloroacetic acid. Right-hand ordinate: oxytocin (OX-) and vasopressin (VP-) activity [units] (after [22]).

mone[19]. This specificity was confirmed by the reconstitution of the complex from its components, neurophysin, oxytocin and vasopressin, at the same ratio as that observed in the initial complex[23]. Furthermore, "hybrid" complexes were obtained with the neurophysin from one species and the hormones from another; mammalian neurophysins were thus used as selective adsorbents in the purification of active principles of lower vertebrates[24].

Neurophysin-hormone complexes were prepared from the glands of various mammalian species and it seems that this type of association is general among vertebrates. In the case of the whiting-pout[25], the precipitation of the complex required a higher sodium chloride concentration than in mammals. This might suggest a different constitution of the neurophysins of lower vertebrates or a degradation. In general, the yield in these species was increased by the addition of bovine neurophysin to the extracts.

3. Characterization of Neurophysins

3.1. Purification of Neurophysins

In spite of the fact that a certain heterogeneity of the neurophysin became apparent in the course of the counter-current distribution (Fig. 3) and paper electrophoresis experiments at alkaline pH, the protein separated from the complex seemed to correspond to a single molecular species in the course of ultracentrifugation. However, during starch-gel electrophoresis at pH 8.1, *Hope*[16] observed that the neurophysin isolated under our conditions contained several constituents. He attributed a part of these to proteolytic degradation occurring during the extraction at pH 4.0, and recommended acid extraction by means of 0.1 N hydrochloric acid in order to denature the proteolytic enzymes irreversibly. However, under these conditions, some contaminating proteins of higher molecular weight are extracted together with the complex and must be eliminated by a supplementary step of molecular sieving. *Hope*[16] recognized the presence of two major components and one minor component in the neurophysins of beef and pig and proposed for them the names Neurophysin I, II, *etc.*, in the order of their decreasing mobility toward the anode. This nomenclature, thus far accepted, can however suggest erroneous homologies between one species and another, since the number and mobility of the components vary in each species and since it is difficult to distinguish the authentic molecular species from degradation products. Thus one observed several neurophysins in the sheep although only one major protein can be detected[26, 26a, 27, 27a]. Polymorphism has been noted in several mammals, including man[28] and rat[29]; however, it is important to note that in the guinea pig, *Sachs et al.*[30] demonstrated only a single neurophysin.

In the meantime at least two sequentially different neurophysins have also been found in guinea pig[42a].

The purification of neurophysins is primarily accomplished by following two kinds of procedures which differ essentially in the first steps. In general, the initial material is an acetone powder of posterior lobes, but it can consist of fresh or frozen glands. An essential factor seems to be the speed with which the glands are removed after death. In the first process[20, 27], the powder is extracted at 4 °C with 0.01 N sulfuric acid, the pH being about 4. Under these conditions, the major part of the extracted material consists of the neurophysin-neurohypophysial hormone complex, which is then purified by fractionated precipitation with sodium chloride at pH 3.9 (Table 1).

After removal of the salts, the complex is dissociated into the proteins and peptide hormones by gel filtration on Sephadex G-25 with 0.2 M acetic acid. The proteins consist essentially of neurophysins, which are then separated by chromatography on a basic ion-exchanger, diethylaminoethyl-Sephadex A-50, using a gradient ionic strength (0.2—1 M pyridine acetate buffers) (Fig. 6). Under these conditions two well

Table 1. Neurophysin-neurohypophysial hormones complexes from mammalian species. OX = oxytocin, VP = vasopressin. The amount by weight of the complex is referred to the powder.

Species	Posterior pituitary powder Activities [U/mg] OX	VP	VP/OX	Complex Activities [U/mg] OX	VP	VP/OX	Weight [g/100 g]	Yield in activities [%]	
Ox	1.0	1.1	1.1	18—20	18—20	1.0	1.5	27	30
Calf (new born)	0.4	1.0	2.5	9	21	2.3	3.0	61	67
Sheep	0.8	0.8	1.0	18	18	1.0	4.2	92	90
Pig	1.4	1.4	1.0	18	18	1.0	1.5	19	19
Horse	0.9	0.8	0.9	20	10	0.5	0.8	18	10
Whale	0.5	2.5	5.0	5	20	4.0	6.0	47	57
Rat	1.2	1.4	1.2						
Rabbit	0.9	1.7	1.9						

separated fractions are obtained: Fraction A in the case of beef, sheep, and pig contains a neurophysin which, according to the nature of the amino acids in positions 2, 3, 6 and 7, we call MSEL-neurophysin (cf. Table 2). This material, depending on the conditions of preparation of the acetone powder, may contain derivatives truncated by several residues at the N- and C-terminus. Fraction B usually contains a second type of neurophysin (VLDV-neurophysin), as well as degradation products that have not yet been clearly identified.

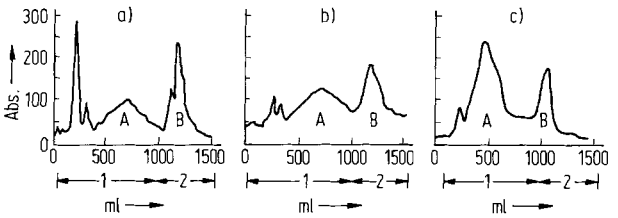


Fig. 6. Isolation of a) bovine, b) equine and c) ovine MSEL-neurophysins by gradient chromatography on DEAE-Sephadex A-50. Ordinate: absorption at 700 nm (Folin). A, B see text. 1: 0.2 M→0.4 M; 2: 0.4 M→1.0 M. pH = 5.9 (after [27]).

In the second procedure used by *Hope et al.*[16], *Breslow*[17] and *Watkins*[26], the extraction of the acetone powder is carried out with 0.1 N HCl at a pH of about 2.0. Neutralization to pH 7.0 leads to formation of a precipitate which can be separated by centrifugation. Readjustment of the pH to 3.9 and precipitation with sodium chloride furnishes a material containing the complex together with contaminating proteins of higher molecular weight. The peptide fraction of the extract is separated off by gel filtration on Sephadex G-25 in 0.1 M formic acid; the protein fraction is then passed through a gel of Sephadex G-75 once again so as to remove the proteins of higher molecular weight. The "neurophysin" fraction is then chromatographed on the basic ion-exchanger diethylaminoethyl-Sephadex A-50 at a constant pH of 8.1 (Tris-HCl) with increasing sodium chloride gradient. Two or three fractions are thus separated, from which at least three components possessing different electrophoretic mobilities can be isolated by repeated chromatography. Nevertheless, so far only two distinct neurophysins have been identified beyond doubt by means of sequential analysis of proteins from beef, pig and sheep glands. Other purification procedures, including selective extraction, isoelectric focusing or affinity chromatography on "immobilized" hormones, have been tried occasionally, but have thus far not been used extensively.

3.2. Amino Acid Sequence of the Neurophysins

The molecular weight of the neurophysins is still under discussion. By ultracentrifugation at pH 4.8, *Hope et al.* obtained values of 19000 and 21000, respectively, for bovine neurophysins I and II[16]. On assuming a molecular weight of 25000—30000 for the complex one could roughly calculate that one molecule of neurophysin is associated with one molecule of oxytocin and one molecule of arginine vasopressin. If the molecular weight is measured by molecular sieving on Sephadex G-75 at pH 7.0, values of the order of 15000—20000 are obtained, both for the complex as well as the "crude" or purified neurophysins[26,31,32]. In contrast, the molecular weight determinations by electrophoresis on polyacrylamide gel in the presence of sodium dodecyl sulfate give lower values of the order of 12500 for the neurophysins[32]. Finally, sequential analysis of the peptides furnished by trypsin hydrolysis of the oxidized neurophysins has revealed that the molecular weight of the monomer lies around 10000. A "dimerization" might therefore easily occur at pH 4 to 8, yielding associations stable in the course of molecular sieving or of ultracentrifugation.

Another interpretation might be that the molecular weights evaluated by ultracentrifugation or by gel filtration are too high owing to the unusual conformation of the molecule[44a].

Table 2. Amino acid sequence of the MSEL neurophysins of sheep [34, 34a], ox [34, 34a], pig [37, 37a, b], horse [37c] and whale [37d].

	1	5	10
Sheep	Ala-Met-Ser-	Asp-Leu-Glu-Leu-Arg-Gln-Cys-Leu-Pro-	
Ox			
Pig			
Horse			
Whale			

	15	20	21	25
Sheep	Cys-Gly-Pro-Gly-Gly-Lys-	Gly-Arg-	Cys-Phe-Gly-Pro-Ser-Ile-	Cys-
Ox				
Pig				
Horse				
Whale				

	30	35	36	40	41
Sheep	Cys-Gly-Asp-Glu-Leu-Gly-	Cys-Phe-	Val-Gly-Thr-Ala-	Glu-Ala-	Leu-
Ox					
Pig					
Horse					
Whale			- Met -		

	45	48	50	55
Sheep	Arg-Cys-Gln-Glu-Glu-	Ile-	Tyr-Leu-Pro-Ser-Pro-Cys-Gln-Ser-Gly-	
Ox		- Asn -		
Pig		- Asn -		
Horse		- Asn -		
Whale		- Asn -		

	60	61	65	70
Sheep	Gln-Lys-Pro-	Cys-Gly-Ser-	Gly-Gly-Arg-Cys-Ala-Ala-Ala-Gly-	Ile-
Ox				
Pig				
Horse				
Whale				

	75	80	81	85
Sheep	Cys-Cys-Asn-Asp-Glu-Ser-	Cys-Val-	Thr-Glu-Pro-Glu-Cys-Arg-Glu-	
Ox				
Pig				
Horse				
Whale				

	89	90	91	92	95
Sheep	Gly-Ile-	Gly-	Phe-	Pro-Arg-Arg-	Val
Ox		Ile / Val			
Pig	- Ala -	Ser -		Leu -	- Ala
Horse	- Ala -			Leu -	- Ala
Whale	- Ala -	Ser -			- Ala

The neurophysins isolated thus far are acid proteins having isoelectric points between 4 and 5. They are distinguished from other proteins by a very high content of cystine (seven disulfide bridges for a chain of 93—95 residues) and proline (seven to eight residues) and by a very low content of aromatic amino acids: they do not contain tryptophan, and have only one tyrosine residue, and two to four phenylalanine residues per molecule. This explains the atypical absorption spectrum in the ultraviolet with a 260/280 nm absorbance ratio greater than unity.

According to *Hope et al.*[16] the three neurophysins demonstrable in beef and pig glands all possess an N-terminal alanine. A comparable result was then obtained for the three components of sheep[26]. On the other hand, in the case of the beef neurophysins, amino acid analyses have shown that neurophysin I contains histidine but no methionine, whereas neurophysins II and C contain methionine but no histidine[16]. In the pig, none of the three neurophysins contains histidine and only two of them contain methionine. The presence or absence of methionine often serves for the distinction of the different neurophysins in a given species.

The actual data concerning complete amino acid sequences of neurophysins are so far limited to those of beef, sheep, pig, horse and whale. N-terminal sequences are known for the neurophysins of rat, dog, cod and man. It seems that every species possesses at least two neurophysins which differ essentially from each other by the N- and C-terminal sequences. Consequently, it has been proposed to distinguish between two families, the MSEL-neurophysins and the VLDV-neurophysins, according to the residues in positions 2, 3, 6 and 7[33]. All neurophysins are single-chained polypeptides of 93—95 amino acids.

The MSEL-neurophysins are actually the best known. The complete amino acid sequences that have so far been determined are collected in Table 2. The amino acid sequence proposed by *Walter et al.*[35,36] for beef MSEL-neurophysin would appear by way of analogy[38] to be less likely than the sequence in Table 2. The amino acid sequence suggested by *Chauvet et al.*[34] for beef MSEL-neurophysin has been confirmed by *Wuu* and *Crumm*[34b].

The MSEL-neurophysins characterized up to now (ox, sheep, pig, horse and whale) consist of a single polypeptide chain of 95 residues. A large N-terminal part (residues 1—88) is nearly invariant since substitutions occur only once in position 36 (valine in all, except methionine in whale) and position 48 (asparagine in all, except isoleucine in sheep). In contrast, for the C-terminal part of the chain, variations can be observed in positions 89, 90, 91, 92 and 95. In the ox, a microheterogeneity is found in position 89, since two forms of MSEL-neurophysins are found, one with isoleucine, the other with valine.

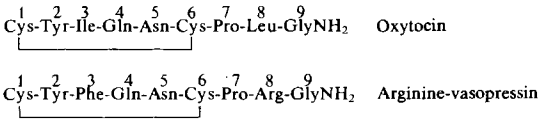
Except for position 90 in which glycine or serine is found, the "mutable" positions of the C-terminal sequence are occupied by hydrophobic residues. Curiously, positions 89 and 95 seem related since both are occupied either by alanine (pig, horse, whale) or by isoleucine or valine (ox and sheep).

The five species examined belong to three orders of eutherian mammals: Artiodactyla (ox, sheep, pig), Perissodactyla (horse) and Cetacea (whale). These orders diverged about 70—80 million years ago. If the sheep is taken as reference, the percentage of substitutions between two different orders is 4—5%. The "drift" of MSEL-neurophysin in the course of evolution is small when compared with those of hemoglobin chains (12—20%). On the other hand, the close resemblance between ox and sheep MSEL-neurophysins is reminiscent of the similarity found for several pituitary polypeptide hormones (Table 3). A "neutral" drift is hard to imagine because both species (which belong to the suborder Ruminantia) diverged perhaps 30 million years ago and the number of substitutions is not proportional to time.

All the MSEL-neurophysins contain 14 cysteine residues per molecule (monomer) which form seven disulfide bonds; a certain mode of bonding has been suggested in the case of the ox protein[39], but since the sequence from which it was deduced is questionable, the definite location of the disulfide bridges still remains unclear.

The VLDV-neurophysins seem less abundant than the MSEL-neurophysins and the proportion of them appears to vary from species to species, so that their characterization is less advanced. The complete amino acid sequence of pig VLDV-neurophysin (neurophysin II) has been indicated[40]. The N-terminal sequences of VLDV-neurophysins from ox (neurophysin I)[41], man (neurophysin I)[42], rat (neurophysin II)[42a] and dog (neurophysin I)[42b] are known. VLDV-neu-

Table 3. Amino acid sequence of the neurohypophysial hormones.

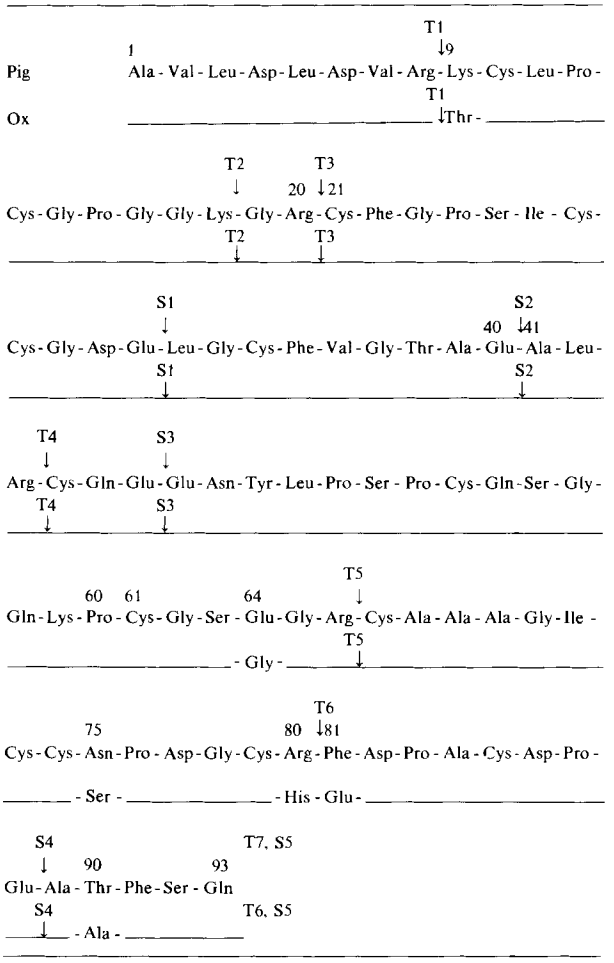


	Oxytocin type 4	8		Vasopressin type 3	8	
Mammals (except pig)	Gln	Leu	Oxytocin	Phe	Arg	Arginine-vasopressin
Pig	Gln	Leu	Oxytocin	Phe	Lys	Lysine-vasopressin
Birds, reptiles, Amphibians, lung fishes	Gln	Ile	Mesotocin	Ile	Arg	Vasotocin
Bony fishes (*paleopterygia* and *neopterygia*)	Ser	Ile	Isotocin	Ile	Arg	Vasotocin
Cartilaginous fishes (rays)	Ser	Gln	Glumitocin	Ile	Arg	Vasotocin (?)
Cartilaginous fishes (sharks)	Gln	Val	Valitocin	Ile	Arg	Vasotocin (?)
	Asn	Leu	Aspargtocin	Ile	Arg	Vasotocin (?)

rophysins contain 93 residues per molecule and 14 cysteine residues, *i. e.* they resemble the MSEL-neurophysins.

The complete amino acid sequences of pig[40a] and ox[40a,41a] VLDV-neurophysins have recently been published (Table 4)[40a]. The sequence for bovine VLDV-neurophysin in Table 4 differs from that published by *Schlesinger et al.*[41a]

Table 4. Amino acid sequence of porcine and bovine VLDV-neurophysin. The arrangement of the tryptic peptides (pig: T1—T7; ox: T1—T6) has been determined with overlapping peptides which were obtained with the protease from Staphylococcus (S1—S5) and by sequencing (N-terminal sequence) (after [40a]).



by the C-terminal residue: glutamine instead of leucine. Table 5 compares the five MSEL-neurophysins and the two VLDV-neurophysins known to date. The homology between the MSEL- and VLDV-neurophysins of the same species is about 80%. The homology within the MSEL-family (five species) ranges from 95 to 99%. The two types of neurophysins have now been recognized also in man[40b]; so the duality exists in all the mammalian species investigated.

The two families of neurophysins have in common a long central sequence of about 65 residues (between positions 10 to 75) and seem to differ mainly in their N-terminal and C-terminal sequences. This fact strongly suggests that the origin of the polymorphism is duplication. On the other hand an internal homology between two parts of the same chain has led to the hypothesis that the chain is formed by partial duplication of a primitive gene coding for 55—60 residues and fusion of the daughter genes[41].

Table 5. Comparison of MSEL and VLDV neurophysins. Upper series: Sequence of the MSEL neurophysins of sheep, ox, pig, horse and whale. Lower series: Sequence of the VLDV neurophysins of pig and ox. Interchanged amino acids within the two groups are given (after [40a]).

	1	2	3		5	6	7		9	10																
MSEL	Ala	-	Met	-	Ser	-	Asp	-	Leu	-	Glu	-	Leu	-	Arg	-	Gln	-	Cys	-	Leu	-	Pro	-	Cys	-
VLDV	—	-	Val	-	Leu	-	—	-	—	-	Asp	-	Val	-	—	-	Lys / Thr	-	—							

15						20	21						25													
Gly	-	Pro	-	Gly	-	Gly	-	Lys	-	Gly	-	Arg	-	Cys	-	Phe	-	Gly	-	Pro	-	Ser	-	Ile	-	Cys	-	Cys	-

30								35	36							40	41									
Gly	-	Asp	-	Glu	-	Leu	-	Gly	-	Cys	-	Phe	-	Val / Met	-	Gly	-	Thr	-	Ala	-	Glu	-	Ala	-	Leu	-	Arg	-
														- Val -															

45					48		50										55											
Cys	-	Gln	-	Glu	-	Glu	-	Asn / Ile	-	Tyr	-	Leu	-	Pro	-	Ser	-	Pro	-	Cys	-	Gln	-	Ser	-	Gly	-	Gln	-
						- Asn -																							

60	61			64	65										70											
Lys	-	Pro	-	Cys	-	Gly	-	Ser	-	Gly / Glu	-	Gly	-	Arg	-	Cys	-	Ala	-	Ala	-	Ala	-	Gly	-	Ile	-	Cys	-
								-		-																			

75								80	81	82						85											
Cys	-	Asn	-	Asp	-	Glu	-	Ser	-	Cys	-	Val	-	Thr	-	Glu	-	Pro	-	Glu	-	Cys	-	Arg	-	Glu	-	Gly	-
—	-	Asn / Ser	-	Pro	-	Asp	-	Gly	-	—	-	Arg / His	-	Phe / Glu	-	Asp	-	—	-	Ala	-	—	-	Asp	-	Pro	-	Glu	-

89	90	91	92	93		95
Ile	Gly	Phe	Pro			Val
Val -	-	-		- Arg -	Arg -	
Ala	Ser	Leu	Leu			Ala
Ala -	Thr / Ala	- Phe	- Ser	- Gln		

3.3. Conformation of the Neurophysins

The three-dimensional structure of the neurophysins has not yet been determined. The CD spectrum of beef MSEL- and VLDV-neurophysins are very similar and suggest a small percentage of α-helix (about 5%) but a very high percentage of β-structure (about 40%)[17,43]. The marked accessibility of the disulfide bonds to reducing agents in the absence of urea[44,44a] suggests a conformation of low compactness. In the absence of urea, routinely used to unfold proteins, the seven disulfide bonds of the molecule are entirely reduced by dithiothreitol, which could be explained if the protein had a naturally extended structure. Its cleavability by enzymes leads to the same conclusion: the protein with its seven disulfide bonds intact is split by trypsin or chymotrypsin in practically the same way as in the unfolded state after reduction and alkylation[44a]. This extended (or easily extendable) conformation can be explained by the great number of proline residues, which for proteins of animal origin is most uncommon.

Molecular weight determinations in the absence of dissociating agents suggest that at pH 3 to 8 two subunits are associated to form a dimer, and even more aggregated forms could exist. It seems probable that the binding of the hor-

mones takes place on the dimer, but the latter's conformation is still unknown.

4. Interactions between Neurophysins and Neurohypophysial Hormones

The relatively small size of the neurophysins and especially of the neurohypophysial hormones, which belong to the smallest biologically active peptides, makes the complex a particularly simple model for the study of protein-protein interactions. Besides, the association is not followed by a chemical modification, as for example in proteolysis, which would complicate the observations. A very large spectrum of synthetic analogues of the hormones (over 300) has been prepared, primarily due to the efforts of *du Vigneaud, Boissonnas* and their co-workers, and it has been possible to determine the residues that intervene in the association. Though complexes of beef neurophysin with arginine vasopressin have been obtained in crystalline form by *Hope et al.*[16], the crystals have thus far not lent themselves for a radiocrystallographic X-ray study, so the three-dimensional structure of the complex has not yet been established. Indirect information is obtainable, however, from equilibrium dialysis studies as well as from variations in ultraviolet absorbance, circular dichroism, and nuclear magnetic resonance following the binding of the hormones to the neurophysins.

4.1. Stoichiometry of the Association

According to the experiments of *Breslow*[17,45] the changes in the CD spectrum reach their maximum when one mole of oxytocin or one mole of lysine vasopressin is combined with one mole of monomeric neurophysin (molecular weight of 10000) (Fig. 7—9). By means of an equilibrium dialysis study at pH 7.4 using labeled oxytocin, lysine vasopressin and beef neurophysin II (MSEL-neurophysin), *Breslow* and *Walter*[46] found that the binding of the two hormones is

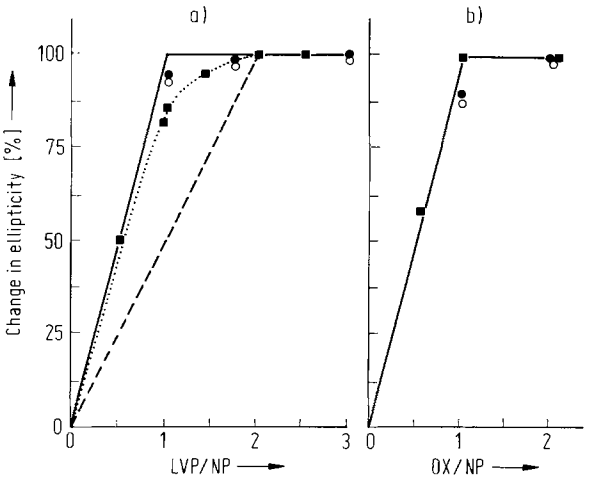


Fig. 7. Alteration of CD spectrum on titration of native or nitrated bovine neurophysin II (MSEL-neurophysin, NP) with a) lysine-vasopressin (LVP) and (b) oxytocin (OX). Results are expressed as the percentage of the total change in ellipticity generated by different hormone/protein ratios, where the total change is defined as the ellipticity of the saturated protein minus the sum of its isolated components. — One high affinity site, ···· one site with $K = 2 \times 10^5$, ---- two equal high affinity sites. • 280 nm, native bovine NP-II; ○ 245 nm, native bovine NP-II; ▪ 350 nm, nitrated bovine NP-II (after [45]).

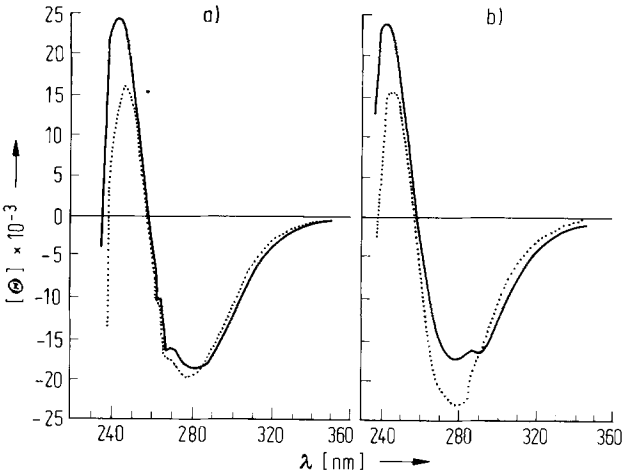


Fig. 8. Near-ultraviolet CD spectra of bovine neurophysin II (MSEL-neurophysin) in the presence of a) 1×10^{-3} M *S*-methyl-Cys-Phe-IleNH$_2$ and b) Met-Tyr-PheNH$_2$. — observed, ···· theoretical. "Theoretical" curves represent calculated spectra for a solution of bovine neurophysin II that is 1×10^{-3} M in the appropriate peptide with neglection of interactions (after [43]).

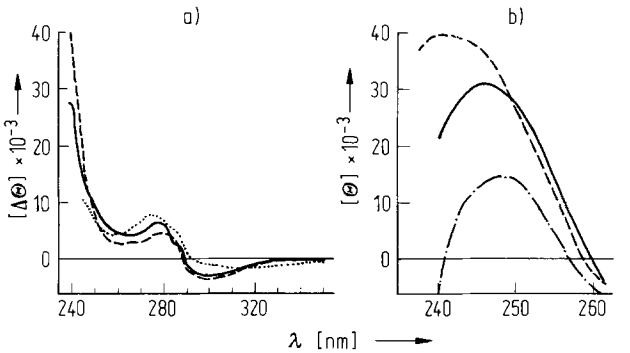


Fig. 9. a) Difference CD spectrum obtained by subtracting the CD spectra of the individual components of the mixture from the spectrum of the protein-peptide complex. Spectra obtained in the presence of oxytocin (—) or of lysine-vasopressin (– – –) represent 100% saturation of protein with hormone. Spectra obtained in the presence of *S*-methyl-Cys-Tyr-PheNH$_2$ (····) represent 90% saturation of the protein. b) Direct circular dichroism spectra of neurophysin II alone (–·–·–) and in the presence of 2 equivalents of oxytocin (—) or lysine-vasopressin (– – –) (after [45]).

competitive, with association constants of 1.2×10^4 M^{-1} for oxytocin and 8×10^3 M^{-1} for lysine vasopressin. Moreover, the authors point out that the affinities for neurophysin I (VLDV-neurophysin) are similar, so that it is not possible to demonstrate the specificity of association of one neurophysin with one given hormone.

On the other hand, the competition and the very similar association constants suggest that the binding sites of the neurophysin for the hormones largely overlap and are perhaps even identical; one direct deduction from this is that the binding sites of the hormones comprise especially the residues which they have in common (seven residues out of nine). The interpretation by *Breslow* and *Walter* does not take into account the fact that, at the pH at which the binding takes place, neurophysin is likely to be present in the form of a dimer, and assumes implicitly that each monomer fixes its ligand in an independent manner. However, the existence of cooperative effects in the binding process has recently been evoked[47,48]. If one assumes a stoichiometric relationship of 1:1 for neurophysin and hormone, one is led to reckon with a separate binding site in each monomer, and to identify the residues that constitute it. The relative instability

of the complexes, shown by the weak association constants, makes it difficult to identify the shielded residues as was possible in the case of the associations of trypsin or chymotrypsin with the pancreatic Kunitz inhibitor[49,50].

4.2. Binding Site of the Hormones

Beef neurophysins bind not only the mammalian neurohypophysial hormones (oxytocin, arginine vasopressin, lysine vasopressin) but also the six active peptides found in the other classes of vertebrates (see Table 3). All these hormones are nonapeptides, in which only the amino acids in positions 3, 4 and 8 vary[24]. The investigations carried out to date have mainly demonstrated the role of the first, second and third amino acid residues of the hormones in the binding to the neurophysins.

Amino Acid Residue No. 1: Acher, Chauvet and *Olivry*[20] had observed that dialysis at pH 2.75 against 0.1 M acetic acid leads to dissociation of the complex, permitting the passage of the hormones from the dialysis sac, whereas the same procedure against water elicits practically no dissociation. This observation suggested the existence of ionic binding between hormones and neurophysins. Since active peptides possess all their carboxy groups in amide form, the only possible group with a charge at the pH of fixation is the α-amino group, which in all cases belongs to a cysteine residue.

The discovery by *du Vigneaud et al.*[51] that this group is not only unnecessary for hormonal activity, but that its suppression even leads to an increase in activity, has naturally led to the examination of the binding of deamino-oxytocin to neurophysin. *Stoufer, Hope* and *du Vigneaud*[52] observed that deamino-oxytocin, in contrast to oxytocin, does not associate itself with beef neurophysins if these are precipitated at pH 3.9 with sodium chloride, nor does it accumulate in the sac containing the neurophysins if these are dialyzed against a solution containing the peptide.

These observations were confirmed by *Breslow* and *Abrash*[53] who have shown that the side chain of the cysteine in position 1 could be lengthened without disturbing the binding since 1-homocysteine oxytocin attaches itself to the protein as well as the oxytocin. Subsequently, *Breslow et al.*[54,55] observed that tripeptide analogues of the N-terminal sequence, which contain *S*-methylcysteine or methionine in position 1, were likewise bound, whereas the replacement by glycine reduces the association constant thirty-fold. The nature of the amino acid in position 1 does not seem to be exactly defined, but the presence of methylene groups in the β- and γ-position, participating in hydrophobic bonds, and certainly that of an α-amino group, implicated in the electrostatic binding, seem necessary.—It must be pointed out that the deamino-hormones are active, but substitution of the first residue causes inactivation.

Amino Acid Residue No. 2: Oxytocin containing the hydrophobic aliphatic isoleucine or glycine residue instead of tyrosine in position 2 is not bound whereas the 2-phenylalanine oxytocin is[53]. The presence of one aromatic amino acid in position 2 thus seems essential and this has been confirmed with the aid of di- and tri-peptides[54,55]. These data would suggest the necessity of precise hydrophobic contacts and perhaps the existence of π-π interactions. Finally, D-tyrosine oxytocin is not bound[53].

Tyrosine-2 is present in all known neurohypophysial hormones and this constancy probably indicates a participation in the association with the protein receptors of the cellular membranes.

Amino Acid Residue No. 3: Residue No. 3 is isoleucine in all known neurohypophysial hormones with the exception of vasopressin in which phenylalanine occupies this position. The oxytocin with glycine in position 3 has an affinity thirty-fold smaller[53]. Likewise, a glycine residue in position 3 of tri- and tetrapeptides reduces the binding affinity[55]. It would seem then that the presence of a hydrophobic aliphatic or aromatic amino acid in position 3 is necessary for binding with neurophysin.

Interestingly, the presence of isoleucine in position 3 seems essential for a marked association of hormones with the uterine receptor, while phenylalanine favors the renal receptor. The antidiuretic specialization of mammalian arginine vasopressin, derived from the arginine vasotocin of the other vertebrates, has come about during evolution precisely by this substitution[24].

Amino Acid Residues Nos. 4—9: Residues 4 to 9 do not appear to be essential for the binding with the neurophysins. The 4-glycine oxytocin binds almost as well as oxytocin[53], and so does the 5-valine oxytocin[46]. Replacement of glycinamide in position 9 by glycine reduces the fixation by 50%[46]. Position 8 is occupied by leucine in oxytocin, and by lysine or arginine in the vasopressins without giving rise to a marked difference in binding power. Finally, the tripeptide *S*-methyl-Cys-Tyr-PheNH_2, an analogue of the sequence of the first three residues of vasopressin, binds with mononitro-neurophysin II of beef with two-thirds of the free energy of oxytocin or lysine vasopressin[45]. Hence, it would seem that fixation to neurophysins implicates essentially the first three residues of the nonapeptides, whereas the activities of the hormones tolerate only very slight variations of sequence, and particularly no "truncation". The zone of interaction between the peptide and the protein is thus extremely limited in comparison with other known models of binary protein-protein association. The weak association constants are in agreement with a relatively small number of contacts, but location of the site of "anchorage" of the peptide is still not possible because of a lack of direct structural data.

4.3. Binding Site of Neurophysins

The identification of certain amino acid residues of hormones associating with neurophysins has led to the search for the protein residues that serve them as binding partners. Thus, a carboxyl group implicated in ionic binding has received particular attention; in addition the single tyrosine (tyrosine-49) present in all neurophysins has been studied in detail.

4.3.1. Aspartic Acid-30, Glutamic Acids-31 and -47

The participation of at least one carboxyl group in the association is shown by the fact that blockage of the acidic residues of the neurophysins furnishes a derivative that no longer binds the hormones[32]. According to the degree of proton displacement accompanying the binding of oxytocin or lysine vasopressin to beef neurophysin II, this binding carbox-

yl group can be assigned a pK value of 4.3[17]. This would indicate binding at a side chain rather than at the free terminal α-carboxy group of the protein (pK = 3—3.5). In fact, there exist variations in length and sequence in the C-terminal region of the chain[34] which make binding at this site unlikely. *Walter* and *Hoffman*[56] announced that they were able to couple the α-amino group of arginine vasopressin with a carboxy group of neurophysin II covalently, with the aid of a water soluble carbodiimide, and to identify the residue involved as Asp-30 or Glu-31. Either one of these could, in the non-covalent complex, be linked by ionic binding with the amino group of the hormone. However, *Breslow*[45] suggested the participation of Glu-47 on the basis of molecular models. In fact, localization of the acidic residue intervening in the electrostatic binding has not yet been definitely established.

4.3.2. Tyrosine-49

All neurophysins analyzed up to now possess a single tyrosine residue in position 49. The ease of detection of this amino acid by ultraviolet spectroscopy, circular dichroism, and nuclear magnetic resonance, has focused attention on Tyr-49 as a residue playing an essential role in the binding of the protein. The first observation supporting this participation was made by *Furth* and *Hope*[57] who transformed the residue to mononitrotyrosine by treatment with tetranitromethane, and showed that the absorption spectrum of the nitrotyrosine changed during the binding of arginine vasopressin in a manner which suggested a lowering of its pK_a value. The lowering of the pK was attributed to the approach of a positively charged group, the guanidine group in arginine-8, or approach of a positively charged group of the protein following a change in the conformation. The authors also suggested that the environment of the nitrotyrosine became more hydrophobic after the association. *Breslow* and *Weis*[43] repeated this experiment using CD measurements and spectrophotometric titration. The results indicated that the arginine vasopressin lowered the pK_a of the nitrotyrosine from 7.45 to 6.85 and produced changes in the ellipticity of the tyrosine. Since these alterations were brought about also by oxytocin or by analogues involving the sequence of the first three residues of the hormones, they could not be due to arginine-8. According to NMR investigations by *Breslow et al.*[58,59] the *ortho* and *meta* protons of Tyr-49 are affected by the association with the tripeptide *S*-methyl-Cys-Phe-IleNH_2, thus confirming that the environment of this residue is modified by the binding. Application of the nuclear Overhauser effect to this system established that the changes in the environment of Tyr-49 on complex formation are attributable to the approach of the peptide residue in position 2[59]. In the case of the above mentioned tripeptide, the intensity of the phenylalanine ring proton resonances decreases after irradiation in the presence of neurophysin II; this is not observed in the absence of neurophysin II. The effect occurs also in the case of hormones with tyrosine in position 2. It would appear that the changes are not due to a stacking, one above the other, of the phenol rings of Tyr-49 of the neurophysin and Tyr-2 of the hormones, but rather to the fact that Tyr-49, masked in the free protein perhaps by a phenylalanine residue, is displaced from this position, either directly by Tyr-2 or by a more general change in conformation[45]. The finding that Tyr-49 can be di-nitrated[45] or acetylated[57] without effect on the binding capacity, does not speak in favor of stacking between Tyr-49 and Tyr-2. In fact, the Tyr-49 of neurophysin would not be in direct contact with the Tyr-2 of the hormone, but in its immediate vicinity. The essential conclusions of *Breslow* and her group have subsequently been confirmed by other investigators[60].

4.4. Conformational Changes during Binding

The fact that the association between hormones and neurophysins favors precipitation by sodium chloride[52] and markedly increases the sedimentation constant[55] can be interpreted either in terms of a modification of the tertiary structure of the protein, or of a displacement of the equilibrium towards dimerization. It is actually difficult to distinguish between the effects of the interaction between hormone and monomer and those of the interaction between two monomers. It is also unclear whether these two interactions are independent of each other. If this were the case, the protein would possess, aside from the binding site for the hormone, a binding site for the second subunit (for the structure of the neurophysins cf. Sections 3.2 and 3.3).

The nature of the contacts and the possible conformational changes resulting from the interaction between hormone and neurophysin are a matter of speculation. Since the side chains of residues 1, 2 and 3 of the hormones are implicated, one can suppose that the disulfide bridge 1—6 and the phenol ring of the invariant tyrosine-2 are affected. *Breslow*[17,43,45,61], attributes the effects measured by analysis of the circular dichroism spectra of free and associated bovine neurophysin II to the following phenomena:

(1) the increase in ellipticity at 195 nm and 240 nm to a disturbance of the disulfide bonds in the course of association,
(2) the increase in ellipticity centered near 280 nm to a disturbance of the tyrosine of the hormone, with perhaps a small contribution by the tyrosine of the protein[43],
(3) the variations in the far-ultraviolet spectrum to changes in the tertiary structure of the protein, or to direct disturbances of different chromophores by the bound peptide.

The shifts of the amino acid residues of the protein, with the exception of the change in orientation of Tyr-49 (see Section 4.3.2), cannot actually be determined.

On the other hand, the possibility should be considered that the decrease in binding affinity between pH 6 and pH 2 may be the consequence of a carboxyl-dependent change in protein conformation[61a]. From measurements of temperature-jump relaxation it has recently been deduced that oxytocin and vasopressin bind with greater affinity to the neurophysin dimer than the monomer and that the binding of oxytocin and vasopressin in neurophysin dimer at pH 7.4 is nearly identical for each hormone[62a].

5. The Possible Common Precursor of Neurophysins and Neurohypophysial Hormones

The stoichiometric association of neurohypophysial hormones and neurophysins may be fortuitous, and the complexes isolated by extraction may be artefacts. Nevertheless, there are a number of arguments indicating that the two

types of substances are already associated in the secretory granules. One must consider the possibility that cleavage of an inactive protein precursor furnishes one neurophysin and one active peptide which remain associated. This happens *e.g.* in the cleavage of ribonuclease into peptide S and truncated protein by subtilisin. However, this hypothesis, which would account for a certain number of cytological and biochemical observations, has not yet been proven (Fig. 10).

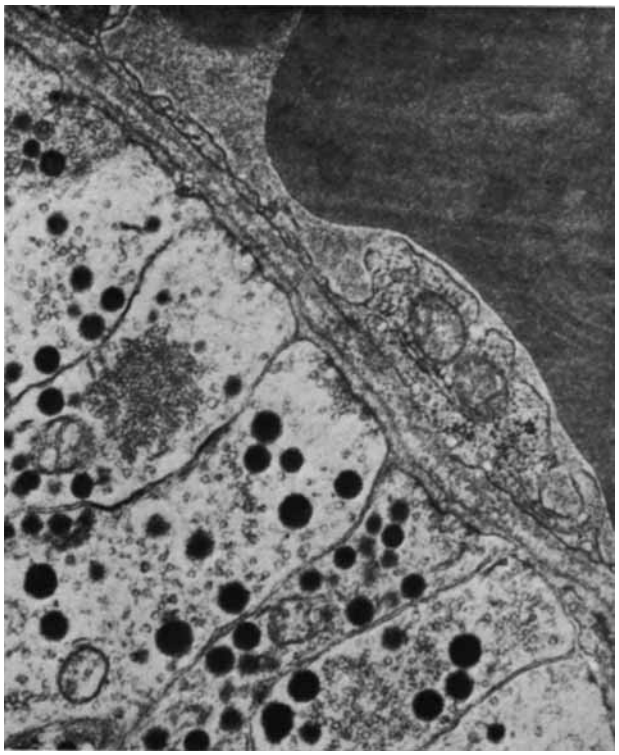


Fig. 10. Neurohypophysial terminals abutting a capillary containing (upper right) a red blood cell. The arrangement is conventional with the terminal regions of the neurons separated from the fenestrated capillary wall by the parenchymal and endothelial basement membranes. Terminals show evidence of secretory activity: paucity of large electron-dense neurosecretory granules and abundance of microvesicles (synaptic vesicles) (after [80]).

In the neurohypophysis of mammals, among which most species have been studied from different points of view, one finds generally two hormones, oxytocin and arginine vasopressin, which very often occur in roughly equal proportions. It is reasonable to assume that the two putative protein precursors would have similar though only slightly different sequences, and consequently, if the neurophysins represent inactive ballast, that they ought to exist in the gland in the same numbers as the hormones and probably in equivalent proportions. In fact, this argument is difficult to substantiate because, on the one hand the actual number of distinct neurophysins can be established only by sequential studies, and on the other hand the proportions can be affected by degradation or selective secretion.

5.1. Biosynthesis of Neurophysins and Hormones

There are a number of data proving that the neurohypophysial hormones and the neurophysins are synthesized in cell bodies located in the hypothalamus. Destruction of the supraoptic and paraventricular nuclei leads to the disappearance of the two types of substances, as determined by their biological activities and cytochemical reactions.

Sachs et al.[62] have studied the biosynthesis of vasopressin. They injected cysteine labeled with ^{35}S into the third ventricle of dogs and removed the hypothalamus 1.5 h later. One half of the tissue, examined right away, contained proteins but practically no vasopressin. The other half, after incubation for 4.5 h in a medium containing puromycin (which blocks the synthesis) and unlabeled cystein, yielded a significant amount of labeled vasopressin. These experiments suggest the biosynthesis of an inactive macromolecular precursor which is subsequently split to yield active vasopressin. *Sachs* assumed that the precursor is formed on the ribosomes of the perikarya of the hypothalamic nuclei and that the "maturation" (cleavage) takes place in the secretory granules during their axonal transport to the neurohypophysis. On the other hand, *Sachs et al.*[63] demonstrated on the dog hypothalamus, after infusion of labeled cysteine, the presence of a labeled neurophysin whose molecular weight (determined by molecular sieving), electrophoretic mobility (on cellulose acetate) and immunological characteristics were very similar to those of bovine neurophysins.

During subcellular fractionation, the labeled protein followed the vasopressin; in the case of animals kept alive for 10—21 days with free access to water, the protein could be recovered from the posterior lobe. Incubation of the latter *in vitro* with a high content of K^+ led to simultaneous secretion of vasopressin and labeled protein. *In vivo*, simultaneous se-

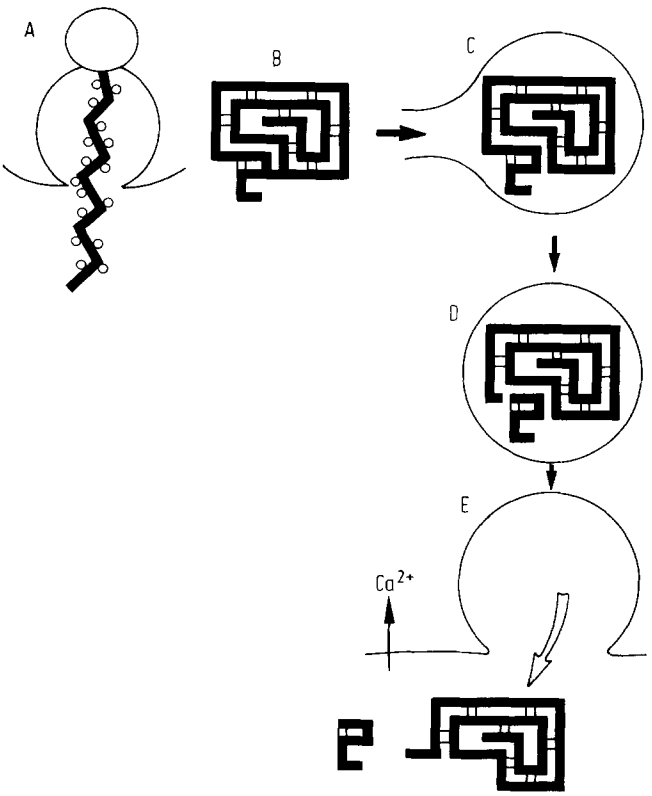


Fig. 11. A model for the biosynthesis, transport, and release of posterior pituitary hormones and neurophysins. A: synthesis of precursor in rough endoplasmic reticulum; B: folding of precursor; C: formation of neurosecretory granules in the Golgi apparatus; D: axonal transport (2—3 mm/h); hormone bound to neurophysin within granules; E: exocytosis; depolarization of the neuronal plasma membrane by propagated action potential; release of hormone and of neurophysin (possible conformational change) (after [16]).

cretion of the two substances and their release into the circulation occurred in dogs subjected to a severe hemorrhage. These experiments would indicate that the biosynthesis and secretion of vasopressin and of one neurophysin are parallel events.

Recently, *Gainer et al.*[63a] have shown that [^{35}S]-cysteine injected adjacent to the supraoptic nucleus of the rat is rapidly incorporated into a 20000-dalton protein which, in time is converted into a 12000-dalton labeled protein, neurophysin, and several small peptides including possibly oxytocin and vasopressin.

Brownstein et al.[63b] have also shown that two putative neurophysin precursors (pI 5.4 and 6.1) with molecular weights of about 20000, and two "intermediates" (pI 5.1 and 5.6) with molecular weights of about 17000, extracted from supraoptic nuclei, bind specifically to anti-rat neurophysin antiserum.

The localization of the neurophysins and the neurohypophysial hormones within the neurons seems to confirm the parallelism and favors the hypothesis of the common precursor (cf. Fig. 11).

5.2. Intracellular Localization of Neurophysins and Hormones

5.2.1. Localization in the Neurons by Immunocytological Methods

The identification of neurophysins in the perikarya of the supraoptic nucleus of the rat by immunofluorescence was accomplished by *Hope*[16] using anti-pig neurophysin II. Furthermore, in dog with anti-pig neurophysin he could demonstrate by this technique the transport of the neurosecretory material by axoplasmic flow in the hypophysial stalk of the dog: twenty hours after constriction of the stalk, he observed an accumulation of immunofluorescent material in the proximal, but not in the distal portion[16] (Fig. 12). In the rat it was even possible to estimate the speed of transport of a labeled protein similar to a neurophysin to be 2—3 mm/h[64].

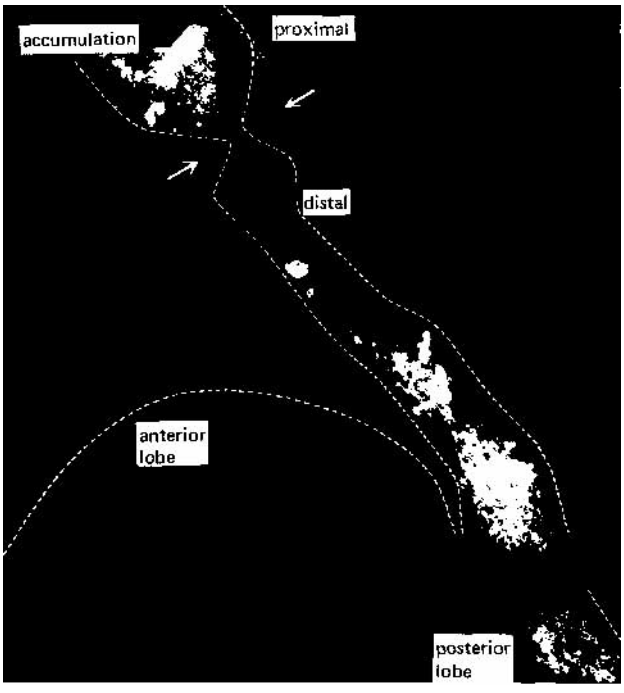


Fig. 12. The distribution of neurophysin immunofluorescence in the neurohypophysial stalk both proximal and distal to the site of a constriction. Note accumulation of fluorescence proximal to the point of constriction (arrows), its absence from axons in the tract immediately distal to the constriction, and its depletion in the proximal neurohypophysis (after [81]).

The intracellular distribution of neurophysins in the hypothalamus and posterior lobe of normal rats (Long-Evans) and of rats with a vasopressin deficiency and considerable diabetes insipidus (Brattleboro strain) has been examined by *Sokol et al.*[64a] using the immunoperoxidase technique (Fig. 13). In the homozygous Brattleboro rats, in contrast to normal rats, about 50% of the magnocellular neurons of the supraoptic and paraventricular nuclei lacked immunoreactive neurophysin. It was suggested that the neurons deficient in vasopressin also lacked neurophysin, which once again speaks in favor of a common biosynthesis.

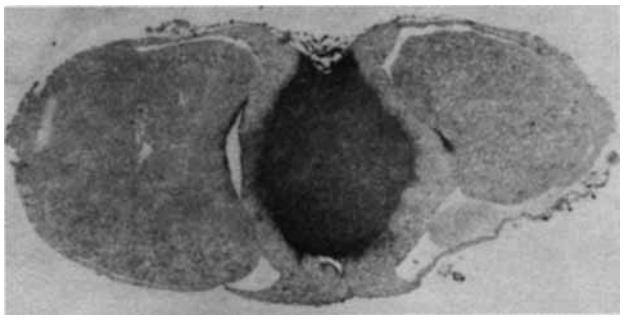


Fig. 13. Low power photomicrograph of mouse pituitary gland sectioned coronally. Immunoperoxidase stain using anti-human estrogen-stimulated neurophysin. There is heavy staining throughout the posterior lobe. The intermediate and the large anterior lobes are essentially free of reaction products (after [82]).

5.2.2. Localization within Neurosecretory Granules

After isolation of secretory granules from bovine posterior lobes by prolonged ultracentrifugation in a density gradient of sucrose it could be demonstrated by electrophoresis that the two major components of the bovine neurophysin, as also the two hormones, are present in about the same ratio[65]. *Dean* and *Hope*[65] found that the two neurophysins represent about 50% of the "granular" proteins. Furthermore, the two neurophysins were simultaneously present in each of the 15 glands individually examined, thus ruling out a genetic heterogeneity. The amino acid content of the crude "granular" neurophysin corresponds to that of a mixture of neurophysins I and II in equal proportions[65]. In addition, the distribution of oxytocin and vasopressin in the sucrose gradient suggests that the two hormones are stored in separate granules[65]. Moreover, neurophysin I is presumably present in the granules containing oxytocin, and neurophysin II in those containing vasopressin[66]. The existence of two categories of granules each possessing one type of hormone and one type of neurophysin also supports the hypothesis of a common precursor of the two substances. In the pig, lysine vasopressin is associated within the granules with neurophysin I[67]. This neurophysin (which is a truncated MSEL-neurophysin) is diminished selectively during the dehydration of the animal which leads to the secretion of lysine vasopressin[68]. All of the available data suggests affiliation of the MSEL-neurophysin with vasopressin, and it is interesting to note that in the bovine fetus the excess of vasopressin (in re-

lation to oxytocin) in the posterior lobe is accompanied by an excess of MSEL-neurophysin[38]. The simultaneous release of one hormone and one type of corresponding neurophysin can be explained by the mechanism of exocytosis[69]. The fact that the neurophysins of one species do not reveal a particular specificity of binding vis-à-vis the one or the other hormone leads one to think that the association does not have a biological significance related to the transport of the material but rather that it results from a juxtaposition due to the phenomenon of biosynthesis.

In the higher vertebrates the neurons terminating in the neurohypophysis have their origins in two hypothalamic regions, the supraoptic and paraventricular nuclei, which made it possible to assume a specialization whereby each of them would synthesize one hormone. However, recent investigations do not speak in favor of such a specialization[70,71]. This does not weaken the hypothesis of "one neuron-one hormone", since each nucleus may contain both types of neurons, a situation that is supported by the cytological analysis of Brattleboro rats which, being afflicted by hereditary diabetes insipidus, show a dispersion of neurons with and without granules[72].

5.3.3. Common Genetic Control of Vasopressin and One Neurophysin

One mutant of rats known as "Brattleboro strain" presents a hereditary diabetes insipidus caused by a deficiency either in the biosynthesis of vasopressin or in its liberation from an inactive precursor[73,74]. This deficiency affects only a single gene, and the heterozygous animals manifest a control over diuresis intermediary between that of normal animals and homozygous mutants. It is, therefore, important to verify if the absence of vasopressin is accompanied by a deficiency in one neurophysin. In the normal rat, three neurophysins (I or A, II or B, III or C) have been detected by means of polyacrylamide gel electrophoresis[75,76]. By injection of [^{35}S]-Cysteine before sacrifice, *Pickering et al.* observed that the ratio between the quantities of radioactivity incorporated in neurophysins I and II is very close to that of the amounts of vasopressin and oxytocin present in the gland[75]. On the other hand, in the homozygous Brattleboro rat, neurophysin I is absent, and in the heterozygote its quantity is lower than that of neurophysin II. *Pickering et al.*[29,75] concluded from this observation that vasopressin is synthesized with neurophysin I (or A) and oxytocin with neurophysin II (or B). *Pickering* attempted to determine the respective quantities of neurophysin I and II by using antiserums. Even though the specificity is imperfect—the antiserum for neurophysin I also precipitates 20% of neurophysin II — he concluded that vasopressin and neurophysin I (or A) are present in the gland in approximately equivalent amounts. These data argue in favor of the existence of a provasopressin which, by cleavage, gives rise to vasopressin and neurophysin I; this is in agreement with the conclusions of *Sachs et al.*[62,63].

Sunde and *Sokol*[76] also compared the neurophysins of the normal rat with those of the Brattleboro homozygote by polyacrylamide gel electrophoresis and likewise observed the disappearance of neurophysin I (neurophysin A of *Pickering*) in the strain manifesting diabetes insipidus. In spite of this, according to their experimental results neurophysin II (B) and neurophysin III (C) are present in equal proportions. The authors have examined the molar ratios of vasopressin/neurophysin I and oxytocin/neurophysin II + neurophysin III and have found the values to be 0.91 and 1.8 for the normal rat, and (0.0) and 1.77 for the Brattleboro homozygote. Furthermore, in the dehydration experiments, where the amount of vasopressin in the posterior lobe of the rat is considerably reduced, the molar ratio vasopressin/neurophysin I is 1.37 for the control animal (free access to water) and 1.31 for the animal deprived of water for three days. Even if the ratio between oxytocin and neurophysins II + III is debatable, that between vasopressin and neurophysin I appears, by way of contrast, to be very constant. It remains open whether rat neurophysin I belongs to the MSEL- or VLDV-family of neurophysins.

The sum total of observations made on the Brattleboro rat would indicate that a single gene controls the biosynthesis of vasopressin and of one neurophysin and that the two substances could be fragments derived from a common protein precursor.

6. Conclusions

The problem of the biosynthesis of the neurohypophysial hormones extrapolates to the more general topic of the biosynthesis of polypeptide hormones, and in a still broader sense to that of protein secretion. Since the work of *Steiner et al.*[77] one knows that most of the polypeptide hormones are synthesized in the form of an inactive precursor of larger size: thus proinsulin, proparathormone, proglucagon, the progastrins, *etc.*, have been characterized, in small quantity, in the secretory cells. One is dealing here with a general characteristic concerning the secretory proteins since one has equally been able to identify a proalbumin, proenzymes, *etc.* Furthermore, it has recently been observed that the proproteins are themselves cleavage products of very short-lived chemical compounds which are called pre-proproteins. *Habener et al.*[78]—inspired by experiments on pre-proparathormone—have proposed a general scheme of the biosynthesis and conversion. The initial protein chain, resulting from the transcription of messenger RNA, leaves the ribosome at its NH_2-terminus and penetrates the membrane of a cistern of the endoplasmic reticulum. An N-terminal sequence consisting of about 20 amino-acid residues, generally hydrophobic, represents the "perforator" of the membrane which is itself hydrophobic, and the rest of the chain can then penetrate the canal thus formed. The N-terminal sequence, called pre-peptide, becomes detached from the chain after 1—2 min, probably by enzymatic action. The isolation of the preproprotein and the characterization of the N-terminal sequence require microtechniques (radioactive labeling, special degradation procedures) that can be applied to quantities of the order of a nanomol. It was in this way that the sequences of the prepeptides of pre-proparathormone[78] and of pre-proinsulin[79] were determined.

Inside the cistern the chains, once liberated from the ribosome, acquire the native conformation of the prohormone. At the ends of the cisterns, vesicles detach themselves which then become fused to form secretory granules. Inside these granules a second proteolytic cleavage converts the prohormone into the hormone. Despite the fact that the enzymes responsible for these cleavages have not yet been isolated, they

seem to have a "trypsin-like" specificity. The life span of the prohormone in the granule is of the order of 1—2 h; in the case of insulin, for example, 95% of the proinsulin is converted into the active hormone whereby a peptide (peptide C) is liberated. The secretory granules reach the secretory pole of the cell and probably their entire content is discharged from the cell by the phenomenon of exocytosis (Fig. 14).

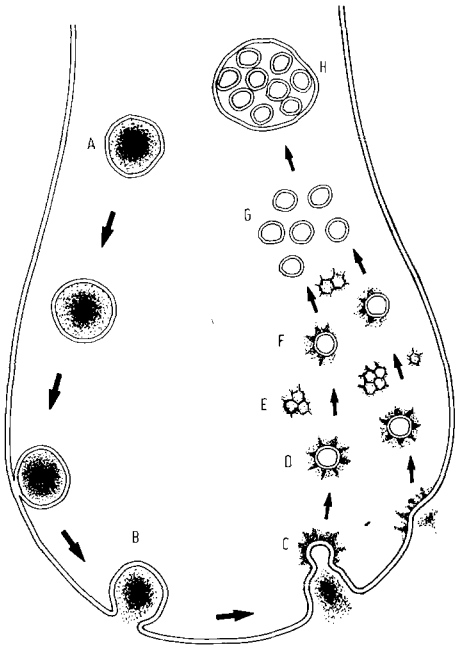


Fig. 14. Scheme depicting exocytosis-vesiculation sequence suggested to operate in neurohypophysial terminals. Contents of neurosecretory granules (A) are emptied directly into extracellular space by exocytosis (B). Granule membrane is retrieved from terminal surface by micropinocytosis-like activity (vesiculation), producing coated caveolae (C) which pinch off as coated microvesicles (D) and then shed coat fragments (E) to become partially coated microvesicles (F) and, finally, smooth (synaptic) microvesicles (G). These in turn are incorporated in lysosomal bodies (H) (after [80]).

This general scheme can also be accepted in the special case of neurosecretion; the neurosecretory neurons function like gland cells[80]. However, here the axoplasmic pathway for the transport of the granules from the cell body in the hypothalamus to the axon terminal in the neurohypophysis is particularly long and the transformations which the proteins undergo within the granules ("maturation") can be especially important. It seems reasonable to assume that the hormonal nonapeptides of the neurohypophysis are synthesized in the form of much longer chains, and that a sequence of cleavages, similar to those observed in several other polypeptide hormones, leads to active stable compounds which one can isolate in relatively important amounts. The simultaneous presence of hormones and neurophysins in the perikarya of the neurosecretory neurons, as revealed by the immunocytological technique; their close association within the granules, proved by the isolation of the latter and by chemical characterization; the indirect demonstration, by the incorporation of labeled amino acids, of the existence of a macromolecular precursor of vasopressin; the simultaneous disappearance of vasopressin and one neurophysin as a consequence of a unique mutation in the rat: all these observations provide a very strong argument in favor of the existence of a common precursor yielding one hormone and one neurophysin by cleavage.

The author is indebted to Prof. Bertha Scharrer for her help in the composition of the manuscript.

Received: February 1978 [A 294 IE]
German version: Angew. Chem. *91*, 905 (1979)

[1] *E. Scharrer*, Z. Vgl. Physiol. *7*, 1 (1928).
[2] *H. Waring*, Biol. Rev. *17*, 120 (1942).
[3] *W. Bargmann*, Z. Zellforsch. Mikroskop. Anat. *34*, 610 (1949).
[4] *G. Gomori*, Am. J. Pathol. *17*, 395 (1941).
[5] *W. Bargmann, E. Scharrer*, Am. Sci. *39*, 255 (1951).
[6] *J. J. Abel*, J. Pharmacol. Exp. Ther. *40*, 139 (1930).
[7] *M. Rosenfeld*, Bull. Johns Hopkins Hosp. *66*, 398 (1940).
[8] *H. B. Van Dyke, B. F. Chow, R. O. Greep, A. Rothen*, J. Pharmacol. Exp. Ther. *74*, 190 (1942).
[9] *O. Kamm, T. B. Aldrich, I. W. Grote, L. W. Rowe, E. P. Bugbee*, J. Am. Chem. Soc. *50*, 573 (1928).
[10] *V. du Vigneaud*, Harvey Lect. *50*, 1 (1954/1955).
[11] *R. Acher, C. Fromageot*, Ergeb. Physiol. Biol. Chem. Exp. Pharmakol. *48*, 287 (1955).
[12] *E. Scharrer, B. Scharrer*, Recent Progr. Horm. Res. *10*, 183 (1954).
[13] *W. Hild, G. Zetler*, Z. Gesamte Exp. Med. *120*, 236 (1953).
[14] *C. W. M. Adams, J. C. Sloper*, J. Endocrinol. *13*, 221 (1956).
[15] *R. Acher* in *W. Bargmann, B. Hanstrom, B. Scharrer, E. Scharrer:* Proc. II. Int. Conf. Neurosecretion. Springer, Berlin 1958, p. 71 ff.
[16] *D. B. Hope, J. C. Pickup:* Handbook of Physiology. Section 7: Endocrinology. Vol. IV, Part 1. Am. Physiol. Soc., Washington 1974, pp. 173 ff.
[17] *E. Breslow*, Adv. in Enzymol. *40*, 271 (1974); *B. T. Pickering, C. W. Jones* in *C. H. Li:* Hormonal Proteins and Peptides. Vol. 5. Academic Press, New York 1978; *E. Breslow*, Annu. Rev. Biochem. *48*, 251 (1979); *S. M. Seif, A. G. Robinson*, Annu. Rev. Physiol., *40*, 345 (1978).
[18] *R. Walter:* Neurophysins: Carriers of Peptide Hormones. Ann. N. Y. Acad. Sci. *248*, 512 (1975).
[19] *R. Acher, G. Manoussos, G. Olivry*, Biochim. Biophys. Acta *16*, 155 (1955).
[20] *R. Acher, J. Chauvet, G. Olivry*, Biochim. Biophys. Acta *22*, 421 (1956).
[21] *G. W. Irving, Jr., V. du Vigneaud*, J. Biol. Chem. *123*, 485 (1938).
[22] *R. Acher, A. Light, V. du Vigneaud*, J. Biol. Chem. *233*, 116 (1958).
[23] *J. Chauvet, M. T. Lenci, R. Acher*, Biochim. Biophys. Acta *38*, 266 (1960).
[24] *R. Acher* in [16], pp. 119 ff.
[25] *R. Acher, J. Chauvet, M. T. Chauvet, D. Crepy*, Biochim. Biophys. Acta *51*, 419 (1961).
[26] *W. B. Watkins*, J. Endocrinol. *59*, 17 (1973).
[26a] *M. Chretien, C. Gilardeau*, Acta Endocrinol. (Copenhagen) *74*, 226 (1973).
[27] *M. T. Chauvet, G. Coffe, J. Chauvet, R. Acher, FEBS Lett. 53*, 331 (1975).
[27a] *M. T. Chauvet, G. Coffe, J. Chauvet, R. Acher*, C. R. Séances Soc. Biol. Paris *170*, 257 (1976).
[28] *K. W. Cheng, H. G. Friesen*, J. Clin. Endocrinol. Metab. *34*, 165 (1972).
[29] *G. D. Burford, C. W. Jones, B. T. Pickering*, Biochem. J. *124*, 809 (1971).
[30] *H. Sachs, D. Pearson, A. Nureddin*, Ann. N. Y. Acad. Sci. *248*, 36 (1975).
[31] *K. W. Cheng, H. G. Friesen*, J. Biol. Chem. *246*, 7656 (1971).
[32] *M. T. Chauvet, J. Chauvet, R. Acher*, unpublished results.
[33] *M. T. Chauvet, J. Chauvet, R. Acher*, FEBS Lett. *52*, 212 (1975).
[34] *M. T. Chauvet, J. Chauvet, R. Acher*, FEBS Lett. *58*, 234 (1975).
[34a] *M. T. Chauvet, J. Chauvet, R. Acher*, Eur. J. Biochem. *69*, 475 (1976).
[34b] *T. C. Wuu, S. E. Crumm*, Biochem. Biophys. Res. Commun. *68*, 634 (1976).
[35] *R. Walter, D. H. Schlesinger, I. L. Schwartz, J. D. Capra*, Biochem. Biophys. Res. Commun. *44*, 293 (1971).
[36] *D. H. Schlesinger, M. Ernst, A. Nicholas, W. B. Watkins, R. Walter*, FEBS Lett. *57*, 57 (1975).
[37] *T. C. Wuu, S. Crumm, M. Saffran*, J. Biol. Chem. *246*, 6043 (1971).
[37a] *T. C. Wuu, S. E. Crumm*, J. Biol. Chem. *251*, 2735 (1976).
[37b] *M. T. Chauvet, P. Codogno, J. Chauvet, R. Acher*, FEBS Lett. *71*, 291 (1976).
[37c] *M. T. Chauvet, P. Codogno, J. Chauvet, R. Acher*, FEBS Lett. *80*, 374 (1977).
[37d] *M. T. Chauvet, P. Codogno, J. Chauvet, R. Acher*, FEBS Lett. 88, 91 (1978).
[38] *M. T. Chauvet, J. Chauvet, R. Acher*, FEBS Lett. *62*, 89 (1976).
[39] *D. H. Schlesinger, B. Frangione, R. Walter*, Proc. Nat. Acad. Sci. USA *69*, 3350 (1972).
[40] *T. C. Wuu, S. Crumm*, 9th Int. Congr. Biochem. Stockholm 1973, Abstract Db 9.
[40a] *M. T. Chauvet, P. Codogno, J. Chauvet, R. Acher*, FEBS Lett. *98*, 37 (1979).

[40b] *M. T. Chauvet, J. Chauvet, R. Acher, A. G. Robinson,* FEBS Lett. *101*, 391 (1979).
[41] *J. D. Capra, J. M. Kehoe, D. Kotelchuck, R. Walter, E. Breslow,* Proc. Nat. Acad. Sci. USA *69*, 431 (1972).
[41a] *D. H. Schlesinger, T. K. Audhya, R. Walter,* J. Biol. Chem. *253*, 5019 (1978).
[42] *W. G. North, R. Walter, D. H. Schlesinger, E. Breslow, J. D. Capra,* Ann. N. Y. Acad. Sci. *248*, 408 (1975).
[42a] *D. H. Schlesinger, G. T. Pickering, W. B. Watkins, J. C. Peek, L. G. Moore, T. K. Audhya, R. Walter,* FEBS Lett. *80*, 371 (1977).
[42b] *R. Walter, T. K. Audhya, D. H. Schlesinger, S. Shin, S. Saito, H. Sachs,* Endocrinology *100*, 162 (1977).
[43] *E. Breslow, J. Weis,* Biochemistry *11*, 3474 (1972).
[44] *C. J. Menendez-Botet, E. Breslow,* Biochemistry *14*, 3825 (1975).
[44a] *M. T. Chauvet, J. Chauvet, R. Acher,* FEBS Lett. *71*, 96 (1976).
[45] *E. Breslow,* Ann. N. Y. Acad. Sci. *248*, 423 (1975).
[46] *E. Breslow, R. Walter,* Mol. Pharmacol. *8*, 75 (1972).
[47] *V. Pliška, H. Sachs,* Eur. J. Biochem. *41*, 229 (1974).
[48] *D. B. Hope, M. Wälti, D. J. Winzor,* Biochem. J. *147*, 377 (1975).
[49] *J. Chauvet, R. Acher,* J. Biol. Chem. *242*, 4274 (1967).
[50] *J. Chauvet, R. Acher,* Eur. J. Biochem. *54*, 31 (1975).
[51] *D. B. Hope, V. V. S. Murti, V. du Vigneaud,* J. Biol. Chem. *237*, 1563 (1962).
[52] *J. E. Stouffer, D. B. Hope, V. du Vigneaud* in *C. F. Cori, G. Foglia, L. F. Leloir, S. Ochoa:* Perspectives in Biology. Elsevier, Amsterdam 1963, pp. 75 ff.
[53] *E. Breslow, L. Abrash,* Proc. Nat. Acad. Sci. USA *56*, 640 (1966).
[54] *E. Breslow, H. L. Aanning, L. Abrash, M. Schmir,* J. Biol. Chem. *246*, 5179 (1971).
[55] *E. Breslow, J. Weis, C. J. Menendez-Botet,* Biochemistry *12*, 4644 (1973).
[56] *R. Walter, P. L. Hoffman,* Fed. Proc. *32*, 567 (1973).
[57] *A. Furth, D. B. Hope,* Biochem. J. *116*, 545 (1970).
[58] *P. Balaram, A. A. Bothner-By, E. Breslow,* Biochemistry *12*, 4695 (1973).
[59] *P. Balaram, A. A. Bothner-By, E. Breslow,* J. Am. Chem. Soc. *94*, 4017 (1972).
[60] *P. Cohen, M. Camier, J. Wolff, R. Alazard, J. S. Cohen, J. H. Griffin,* Ann. N. Y. Acad. Sci. *248*, 463 (1975).
[61] *E. Breslow,* Proc. Nat. Acad. Sci. USA *67*, 493 (1970).
[61a] *E. Breslow, P. Gargiulo,* Biochemistry *16*, 3397 (1977).
[62] *H. Sachs, Y. Takabatake,* Endocrinology *75*, 943 (1964).
[62a] *A. F. Pearlmutter, C. McMains,* Biochemistry *16*, 628 (1977).
[63] *C. P. Fawcett, A. E. Powell, H. Sachs,* Endocrinology *83*, 1299 (1968).
[63a] *H. Gainer, Y. Sarne, M. J. Brownstein,* Science *195*, 1354 (1977).
[63b] *M. J. Brownstein, A. G. Robinson, H. Gainer,* Nature *269*, 259 (1977).
[64] *A. Norström, J. Sjöstrand,* J. Neurochem. *18*, 29 (1971).
[64a] *H. W. Sokol, E. A. Zimmerman, W. H. Sawyer, A. G. Robinson,* Endocrinology *98*, 1176 (1976).
[65] *C. R. Dean, D. B. Hope,* Biochem. J. *106*, 565 (1968).
[66] *C. R. Dean, D. B. Hope, T. Kazic,* Br. J. Pharmacol. Chemother. *34*, 192 (1968).
[67] *J. C. Pickup, C. I. Johnston, S. Nakamura, L. O. Uttenthal, D. B. Hope,* Biochem. J. *132*, 361 (1973).
[68] *H. G. Friesen, E. B. Astwood,* Endocrinology *80*, 278 (1967).
[69] *W. W. Douglas* in [16], pp. 191 ff.
[70] *E. A. Zimmerman, K. C. Hsu, A. G. Robinson, P. W. Carmel, A. G. Franz, M. Tannenbaum,* Endocrinology *92*, 931 (1973).
[71] *G. D. Burford, R. E. J. Dyball, R. L. Moss, B. T. Pickering,* J. Anat. *2*, 261 (1974).
[72] *H. Valtin, J. Stewart, H. W. Sokol* in [16], pp. 131 ff.
[73] *J. J. Jones, J. Lee,* J. Endocrinol. *37*, 335 (1967).
[74] *H. Valtin,* Am. J. Med. *42*, 814 (1967).
[75] *B. T. Pickering, C. W. Jones, G. D. Burford, M. McPherson, R. W. Swann, P. F. Heap, J. F. Morris,* Ann. N. Y. Acad. Sci. *248*, 15 (1975).
[76] *D. A. Sunde, H. W. Sokol,* Ann. N. Y. Acad. Sci. *248*, 345 (1975).
[77] *H. S. Tager, D. F. Steiner,* Annu. Rev. Biochem. *43*, 509 (1974).
[78] *B. Kemper, J. F. Habener, M. D. Ernst, J. T. Potts, Jr., A. Rich,* Biochemistry *15*, 15 (1976).
[79] *S. J. Chan, P. Keim, D. F. Steiner,* Proc. Nat. Acad. Sci. USA *73*, 1964 (1976).
[80] *W. W. Douglas* in [16], pp. 191 ff.
[81] *B. G. Livett,* Ann. N. Y. Acad. Sci. *148*, 112 (1975).
[82] *E. A. Zimmerman, R. Defendini, H. W. Sokol, A. G. Robinson,* Ann. N. Y. Acad. Sci. *248*, 92 (1975).

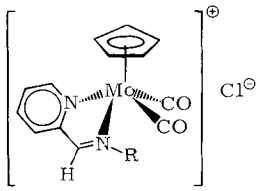
Communications are brief preliminary reports of research work in all areas of chemistry which, on account of its fundamental significance, novelty, or general applicability, should be of interest to a broad spectrum of chemists. Authors of communications are requested to state reasons of this kind justifying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

Synthesis and X-Ray Structure Analysis of a Mo Complex with η^2-Coordinated Benzaldehyde; Transformation of a CO Ligand by Double α-Addition[**]

By *Henri Brunner, Joachim Wachter, Ivan Bernal,* and *Michael Creswick*[*]

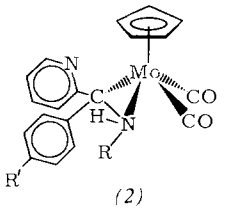
The chelate complexes *(1)*[1], accessible from the Schiff bases of 2-pyridinecarbaldehyde and $C_5H_5Mo(CO)_3Cl$ react with an excess of C_6H_5Li or *p*-$R'C_6H_4MgBr$ under ring contraction to give the neutral complexes *(2)*[2]. Reaction of the *N*-methyl compound *(1)* (R = CH_3) with *p*-$R'C_6H_4MgBr$ (R' = H, CH_3) in the molar ratio 1:2 does not stop at the stage of *(2)* but leads to *(3)* by reduction of a CO group. Whereas in the formation of a carbene ligand from a M—C≡O group the nucleophile adds to the C atom and the electrophile to the O atom[3], the transformation of a C≡O ligand into η^2-benzaldehyde, established for *(3a)* by X-ray structure analysis, requires double α-addition.

In the solid state *(3a)* occurs in two isomeric forms which can be separated manually. Both contain in the IR spectrum (KBr) the ν_{C-O} band at 1830 cm^{-1}; however, they differ in the frequency of the N—H stretching vibrations [*(3a')* 3203 cm^{-1}, *(3a'')* 3181 cm^{-1}]. The molecular structure of *(3a')* in the crystal (Fig. 1), determined by X-ray crystallography, is



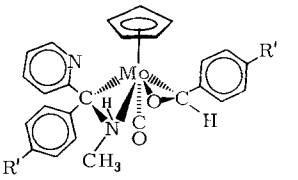
(1)

R = CH_3, C_6H_5, $CH(CH_3)_2$, $CH_2C_6H_5$, $CH(CH_3)C_6H_5$



(2)

R' = H, CH_3, OCH_3, Cl



(3a), R' = H, *(3b)*, R' = CH_3

in accord with the ^{1}H- and ^{13}C-NMR spectra measured in solution at −10 °C (Table 1). Compared with *(2)*, in *(3a)* the δ(^{13}C) values for the MoCN three-membered ring (Δ = −23) and the CO group (Δ = +13) are shifted appreciably. In *(3b)* the *p*-CH_3 signals are nonequivalent.

At room temperature, the orange solutions of *(3)* in chloroform, benzene, and acetone soon turn blue with formation of extremely air sensitive and thermolabile complexes of still unknown structure.

The orange rhombs of *(3a')* crystallize in the space group $P\bar{1}$, $Z = 2$, cell constants $a = 9.035(6)$, $b = 12.314(6)$, $c = 13.220(5)$ Å, $\alpha = 65.91(4)$, $\beta = 71.40(4)$, $\gamma = 72.42(4)°$; $V = 1246.97$ Å^3, $\varrho_{calc} = 1.311$ g·cm^{-3}. From 3154 measured reflections (MoK_α radiation, $\lambda = 0.71073$ Å) 2128 with $I > 2\sigma(I)$ were used for the refinement of the structure [*R*(F) value 4.59%].

Table 1. NMR data of complexes *(3a)* and *(3b)* ($CDCl_3$ solution, TMS int.) [a].

^{1}H-NMR	$C_6H_4CH_3$		NCH_3 ($J_{NH\ CH_3}$)	C_5H_5	CH	NH	H5	C_5H_4N H4, H3	H6	C_6H_4R'
(3a)			^{2}2.63 (5.5)	^{1}4.76	^{1}5.22	^{m}6.30 [b]	^{m}6.49	^{m}6.98	^{m}8.39	^{m}7.32
(3b)	^{1}2.33, ^{1}2.36		^{2}2.56 (5.6)	^{1}4.73	^{1}5.21	^{m}6.24 [b]	^{m}6.54	[c]	^{m}8.31	^{m}7.14
^{13}C-NMR [d]	NCH_3	MoCN	MoCO [e]	C_5H_5	$C_5H_4N + C_6H_4R'$		C—O			
(3a)	39.3	76.9	81.6	100.6	120.0—147.3, 168.3		234.9			

[a] δ values, coupling constants in Hz; Varian T-60 and Bruker WH-90, temperature −10 °C. [b] Broad. [c] Signal obscured. [d] Broad band decoupled. [e] Doublet in the off-resonance spectrum.

[*] Prof. Dr. H. Brunner, Dr. J. Wachter
Institut für Chemie der Universität
Universitätsstr. 31, D-8400 Regensburg 2 (Germany)
Prof. Dr. I. Bernal, M. Creswick
Department of Chemistry, University of Houston
Houston, Texas 77004 (USA)

[**] This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and BASF AG, Ludwigshafen, as well as by the US National Science Foundation and the R. A. Welch Foundation.

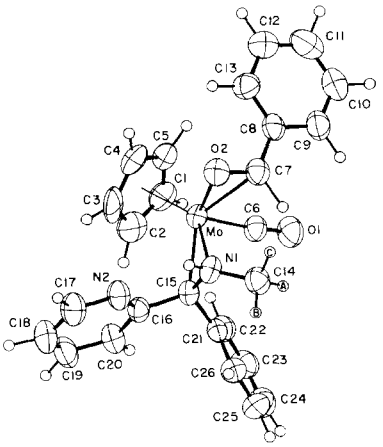


Fig. 1. ORTEP diagram of *(3a')*. Bond lengths: Mo–C6 1.900(11), C6–O1 1.182(13), Mo–C7 2.258(14), C7–O2 1.333(12), Mo–O2 2.071(8), Mo–N1 2.137(9), N1–C15 1.436(17), Mo–C15 2.203(9), Mo–Cp (average) 2.35(3) Å; bond angles: C7–Mo–O2 35.4, Mo–C7–O2 64.5, N1–Mo–C15 38.7, Mo–N1–C15 73.2, Mo–C6–O1 171.7, C6–Mo–C7 69.7, C6–Mo–O2 104.6, C6–Mo–N1 93.4, C6–Mo–C15 88.9°.

Similarly as in *(2)*, in the MoCN three-membered ring of *(3a')* the pyridyl substituent at C15 and the hydrogen atom at N1 lie at the side of the C_5H_5 ring; a hydrogen bridge is formed between N1 and N2[2]. The C_6H_5 substituent at the MoCO three-membered ring is also orientated to the C_5H_5 ring. The plane of the C_5H_5 ring forms angles of 60.36 and 33.58° with the planes of the MoCN and MoCO three-membered rings, whereby in the MoCN ring C15 and in the MoCO ring O2 are closer to the C_5H_5 plane. With an angle of 77.56° the planes of both three-membered rings are nearly perpendicular to each other. With 110.6(8)° the angle C16—C15—C21 is close to the tetrahedral angle. The η^2-bonding of the benzaldehyde in *(3a')* corresponds to the coordination of formaldehyde in $Os(\eta^2\text{-}CH_2O)(CO)_2(PPh_3)_2$[4] and benzaldehyde in $Ni(PPh_3)_2(\eta^2\text{-}C_6H_5CHO)$[5]. Considering the η^2-benzaldehyde a two-electron ligand and the η^2-aminomethyl group a three-electron ligand, *(3a')* can be regarded as a derivative of $C_5H_5Mo(CO)_2(NO)$[6].

Procedure

A solution of $p\text{-}R'C_6H_4MgBr$ ($R'=H$ or CH_3) (11.6 mmol) in 50 ml THF is added dropwise to a suspension of 2.2 g (5.9 mmol) *(1)* ($R=CH_3$) in 100 ml THF at room temperature. After refluxing for 30 minutes the solvent is evaporated off and the residue dissolved in 15 ml benzene. On chromatography on SiO_2 (column 3 × 20 cm) with benzene two very weak zones develop. These are discarded. Thereafter a broad greenish-blue zone develops which contains *(3a)*, *(3b)* and their subsequent reaction products; this is eluted with benzene/ether (1:1). Recrystallization at −35 °C from 100 ml acetone and 20 ml ether affords red orange crystals in 23–25% yield. On further recrystallization from ether/pentane (10:1) analytically pure compounds can be obtained: orange rhombs of *(3a')* (dec. 155 °C, $\nu_{NH}=3203\ cm^{-1}$)[7], red prisms of *(3a'')* (dec. 154 °C, $\nu_{NH}=3181\ cm^{-1}$), and red prisms of *(3b)* (dec. 170 °C, $\nu_{NH}=3181\ cm^{-1}$), respectively.

Received: May 28, 1979 [Z 299 IE]
German version: Angew. Chem. *91*, 920 (1979)

CAS Registry numbers:
(1), R = CH_3, 41308-25-2; *(3a)*, 71888-50-1; *(3b)*, 71888-49-8; C_6H_5Br, 108-86-1; $p\text{-}CH_3C_6H_4Br$, 106-38-7

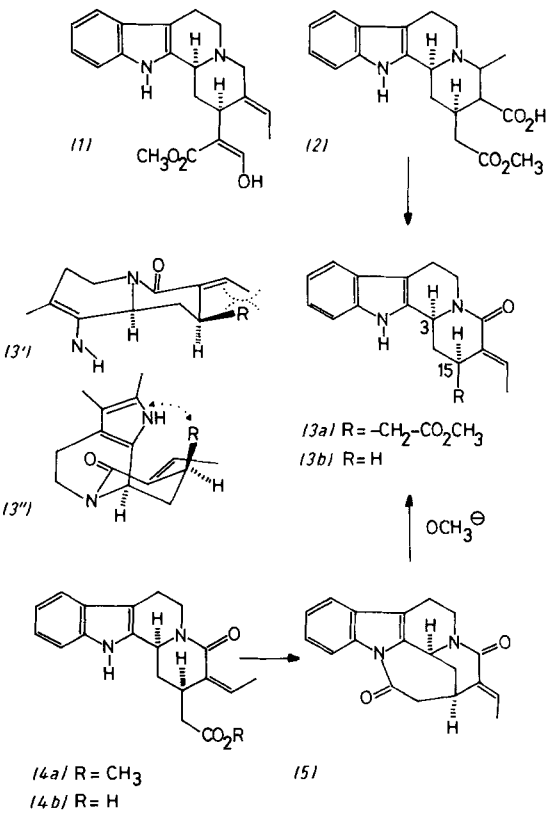
[1] *H. Brunner, W. A. Herrmann*, Chem. Ber. *105*, 3600 (1972).
[2] *H. Brunner, H. Schwägerl, J. Wachter, G. M. Reisner, I. Bernal*, Angew. Chem. *90*, 478 (1978); Angew. Chem. Int. Ed. Engl. *17*, 453 (1978); *H. Brunner, H. Schwägerl, J. Wachter*, Chem. Ber. *112*, 2079 (1979).
[3] *E. O. Fischer*, Angew. Chem. *86*, 651 (1974); Adv. Organomet. Chem. *14*, 1 (1976).
[4] *K. L. Brown, G. R. Clark, C. E. L. Headford, K. Marsden, W. R. Roper*, J. Am. Chem. Soc. *101*, 503 (1979).
[5] *D. Walther*, Z. Chem. *15*, 490 (1975); *T. T. Tsou, J. C. Huffman, J. K. Kochi*, Inorg. Chem. *18*, 2311 (1979).
[6] *M. G. Reisner, I. Bernal, H. Brunner, J. Doppelberger*, J. Chem. Soc. Dalton Trans. *1979*, 1664; *J. L. Atwood, R. Shakir, J. T. Malito, M. Herberhold, W. Kremnitz, W. P. E. Bernhagen, H. G. Alt*, J. Organomet. Chem. *165*, 65 (1979).
[7] The 70 eV mass spectra of *(3a)* and *(3b)* contain as fragments of highest mass number $[M-C_6H_6-CO]^+$. The molecular ions can be observed in the F-D spectrum (Varian 311 A). We thank Dr. *K. K. Mayer* and *F. Fischer* for recording the spectra.

Thermodynamically Controlled Stereoselective Synthesis of Geissoschizine[**]

By *Werner Benson* and *Ekkehard Winterfeldt*[*]

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

We have previously described a total synthesis[1] of the biogenetically important alkaloid[2] geissoschizine *(1)*. The stereoselective methylene-lactam rearrangement of amino acids of type *(2)* may be regarded as the key reaction, which affords the *E*-configurated lactam *(3a)* as main product.



[*] Prof. Dr. E. Winterfeldt, Dipl.-Chem. W. Benson
Institut für Organische Chemie der Universität
Schneiderberg 1 B, D-3000 Hannover (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft (Wi 206/30).

The *Z*-configurated lactam *(4a)* formed as by-product proved to be stable under the reaction conditions, so a chromatographic separation was necessary. In an attempt to avoid this separation step we have studied the possibilities of *E-Z* isomerization.

Whereas in the case of unsaturated C^{15}-unsubstituted lactams [see *(3b)*] only the desired *E*-configuration is formed under kinetically controlled conditions[3] and is thermodynamically stable, in the case of the geissoschizine intermediate *(3a)* competing formation of the *Z*-isomer *(4a)* takes place by steric interaction between CH_3 and R [see conformation *(3')*]. This interaction would be minimized in the conformation *(3'')*—a conformation which however is not populated, unless forcefully so by bonding between R and the indole *N*-atom. This is achieved by treatment of the lactamic acid *(4b)* with trifluoroacetic anhydride. This ring closure is in fact accompanied by a spontaneous isomerization of the double bond with formation of the *E*-configurated dilactam *(5)*. Regioselective ring-opening of the dilactam with sodium methoxide in methanol leads to the lactamate *(3a)* in quantitative yield.

The synthesis becomes stereoconvergent through the intermediate *(5)*. The mixture of the lactamates *(3a)* and *(4a)* is hydrolyzed to the mixture of the lactamic acids, which then cyclize to the single dilactam *(5)* in very high yields. All the steps give excellent yields and can be carried out without resorting to isolation and purification of the intermediates. *(3a)* is cleanly converted into geissoschizine *(1)* by "Borch reduction" and formylation (see [1]).

Experimental

Hydrolysis of *(4a)* to the lactamic acid *(4b)*: NaOH (300 mg) and water (5 ml) were added to a solution of *(4a)* (200 mg, 0.6 mmol) in methanol (10 ml) and the mixture stirred overnight at room temperature. After acidification with 2 M citric acid and extraction of *(4b)* with dichloromethane, the extract was dried over $MgSO_4$ and then evaporated to dryness: 185 mg (96.5%) *(4b)*.—A mixture of *(4b)* (185 mg), dichloromethane (5 ml) and trifluoroacetic acid (20 ml) under nitrogen was stirred overnight at room temperature. After evaporation to dryness the product *(5)* was recrystallized from ether: 150 mg (86%), m.p. 195 °C[4].

Ring-opening to *(3a)*: A mixture of *(5)* (150 mg) and a 2% solution of sodium methoxide in anhydrous methanol (20 ml) was stirred for 1 h at room temperature in the absence of moisture. After addition of 2 M citric acid solution and extraction with dichloromethane the extract was washed with saturated sodium hydrogen carbonate and saturated sodium chloride solutions, dried over $MgSO_4$ and evaporated to dryness. The product *(3a)* was recrystallized from ether: 155 mg (93.6%).

Received: June 13, 1979 [Z 313 IE]
Publication delayed at authors' request
German version: Angew. Chem. *91*, 921 (1979)

[1] *B. Hachmeister, D. Thielke, E. Winterfeldt*, Chem. Ber. *109*, 3825 (1976).
[2] *J. Stöckigt*, J. Chem. Soc. Chem. Commun. *1978*, 1097, and references cited therein.
[3] *D. Thielke, J. Wegener, E. Winterfeldt*, Chem. Ber. *108*, 1791 (1975).
[4] UV (methanol): acylindole spectrum (qualitative).—IR (KBr): C=O 1690, unsaturated lactam 1660, 1610 cm^{-1}.—^{1}H-NMR ($CDCl_3$): $\tau = 1.97$ (1H, m, anisotropy-H (aromatic)), 2.5—2.9 (3H, m, aromatic H), 2.95 (1H, q, $J = 7.5$ Hz, olefinic H), 5.32 (2H, m, quinolizidone H, anisotropy-H), 8.23 (3H, d, $J = 7.5$ Hz).—MS (200 °C): $m/e = 306$ ($M^{\oplus}$, 100%), 278 (32.4%), 263 (18.9%), 235 (32.4%), 169 (51.4%), 156 (32.4%).

Enantioselective Synthesis of α-Methyl-α-aminocarboxylic Acids by Alkylation of the Lactim Ether of *cyclo*-(L-Ala-L-Ala)[**]

By *Ulrich Schöllkopf, Wolfgang Hartwig,* and *Ulrich Groth*[*]

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

Optically active amino acids are of special interest in pure and applied organic chemistry. Asymmetric amino acid syntheses are of preparative importance, but only when they are simple to perform and give high optical yields (>90%). In the case of stoichiometric asymmetric syntheses the chiral agent ought to be recoverable and/or readily available in the "chiral pool".

We recently reported the asymmetric synthesis of α-methyl-α-aminocarboxylic acids [type *(7)*] by alkylation of *N*-1-chirally substituted 4-methylimidazolin-5-one[1a]. In the search for further synthetic routes we have now found that the base-induced alkylation of (3*S*,6*S*)-(+)-2,5-dimethoxy-3,6-dimethyl-3,6-dihydropyrazine *(3)* proceeds with high asymmetric induction (cf. Table 1). The diastereoselectivity

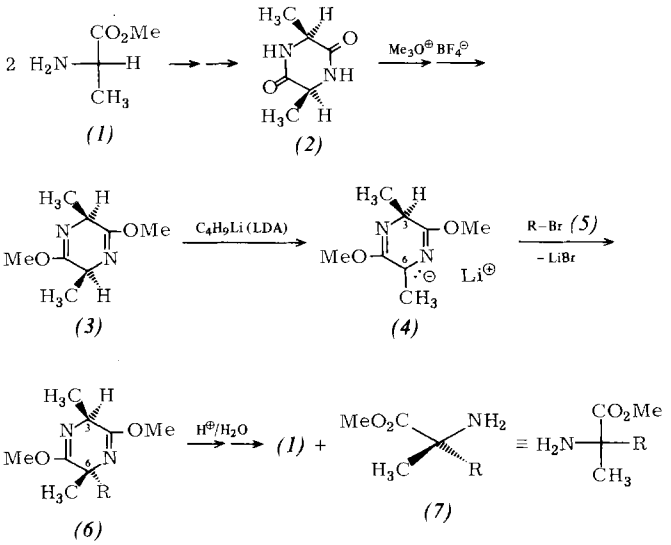


Table 1. Dihydropyrazines *(6)* and α-methyl-α-amino acids prepared by alkylation of *(3)*. e.e. = enantiomeric excess.

(6)	R	Yield [%]	Asymm. induction [%]	Config.	*(7)* e.e.
(a)	$CH_2C_6H_5$	80–90	≈93 [a]	*R*	≈93 [b]
(b)	$CH_2C_6H_3$-3,4-$(OCH_3)_2$	85–90	≈95 [a]	*R*	≈90 [d, g]
(c)	CH_2-2-Naphthyl	≈85	≈93 [a]	*R*	≈90 [d, g]
(d)	CH_2-2-Quinolyl	≈78	≈94 [a]	*R*	≈93 [d, g]
(e)	CH_2-3-Pyridyl	≈90	>95 [a]	*R*	≈90 [d, e]
(f)	$CH_2CH{=}CH_2$	80–85	≈92 [d]	*R* [c]	≈90 [d, e]
(g)	$CH(CH_3)_2$	75–80	≈92 [d]	*R* [c]	
(h)	$C(OH)(C_6H_5)_2$	≈85	>95 [a, f]	*R* [c]	

[a] ^{1}H-NMR spectroscopic on C-3-CH_3 of *(6)*. [b] On α-methylphenylalanine with $Eu(tfc)_3$ and polarometrically. [c] Assumed similarly as *(6a)*. [d] On *(7)* with $Eu(tfc)_3$; e.e. of *(7)* usually slightly lower than asymmetric induction because *(3)* not 100% optically pure. [e] Isolated incompletely free of *(1)*. [f] Synthesized with benzophenone instead of R Br. [g] $[\alpha]_D^{25}$ ($c = 1.0$, EtOH) calculated for optically pure *(7)*: −4.8° for *(7c)*, +7.8° for *(7d)*, −7.90° for *(7e)*.

[*] Prof. Dr. U. Schöllkopf, Dr. W. Hartwig, U. Groth
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Asymmetric Syntheses *via* Heterocyclic Intermediates, Part 2.—Part 1: [1a].

of the alkylation can be determined, either ^{1}H-NMR spectroscopically at the stage of the alkylation product *(6)* or polarimetrically or NMR spectroscopically with chiral shift reagents at the stage of the α-methyl-α-aminocarboxylate *(7)* or α-methyl-α-amino acid.

We obtained 3,6-dihydropyrazine *(3)* by reaction of *cyclo*-(L-Ala-L-Ala) *(2)*[2] with trimethyloxonium tetrafluoroborate. This reaction proceeds without racemization. The lithiation of *(3)* to *(4)* can be smoothly performed at −70 °C (in tetrahydrofuran) with butyllithium or lithium diisopropylamide (LDA). Double metalation at C-3, which would lead to an antiaromatic 8π electron system, does not take place[3]. The alkylation products *(6)* are hydrolyzable with 0.5 N hydrochloric acid even at room temperature. The esters *(1)* and *(7)* can be separated, for instance, by distillation.

In the alkylation *(4)*→*(6)*, the *R*-configuration is induced at C-6, *i.e.* the alkyl moiety prefers the *trans*-position to the methyl group at C-3. For example, (*R*)-(−)-α-methylphenylalanine[1b] is obtained from *(6a) via* the ester *(7a)*. In *(6a)* the *R*-configuration at C-6 is recognizable in the ^{1}H-NMR spectrum: 3-H absorbs at relatively high field strengths (δ = 3.17) because it is situated in the shielding anisotropic region of the phenyl group, which probably lies in a π-complex fashion over the heterocycle[4]. We attribute the high asymmetric induction to the fact that one of the two diastereotopic sides of the probably planar anion of *(4)* is relatively strongly shielded by the methyl group.

Experimental

(2): After washing with ether, the crude product obtained according to [2a] is *ca.* 90% optically pure. Crystallization twice from water yielded almost optically pure *(2)*; $[\alpha]_D^{25}$ = 26.4° (*c* = 1.3, H_2O); after drying in a vacuum over P_2O_5, m.p. 289 °C.

(3): A mixture of *(2)* (14.2 g, 0.1 mol) in anhydrous CH_2Cl_2 (300 ml) and trimethyloxonium tetrafluoroborate was vigorously stirred or shaken for 34 h at room temperature[5]. A buffer solution, consisting of NaH_2PO_4 (40.0 g, 0.3 mol) and Na_2HPO_4 (113.7 g, 0.8 mol) in 500 ml water, was added to the ice-cold mixture, the organic phase was separated off and the aqueous phase extracted three times with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and then evaporated to dryness at 10 torr; yield 14.9 g (88%) of almost optically pure *(3)*, b.p. ≈75 °C/8—10 torr; $[\alpha]_D^{20}$ = +82.6° (*c* = 1.0, ethanol)[6]; IR (film): ν = 1685 cm^{-1} (N=C); ^{1}H-NMR ($CDCl_3$): δ = 1.33 (d, CH_3), 4.04 (q, further split with $J_{1,4}$, CH).

Alkylation of *(3)* to *(6):* A solution of butyllithium (10 mmol, 6.4 ml of a 1.55 N solution in hexane) (or 10 mmol lithium diisopropylamide in a little THF) is cooled to −70 °C and then added dropwise to a solution of *(3)* (1.7 g, 10 mmol) in anhydrous THF (20 ml) at −70 °C. The mixture is stirred for 10 min at this temperature, treated with a solution of *(5)* (10 mmol) in THF (10 mmol) and stirring continued for 2—10 h. The mixture is allowed to warm to room temperature, the solvent removed at 10 torr, the residue treated with 10 ml water (and if necessary 5 g common salt), extracted three times with 30 ml of ether or CH_2Cl_2, the extracts combined, dried over $MgSO_4$ and worked-up in the usual way. Diastereomeric ratios (cf. Table 1) were determined on the crude product. The compounds *(6)* were purified by bulb-to-bulb distillation; example: *(6a)*, b.p. 115—120 °C/0.6 torr; IR (film): ν = 1680 cm^{-1} (N=C); ^{1}H-NMR ($CDCl_3$): δ = 3.62 and 3.60 (each s, OCH_3), 1.44 (s, 6-CH_3), 1.16 and 0.40 (each d, *J* = 7 Hz, 3-CH_3 for *trans-(6a)* and *cis-(6a)*[7], intensity ratio ≈28:1), 3.17 (q, *J* = 7 Hz, 3-H), 3.11 and 2.74 (AB, *J* = 14 Hz, CH_2).

Hydrolysis of *(6)* to *(7):* A suspension of *(6)* (10 mmol) in 0.5 N hydrochloric acid was stirred for 20 min—2 h at room temperature. The solvent was removed in a vacuum (50 °C), the residue [*(7)*·HCl] taken up in a *ca.* 10 ml water, covered with 30 ml ether and treated with conc. ammonia solution (1.6 ml) with vigorous stirring at 0 °C (danger of racemization of recovered *(1)*!). After separation of the ether phase, the aqueous phase was treated with 2 g sodium chloride, extracted five times with ether and the combined extracts dried over sodium sulfate. In the case of water-insoluble esters *(7)*, after hydrolysis the mixture was treated with dilute ammonia solution, extracted twice with ether, and potassium carbonate was added to the aqueous phase. After further extraction with ether the combined ether phases were dried over sodium sulfate. After removal of ether, *(1)* and *(7)* were separated by bulb-to-bulb distillation; example: *(7a)*, b.p. 50—55 °C/0.6 torr [*(1)* was separated in the forerun]; IR (film): ν = 1600 (br., NH_2), 1725 (C=O), 3200, 3320, and 3380 cm^{-1} (NH_2); ^{1}H-NMR ($CDCl_3$): δ = 3.66 (s, OCH_3), 3.13 and 2.78 (AB, CH_2), 1.37 (s, CH_3).

Received: March 19, 1979 [Z 314 IE]
Publication delayed at authors' request
German version: Angew. Chem. *91*, 922 (1979)

[1] a) *U. Schöllkopf, H.-H. Hausberg, I. Hoppe, M. Segal, U. Reiter*, Angew. Chem. *90*, 136 (1978); Angew. Chem. Int. Ed. Engl. *17*, 117 (1978); cf. references cited therein. b) *K. Weinges, G. Graab, D. Nagel, B. Stemmle*, Chem. Ber. *104*, 3594 (1971); *K. Weinges, K. Gries, B. Stemmle, W. Schrank, ibid. 110*, 2098 (1977).

[2] a) *E. Fischer*, Ber. Dtsch. Chem. Ges. *39*, 453 (1906); b) *W. Pickenhagen, P. Dietrich*, Helv. Chim. Acta *58*, 1078 (1975).

[3] Cf. *R. R. Schmidt*, Angew. Chem. *87*, 603 (1975); Angew. Chem. Int. Ed. Engl. *14*, 581 (1975).

[4] Such preferred conformations (folded conformations) have been demonstrated on numerous occasions in the case of benzyl-substituted heterocycles; cf. *A. K. Bose, M. S. Manhas, R. V. Tavares, J. M. van der Veen, H. Fujiwara*, Heterocycles *7*, 1227 (1977).

[5] Triethyloxonium tetrafluoroborate reacts more rapidly (soluble in CH_2Cl_2!). The asymmetric inductions in the case of the diethyl lactim ether are as high as in the case of *(3)*, but the ^{1}H-NMR spectra are less clear.

[6] Hydrolysis of *(3)* gave 93—95% optically pure alanine, *i.e. (3)* is at least 93—95% pure.

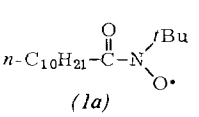
[7] *cis* and *trans* referred to 3-methyl and 6-benzyl.

Enantioselective Oxidation by a Chiral Acylaminyl Oxide

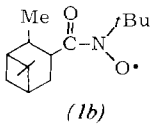
By *Corrado Berti* and *M. John Perkins*[*]

Dedicated to Dr. Robert S. Cahn on the occasion of his 80th birthday

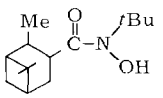
The literature contains relatively few instances of asymmetric induction in atom transfer from carbon, presumably because chirality is lost in the derived carbon radical. However enantioselectivity has been observed, and constitutes a



(1a)



(1b)



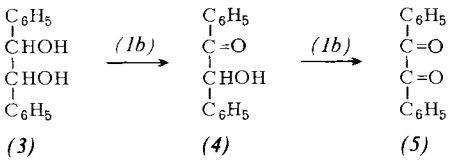
(2)

[*] Prof. Dr. M. J. Perkins, Dr. C. Berti
Dept. of Chemistry, Chelsea College
Manresa Road, London SW3 6LX (England)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1111-0864 $ 02.50/0

simple procedure for obtaining materials enriched in one enantiomer[1]. The present report extends this principle to oxidations with chiral nitroxides (aminyl oxides), *i.e.* radicals of the type RR'NO•.

It has been demonstrated that isolable acyl(*tert*-butyl)aminyl oxides *(1)* are sufficiently reactive to behave as mild selective homolytic oxidizing agents, *e.g.* towards phenols and allylic alcohols[2]. Unlike *Fremy*'s radical $(K^+ {}^-O_3S)_2NO•$[3] they may be employed in non-polar solvents. We recently found that as sensitive compound as Vitamin A alcohol can be oxidized to retinal in *ca.* 90% yield by the radical *(1a)*; there is negligible competition from radical attack on the conjugated pentaene unit, or on the product aldehyde[4].



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

We have now isolated the chiral acylaminyl oxide *(1b)*, and found that it will effect enantioselective oxidation of benzoin *(4)*. Reaction of benzoin with *ca.* 1.5 molar equivalents of *(1b)* in benzene gives benzil *(5)* (*ca.* 0.6 equiv.) together with unreacted benzoin *(4)* (*ca.* 0.4 equiv.) which has $[\alpha]_D^{25}$ $(CHCl_3) = 14°$. This corresponds to an enantiomeric excess of *ca.* 7%[5]. In view of the separation between the radical center and the chiral substituent in *(1b)* the effect seems encouragingly large. The substrate initially selected for study was *meso*-dihydrobenzoin, *meso-(3)*, since it was envisaged that selectivity might be enhanced by hydrogen-bond association with the carbonyl group of the aminyl oxide. In this case, although benzoin *(4)* could be isolated, which was substantially enriched in one isomer, (e.e. *ca.* 15%), the yield was very low (<10%) since the rate of oxidation of benzoin *(4)* to benzil *(5)* proved to be greater than the rate of oxidation of dihydrobenzoin *(3)* to benzoin *(4)*.

The aminyl oxide *(1b)*, a blue oil which is readily prepared from (−)-3-pinanecarboxylic acid *via* the hydroxamic acid *(2)* ($[\alpha]_D^{25}$ (1 g/100 ml $CHCl_3$) = −49°; m.p. 157—158 °C) following a well-established procedure[6], is regarded as the prototype for a series of chiral aminyl oxide oxidizing agents. Manipulation of both reactivity and enantioselectivity by varying the acyl group and by replacing *tert*-butyl with a chiral alkyl group should be straightforward.

Received: August 20, 1979 [Z 315 IE]
German version: Angew. Chem. *91*, 923 (1979)

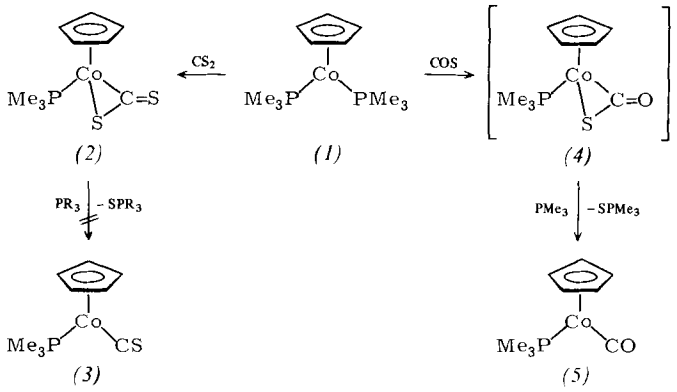
[1] *J. H. Hargis, Huang-Hong Hsu*, J. Am. Chem. Soc. *99*, 8114 (1977).
[2] *T. C. Jenkins, M. J. Perkins, S. A. Hussain*, Tetrahedron Lett. *1977*, 3199; J. Chem. Soc. Perkin Trans. 1 *1979*, in press.
[3] *H. Zimmer, D. C. Lankin, S. W. Horgan*, Chem. Rev. *71*, 229 (1971).
[4] *A. H. Sharma*, unpublished observations.
[5] *J. Kenyon, R. L. Patel*, J. Chem. Soc. *1965*, 435.
[6] *P. F. Alewood, S. A. Hussain, T. C. Jenkins, M. J. Perkins, A. H. Sharma, N. P. Y. Siew, P. Ward*, J. Chem. Soc. Perkin Trans. 1 *1978*, 1066.

Thiocarbonyl-Metal Complexes from CSSe[1]

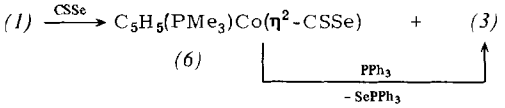
By *Helmut Werner* and *Oswald Kolb*[*]

In the carbon disulfide complex *(2)*, which is formed on reaction of $C_5H_5Co(PMe_3)_2$ *(1)* with CS_2[2], the η^2-CS_2 ligand is tightly bound. Hence, all attempts to obtain the corresponding thiocarbonyl complex *(3)*, as in the case of other CS_2-metal complexes[3] by reaction of *(2)* with PMe_3 or PPh_3, have met without success[4].

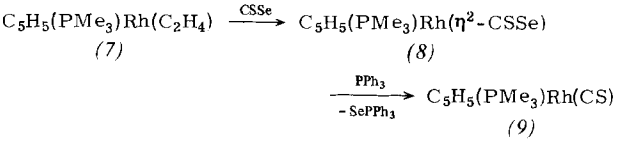
(1) reacts with COS to give $C_5H_5(PMe_3)Co(CO)$ in almost quantitative yield[5]. Possibly the complex *(4)* analogous to *(2)* is formed as labile intermediate, which then undergoes further reaction with the PMe_3 present in the solution with elimination of a sulfur atom to give *(5)*.



Should this be the case, then—assuming an analogous reaction course—the thiocarbonyl complex *(3)* ought to be formed from CSSe and *(1)* *via* the intermediate *(6)*. This expectation is only partially fulfilled. On reaction of *(1)* with thiocarbonyl selenide at −20 °C in toluene a mixture of *(3)* and *(6)* is obtained, which owing to the difference in solubility of the complexes in hexane [*(3)* is readily soluble and *(6)* is only sparingly soluble] can be easily separated. *(6)* reacts with PPh_3 in benzene (50 °C, 1 h) to give *(3)* in quantitative yield.



CSSe is also a very suitable source of CS for the preparation of other thiocarbonyl complexes. Thus, replacement of the ethylene ligand in *(7)*[6] by CSSe (benzene, 50 °C, 5 h) leads to *(8)*[4], which reacts with PPh_3 (benzene, 50 °C, 45 min) to give *(9)* in quantitative yield. The triphenylphosphane complex $C_5H_5(PPh_3)Rh(CS)$ analogous to *(9)* was recently synthesized starting from $(PPh_3)_2Rh(CS)Cl$ and NaC_5H_5[7].



The use of CSSe opens a new synthetic route to thiocarbonyl-metal complexes, which hitherto were mainly obtained from CS_2 or $CSCl_2$[8]. CSSe is of particular advantage if the potential alternative metal-(η^2-CS_2) compound is kinetically inert toward PPh_3 or other sulfur-abstracting agents.

Table 1. Spectroscopic data of the thiocarbonyl complexes *(3)* and *(9)*.

(3): ^{1}H-NMR ([D$_6$]-benzene): δ = 4.74 (5H; d, J_{PH} = 0.9 Hz), 1.14 (9H; d, J_{PH} = 9.8 Hz). IR (CS_2): 1270 cm^{-1} (CS-stretching vibration). MS (70 eV): *m/e* (I_r) = 244 (68; M^+), 200 (100; $C_5H_5CoPMe_3^+$), 168 (16; $C_5H_5CoCS^+$), 124 (50; $C_5H_5Co^+$).

(9): ^{1}H-NMR ([D$_6$]-benzene): δ = 5.24 (5H; d × d, J_{PH} = 0.4, J_{RhH} = 0.7 Hz), 1.24 (9H; d × d, J_{PH} = 10.4, J_{RhH} = 1.6 Hz). IR (CS_2): 1279 cm^{-1}. MS (70 eV): *m/e* (I_r) = 288 (100; M^+), 244 (61; $C_5H_5RhPMe_3^+$), 212 (31; $C_5H_5RhCS^+$), 168 (46; $C_5H_5Rh^+$), 147 (28; $RhCS^+$).

[*] Prof. Dr. H. Werner, Dipl.-Chem. O. Kolb
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

Received: August 2, 1979 [Z 326 IE]
German version: Angew. Chem. 91, 930 (1979)

CAS Registry numbers:
(1), 63413-01-4; (3), 71888-45-4; (6), 71888-44-3; (7), 69178-16-1; (8), 71882-20-7; (9), 71901-53-6

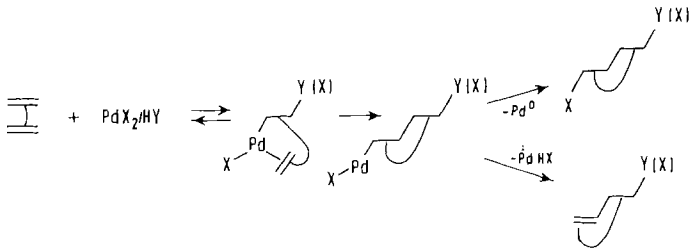
[1] Complexes with Carbon Sulfides and Selenides as Ligands, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie and by gifts of chemicals from BASF AG, Ludwigshafen, and DEGUSSA, Hanau, Germany. – Part 1: [2].
[2] *H. Werner, K. Leonhard, Ch. Burschka*, J. Organomet. Chem. *160*, 291 (1978).
[3] *I. S. Butler, N. J. Coville, D. Cozak*, J. Organomet. Chem. *133*, 59 (1977); *M. Herberhold, M. Süss-Fink*, Chem. Ber. *111*, 2273 (1978).
[4] *O. Kolb*, Diplomarbeit, Universität Würzburg 1979.
[5] *K. Leonhard*, unpublished results.
[6] *H. Werner, R. Feser*, Angew. Chem. *91*, 171 (1979); Angew. Chem. Int. Ed. Engl. *18*, 157 (1979).
[7] *F. Faraone, G. Tresoldi, G. A. Loprete*, J. Chem. Soc. Dalton Trans. *1979*, 933.
[8] *I. S. Butler*, Acc. Chem. Res. *10*, 359 (1977); *B. D. Dombek, R. J. Angelici*, Inorg. Chem. *15*, 1089 (1976); *J. W. Buchler et al.*, Z. Naturforsch. *B 33*, 1371 (1978).

Cyclic Systems by Palladium-Catalyzed Oxidation of Diolefins[**]

By *Andreas Heumann, Marius Reglier*, and *Bernard Waegell*[*]

The direct catalytic oxidation of olefins (except ethylene[1]) in the presence of palladium salts has only recently acquired importance in synthetic organic chemistry[2]. With the system $PdCl_2/CuCl_2$/buffered acetic acid it is possible to add chlorine and the acetoxy group[4] to strained olefins such as norbornene[3a] or apopinene[3b].

We have found that not only compounds from the norbornene series but also monocyclic and acyclic hydrocarbons—providing they contain two double bonds—can be oxidized selectively and in good yields with palladium salts. The reaction is of general utility [examples: *(1)*, *endo-(6)*, *(10)*, 5-methylenecyclooctene[5]] and proceeds according to the following Scheme:

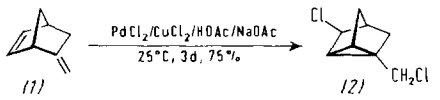


On addition of $CuCl_2$ (2 mol per mol olefin) the reaction becomes catalytic with regard to the palladium salt ($PdCl_2$ 0.03 mol-%); the use of buffered (NaOAc) acetic acid as solvent facilitates the isolation of various types of disubstituted final products. The second double bond in the substrate stabilizes the intermediary (and often isolable) Pd-σ-complex and, moreover, is inserted into the C—Pd bond. C–C coupling, *i.e.* cyclization, occurs and the σ-π complex affords a new σ-complex which can readily react by β-elimination or reductive elimination to give the metal-free final products.

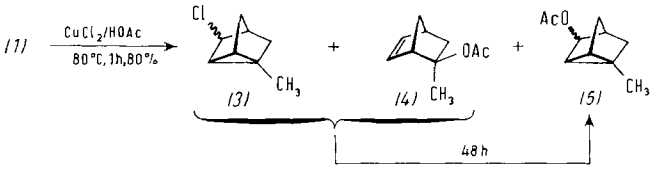
[*] Prof. Dr. B. Waegell, Dr. A. Heumann, Dipl.-Chem. M. Reglier
Laboratoire de Stéréochimie, associé au CNRS
Université d'Aix-Marseille
Centre de St-Jérôme, F-13013 Marseille (France)

[**] This work was supported by the Délégation Générale à la Recherche Scientifique et Technique (DGRST: décision d'aide n° 77.7.0755).

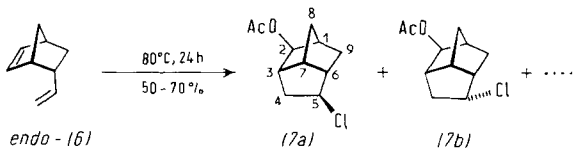
Under these conditions 5-methylenenorbornene *(1)* furnishes only the dichlorinated nortricyclene derivative *(2)*[6].



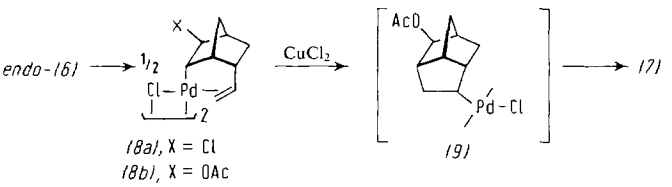
This selective dichlorination is the result of a $PdCl_2/CuCl_2$ catalysis; $CuCl_2$ alone catalyzes only the addition of HCl or HOAc to give *(3)*, *(4)*, and *(5)*.



Reaction of the structurally related 5-vinylnorbornene *(6)* (*exo*/*endo* = 24/76) with $PdCl_2/CuCl_2$/HOAc/NaOAc leads to the isomeric brendane derivatives *(7a)* and *(7b)* in the ratio 7:3; noncyclized chlorides are also formed.

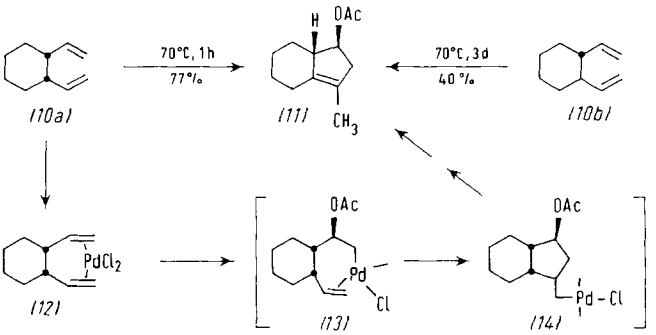


The structures of the compounds *(7)*[7] were confirmed by degradation to the known 2-brendanone[8]; the position of the chlorine can be assigned by mechanistic considerations.



The base-catalyzed cleavage of HCl from *(7)* leads to 4-brenden-2-ol[9]. The complexes *(8a)* and *(8b)* can be isolated[10], and, at 80 °C, form the same products *(7)*.

A formal α,ω'-cyclization is observed on oxidation of *cis*- and *trans*-1,2-divinylcyclohexane *(10a)* and *(10b)* to the bicyclo[4.3.0]non-6-ene derivative *(11)*.



The formation of the isomer *(11)* can be regarded as a sequence of several stereoselective steps proceeding *via* the intermediates *(13)* and *(14)*[2]. Apparently, the *cis*-isomer *(10a)* has the "correct" stereochemistry; according to model considerations, however, the *trans*-isomer *(10b)* should also yield palladium complexes relatively easily. It can be seen that the

chosen models lead not only to synthetically interesting reactions but also give an insight into the reaction mechanism[5].

Experimental

Synthesis of *(11)*: A suspension of $PdCl_2$ (50 mg, 0.28 mmol), anhydrous $CuCl_2$ (2.7 g, 20 mmol) and sodium acetate (800 mg, 10 mmol) in glacial acetic acid (25 ml) is treated with *(10a)* (1.36 g, 10 mmol) and the stirred mixture is warmed to 70 °C for 1 h. After addition of 25 ml of water the mixture is cooled and extracted with pentane (4 × 15 ml). The combined pentane extracts are washed until neutral (1 × $NaHCO_3/H_2O$, 1 × $NaCl/H_2O$) and dried over $MgSO_4$. After removal of solvent in a rotary evaporator the crude product is distilled *in vacuo* (bulb-to-bulb, 80 °C/10 torr); yield 1.5 g (77%) *(11)*[11].

Received: July 16, 1979 [Z 316a IE]
German version: Angew. Chem. *91*, 924 (1979)

CAS Registry numbers:
(1), 694-91-7; *(2)*, 35406-02-1; *(3)*, 71887-53-1; *(4)*, 71887-54-2; *(5)*, 71927-85-0; *exo (6)*, 23890-32-6; *endo (6)*, 25093-48-5; *(7a)*, 71887-55-3; *(7b)*, 71962-06-6; *(10a)*, 1004-84-8; *(10b)*, 33383-06-1; *(11)*, 71887-56-4; *(8a)*, 53433-66-2; *(8b)*, 53433-69-5

[1] Review: *J. Smidt, W. Hafner, R. Jira, R. Sieber, J. Sedlmeier, A. Sabel*, Angew. Chem. *74*, 93 (1962); Angew. Chem. Int. Ed. Engl. *1*, 80 (1962).
[2] Reviews: *P. M. Henry*, Adv. Organomet. Chem. *13*, 363 (1975); *B. M. Trost*, Tetrahedron *33*, 2615 (1977).
[3] a) *W. C. Baird, Jr.*, J. Org. Chem. *31*, 2411 (1966); *R. Baker, D. E. Halliday*, J. Chem. Soc. Perkin Trans. II *1974*, 208; b) *R. M. Giddings, D. Whittacker*, Tetrahedron Lett. *1978*, 4077.
[4] *A. Heumann, B. Waegell*, Nouv. J. Chim. *1*, 277 (1977).
[5] *A. Heumann, M. Reglier, B. Waegell*, Angew. Chem. *91*, 925 (1979); Angew. Chem. Int. Ed. Engl. *18*, 867 (1979).
[6] *C. Lasne, A. Thuillier*, C. R. Acad. Sci. *C 273*, 1258 (1971).
[7] *(7a)*: IR ($CHCl_3$): 1735 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 4.17 (s, 2-H), 4.26 (m, 5-H), 2.04 (s, CH_3), 0.75 (2t, 9-H *"endo"*, J_1 = 14 Hz); *(7b)*: IR ($CHCl_3$): 1725 cm $^{-1}$; ^{1}H-NMR ($CDCl_3$): δ = 4.37 (s, 2-H), 4.40 (m, 5-H), 2.04 (s, CH_3).
[8] *A. Nickon, H. R. Kwasnik, C. T. Mathew, T. D. Swartz, R. O. Williams, J. B. Digiorgio*, J. Org. Chem. *43*, 3904 (1978). We thank Professor *A. Nickon*, The Johns Hopkins University of Baltimore, for the IR- and NMR spectra of 2-brendanone.
[9] The corresponding acetate is well known: *R. S. Bly, R. K. Bly, G. B. Konizer, S. P. Jindal*, J. Am. Chem. Soc. *98*, 2953 (1976).
[10] *W. T. Wipke, G. L. Goeke*, J. Am. Chem. Soc. *96*, 4244 (1974).
[11] *(11)*: IR (Film): 3020, 3000, 1440 (C=C), 1720 (C=O), 1250 cm^{-1} (C—O); ^{1}H-NMR ($CDCl_3$): δ = 4.86 (J_1 = 8, J_2 = 4, J_3 = 4 Hz, 1 H), 2.04 (s, 3 H), 1.6 (s, 3 H), 0.8—2.9 (m, 11 H); ^{13}C-NMR ($CDCl_3$): δ = 171.2 (C), 135.3 (C), 125.0 (C), 79.3 (CH), 53.1 (CH), 43.7 (CH_2), 32.8 (CH_2), 26.6 (CH_2), 26.0 (CH_2), 25.8 (CH_2), 21.3 (CH_3), 13.1 (CH_3); MS: *m/e* = 134 (*M* − 60, 100%).

Mechanistic Aspects of the Palladium-Catalyzed Cyclization of 5-Methylenecyclooctene[**]

By *Andreas Heumann, Marius Reglier,* and *Bernard Waegell*[*]

The palladium-catalyzed cyclization of diolefins represents a simple and direct method for the preparation of substituted bi- and poly-cyclic systems[1]. We report here on a further reaction of this kind, the cyclization of 5-methylenecyclooctene *(1)*, which is readily accessible in four steps from 1,5-cyclooctadiene. Cyclization of *(1)* in the presence of $PdCl_2$ (3 mol-%), $CuCl_2$ [2 mol per mol *(1)*] and HOAc/NaOAc affords the products *(2)* to *(5)* in the ratio 8:35:20:22 (Table 1)[2]. This reaction enables not only the preparation of relatively complex systems from readily accessible olefins but also an insight into the mechanism of this metal-catalyzed oxidative cyclization. The structures were assigned on the basis of the following findings: On base-catalyzed HCl-elimination, hydrolysis, and subsequent hydrogenation the reaction mixture afforded bicyclo[3.3.1]nonan-1-ol[3] and bicyclo[4.2.1]nonan-1-ol[4]. The *endo* configuration of the 4-chloro substituents in *(2)* and *(3)* can be unequivocally assigned by the chemical shift and the coupling constants of the CHX proton[5]. In contrast, the mobility of the C_4-bridge in the bicyclo[4.2.1]nonane system leads to almost identical multiplicities of the CHX protons in the NMR spectra of the 5-*endo*- and 5-*exo*-compounds[6]. Comparison of the CHX signals of *(5)* and of the *endo*-2-chlorobicyclo[4.2.1]nonane *(7)* obtained from *(6)*[6] (Table 1) showed that *(5)* is most probably the *endo* isomer.

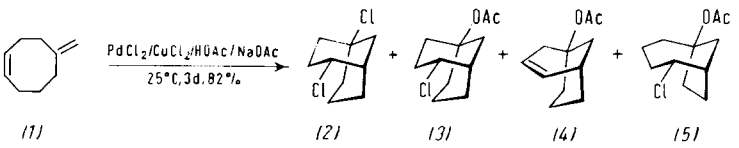
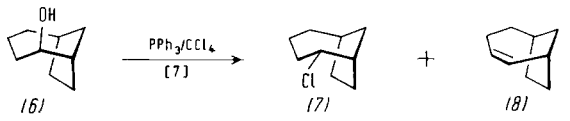


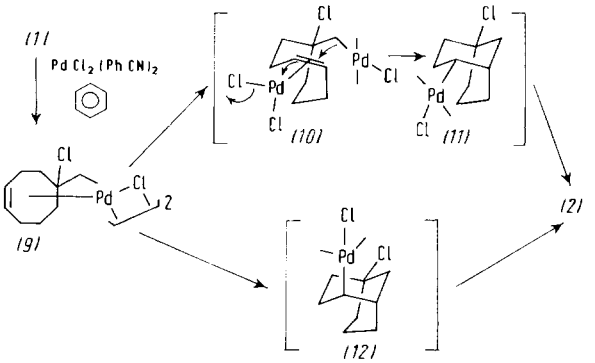
Table 1. Characteristic spectral data of the compounds *(1)*—*(5)* and *(7)*. ^{1}H-NMR in $CDCl_3$, IR in $CHCl_3$.

(1), ^{1}H-NMR: δ = 4.79 (s, 2 H, C=CH_2), 5.56—5.72 (m, 2 H, CH=CH)
(2), ^{1}H-NMR: δ = 4.24 (m, J_1 = 4, J_2 = 8, J_3 = 14 Hz, 1 H, CHCl)
(3), IR: 1720 cm^{-1}; ^{1}H-NMR: δ = 4.24 (m, J_1 = 4.5, J_2 = 9, J_3 = 13 Hz, 1 H, CHCl), 1.96 (s, 3 H, OAc)
(4), IR: 1720 cm^{-1}; ^{1}H-NMR: δ = 5.48—5.82 (m, 2 H, CH=CH), 1.98 (s, 3 H, OAc)
(5), IR: 1730 cm^{-1}; ^{1}H-NMR: δ = 4.04 (d, t, J_1 = J_2 = 4.5, J_3 = 9 Hz, 1 H, CHCl), 1.98 (s, 3 H, OAc)
(7), ^{1}H-NMR: δ = 4.05 (d, t, J_1 = J_2 = 4.5, J_3 = 9 Hz, 1 H, CHCl)



The reaction of *(1)* reveals the paramount importance of the reactivity of the C—Pd bond. In the reaction of *(1)* with $PdCl_2(PhCN)_2$ in benzene we were able to isolate the σ-π complex *(9)* by simple filtration and oxidatively cyclize it to the products *(2)*—*(5)*.

From the structure of *(9)* one could expect during the cyclization step a reaction behavior similar to that of the corre-



[*] Prof. Dr. B. Waegell, Dr. A. Heumann, Dipl.-Chem. M. Reglier
Laboratoire de Stéréochimie associé au CNRS
Université d'Aix-Marseille
Centre de St-Jérôme, F-13013 Marseille (France)

[**] This work was supported by the Délégation Générale à la Recherche Scientifique et Technique (DGRST: décision d'aide n° 77.7.0755). We are grateful to Hüls, Marl, for supplying the 1,5-cyclooctadiene.

sponding 1-methyl-4-cyclooctenyl derivatives[8]; however the exclusive isolation of *endo* derivative and the absence of diacetates are only difficultly reconcilable with an ionic mechanism. It would appear to us that an intermolecular catalyzed cyclization *via (10)* and *(11)* is possible; this reaction is formally comparable with the transannular amination of *N*-ethoxycarbonyl-8-azabicyclo[5.1.0]oct-3-ene to *N*-ethoxycarbonylnortropidine[9]. There is little likelihood, however, that the carbon bonded to palladium in *(10)*, which is much less nucleophilic than the N-atom in the reference compound[9], is capable of effecting formation of the intermediary complex *(11)*. Rather, *(2)* should be formed *via* a *(cis)* insertion to give *(12)* and oxidative cleavage with $CuCl_2$ with reversal of configuration. That the $CuCl_2$-catalyzed oxidation of the C—Pd bond could be a similar process has only recently been shown on singly deuterated olefins[10].

The bridgehead acetates *(3)—(5)* are formed analogously [*(4)* is formed by β-elimination] but it is still unclear at which stage the Cl is replaced by OAc.

Received: July 16, 1979 [Z 316b IE]
German version: Angew. Chem. *91*, 925 (1979)

CAS Registry numbers:
(1), 15890-49-0; *(2)*, 71887-57-5; *(3)*, 71887-58-6; *(4)*, 71887-59-7; *(5)*, 71887-60-0; *(6)*, 14565-34-5; *(7)*, 71887-61-1; *(9)*, 71882-23-0

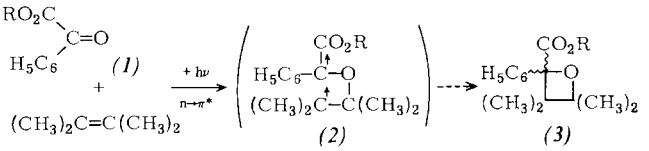
[1] *A. Heumann, M. Reglier, B. Waegell*, Angew. Chem. *91*, 924 (1979); Angew. Chem. Int. Ed. Engl. *18*, 866 (1979).
[2] GC analysis: capillary column PEG 20M, 56m. The mixture also contains an additional 15—20 unidentified products; total amount 10—15%.
[3] *W. G. Dauben, C. D. Poulter*, J. Org. Chem. *33*, 1237 (1968).
[4] *K. B. Becker*, Helv. Chim. Acta *60*, 94 (1977). We thank Dr. *Becker*, Universität Basel, for the spectra and a sample of bicyclo[4.2.1]nonan-1-ol.
[5] Cf. *W. F. Erman, H. C. Kretschmar*, J. Org. Chem. *33*, 1545 (1968); *A. Heumann, W. Kraus*, Tetrahedron *34*, 405 (1978); *C. F. Garbers, H. S. C. Spies, H. E. Visagie, J. C. A. Boeyens, A. A. Chalmers*, Tetrahedron Lett. *1978*, 81.
[6] Cf. *H. Sadlo, W. Kraus*, Tetrahedron *34*, 1965 (1978). We thank Dr. *H. Sadlo*, Universität Hohenheim, for a sample of *(6)*.
[7] *R. G. Weiss, E. J. Snyder*, Chem. Commun. *1968*, 1358.
[8] *M. Hanack, W. Kraus, W. Rothenwöhrer, W. Kaiser, G. Wentrup*, Justus Liebigs Ann. Chem. *703*, 44 (1967).
[9] *G. R. Wiger, M. F. Rettig*, J. Am. Chem. Soc. *98*, 4168 (1976).
[10] *J. E. Bäckvall, B. Åkermark, S. O. Ljunggren*, J. Am. Chem. Soc. *101*, 2411 (1979).

Unusually High Asymmetric Induction in the Photochemical Formation of Oxetanes[**]

By *Hans Gotthardt* and *Wolfgang Lenz*[*]

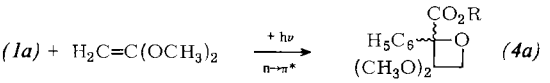
Asymmetric reactions giving products with high optical purity are of special interest in synthetic chemistry. We report here on the asymmetric induction in the photochemical formation of oxetanes according to *Paterno-Büchi*[1].

The optically active phenylglyoxylic acid (−)-menthyl ester *(1a)*[2] (0.025 M in benzene) combines with 2,3-dimethyl-2-butene (0.060 M) on irradiation[3], presumably *via* the intermediate *(2a)*, to give an oily (23.7:76.3)-mixture of the diastereomeric oxetanecarboxylates *(3a)*[4] in 90% yield as a result of a formal [2+2]-photocycloaddition. We have been able to isolate the main component in pure crystal form by gas chromatographic separation[5]. Subsequent hydrolysis with potassium hydroxide/dicyclohexano[18]crown-6 complex in toluene and esterification of the oxetanecarboxylic acid with diazomethane afforded the pure enantiomer *(3b)*



(a), R = (−)-$C_{10}H_{19}$; *(b)*, R = CH_3

with $[\alpha]_{546}^{20} = -15.13°$. In the same way, the diastereomeric mixture *(3a)* obtained on irradiation affords an enantiomeric mixture *(3b)* having a specific optical rotation of $[\alpha]_{546}^{20} = -8.05°$; in accord with the gas-chromatographically determined value this corresponds to an optical purity of 53%.



In an analogous way the irradiation of *(1a)* in the presence of 1,1-dimethoxyethene affords the diastereomeric oxetanecarboxylates *(4a)*[6] in 60% yield with an optical purity of 37% (GC and ^{1}H-NMR nalysis).

This surprisingly high asymmetric induction in an intermolecular photocycloaddition is unusual; for example, optical purities of up to only 17% are achieved in the thietane series[7].

Received: July 13, 1979 [Z 317 IE]
German version: Angew. Chem. *91*, 926 (1979)

CAS Registry numbers:
(1), 20229-41-8; *(3a)*, isomer 1, 71887-47-3; *(3a)*, isomer 2, 71887-48-4; (−)-*(3b)*, 71887-49-5; (±)-*(3b)*, 71887-50-8; *(4a)*, isomer 1, 71887-51-9; *(4b)*, isomer 2, 71887-52-0; 2,3-dimethyl-2-butene, 563-79-1; 1,1-dimethoxy ether, 922-69-0

[1] Paterno-Büchi reaction: *H. Meier* in *Houben-Weyl-Müller:* Methoden der Organischen Chemie. 4nd edit., Vol. IV/5b, p. 838, Thieme, Stuttgart 1975.
[2] *(1a)*: $[\alpha]_{546}^{25} = -50.2°$ (acetone).
[3] Hanau TQ 150 Mercury medium-pressure lamp behind pyrex.
[4] Diastereomeric mixture *(3a)*: b.p. 140—145 °C (bath)/0.005 mbar; IR (CCl_4): 1722 cm^{-1} (C=O).
[5] *(3a)*, main component: m.p. 79—80 °C (from 80% ethanol); $[\alpha]_{546}^{20} = -70.9°$ (acetone); ^{1}H-NMR (90 MHz, CCl_4, TMS): δ=0.30—2.07 (m, 18H), 0.83, 1.21, 1.28, 1.37 (4s, $4CH_3$), 4.39—4.67 (m, 1H), 7.12—7.32 (m, 3 aromatic H), 7.43—7.55 (m, 2 aromatic H).
[6] *(4a)*: b.p. 140—150 °C (bath)/0.005 mbar; IR (CCl_4): 1729 cm^{-1} (C=O); ^{1}H-NMR (C_6H_6): δ=2.84, 3.20 (2s, $2OCH_3$ of main product), 2.82, 3.23 (2s, $2OCH_3$), 4.38, 4.55 (AB, J=6.7 Hz, CH_2 of main product), 4.38, 4.58 (AB, J=6.7 Hz, CH_2).
[7] *H. Gotthardt, W. Lenz*, Tetrahedron Lett. *1979*, 2879.

Multiple Cyclopropylmethyl-Cyclobutyl Rearrangements in a Pentaspirohexadecanol[**]

By *Lutz Fitjer* and *Detlef Wehle*[*]

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

Polycyclic hydrocarbons in which a central *m*-sided ring (m=4, 6, 8...) is coupled to *m* peripheral *n*-sided rings such that each side of the central ring is simultaneously a side of a peripheral ring ([*m.n*]coronanes[1]) have so far not been reported in the literature. These compounds have an unusual

[*] Prof. Dr. H. Gotthardt, Dipl.-Chem. W. Lenz
Lehrstuhl für Organische Chemie der Gesamthochschule
Gaussstr. 20, D-5600 Wuppertal 1 (Germany)

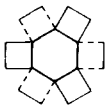
[**] This work was supported by the Fonds der Chemischen Industrie.

[*] Priv.-Doz. Dr. L. Fitjer, D. Wehle
Organisch-chemisches Institut der Universität
Tammannstrasse 2, D-3400 Göttingen (Germany)

[**] Polyspiranes, Part 3. This work was supported by the Deutsche Forschungsgemeinschaft. As Part 1 and 2: *L. Fitjer*, Angew. Chem. *88*, 803, 804 (1976); Angew. Chem. Int. Ed. Engl. *15*, 762, 763 (1976).

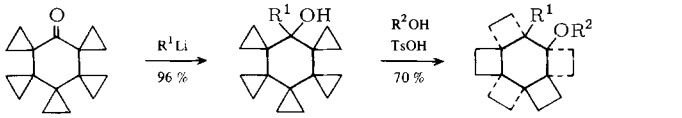
topology and can be shown to exhibit interesting chemical and physicochemical properties. A potentially useful technique for their synthesis is cascade-rearrangement[2], previously unexploited for the construction of repeating partial structures.

We report here on the initiation of a cascade of cyclopropylmethylcyclobutyl rearrangements in 16-methylpentaspiro[2.0.2.0.2.0.2.0.2.1]hexadecan-16-ol *(3)* as a possible key sequence for the synthesis of the [6.4]coronane *(1)*.



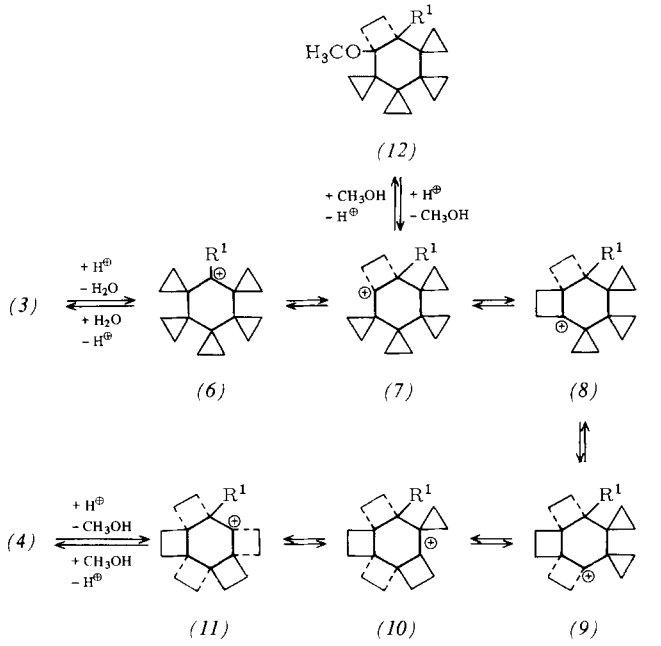
(1)

We obtained *(3)*[3] in 96% yield by reaction of pentaspiro[2.0.2.0.2.0.2.0.2.1]hexadecan-16-one *(2)*[4] with methyllithium in ether. On heating to 60 °C in methanolic solution with catalytic amounts of *p*-toluenesulfonic acid, *(3)* rearranges within 24—48 h *via* four gas-chromatographically detectable intermediates[5] into a preparative gas-chromatographically[5] separable solid to which we assign, on the basis of its mode of formation[6] and physical data[7], the structure of a 1-methoxy-2-methylhexacyclo[12.2.0.0^{2,5}.0^{5,8}.0^{8,11}.0^{11,14}]-hexadecane *(4)*. If the rearrangement is carried out in acetone/water (8:2), under otherwise the same conditions, the alcohol *(5)*[8] is obtained.



(2) *(3)*, R^1 = CH$_3$ *(4)*, R^1, R^2 = CH$_3$; *(5)*, R^1 = CH$_3$, R^2 = H

The formation of *(4)* and of *(5)* can be assumed to involve a five-fold cyclopropylmethyl-cyclobutyl rearrangement proceeding *via* the ionic intermediates *(6)*—*(11)*[6,9]. To confirm the postulated reaction course we interrupted the methanolysis of *(3)*, examined the unreacted *(3)* for accompanying rearrangement products, and isolated and characterized the first gas-chromatographically detectable intermediate product[5]. Since the composition of recovered *(3)* proved to be unchanged, and the first gas-chromatographically detectable intermediate was found to have the structure *(12)*[10], it can be assumed that the rearrangement *(3)*→*(4)* proceeds *via (7)* without previous addition of methanol to *(6)*. The remaining three intermediate products[5] could therefore be the methyl ethers of *(8)*, *(9)*, and *(10)*.



The above results would suggest that a more detailed examination of the utility of cascade rearrangement for the synthesis of [*m.n*]coronanes is certainly justified. Thus, by variation of R^1 the annelation of a further ring to *(11)* and hence a synthesis of the [6.4]coronane *(1)* ought to be possible, whereas using *m.n*-oriented fit, other [*m.n*]coronanes should be attainable from the corresponding polyspirane.

Received: August 7, 1979 [Z 318 IE]
German version: Angew. Chem. *91*, 927 (1979)

CAS Registry numbers:
(1), 71887-40-6; *(2)*, 60538-52-5; *(3)*, 71887-41-7; *(4)*, 71887-42-8; *(5)*, 71887-43-9; *(12)*, 71887-44-0

[1] By definition the proposed trivial name [*m.n*]coronanes (Lat.: corona = wreath, crown) applies only to compounds for which centrosymmetric forms are conceivable.

[2] By cascade rearrangement is meant a sequence of rearrangements, one coupled with the other in a chain-like fashion.

[3] *(3)*, m.p. 276—278 °C (capillary); IR (CCl_4): ν(O H) = 3634, ν(C H) = 3076, 3005 cm^{-1}; ^{1}H-NMR (60 MHz, $CDCl_3$, $CHCl_3$ int.): δ = 1.53 (s, 3H, CH_3), −0.60 to 1.00 (m, 21H); ^{13}C-NMR (25.2 MHz, $CDCl_3$): δ = 1.17, 1.35, 1.78 ($C_{ax.}$), 7.84, 10.97, 12.60 (C_{eq}), 25.12 (CH_3), 25.74, 26.91, 30.09 ($C_{quat.}$), 71.81 (C-16); MS: 244 (M^+, 2%), 216 ($M^+ - C_2H_4$, 100%).

[4] *L. Fitjer*, Angew. Chem. *88*, 804 (1976); Angew. Chem. Int. Ed. Engl. *15*, 763 (1976).

[5] 2.5 m × 1/4″ all-glass system, 10% OV 210 on Varaport 30, 60/80 mesh, 160 °C; relative retention times of the gas-chromatographically detectable products in the order of their appearance: 1.85 *(3)*, 1.52 *(12)*, 1.37, 1.29, 1.15, 1.00 *(4)*.

[6] Cf. also the results obtained on acid-catalyzed rearrangement of spiro[2.4]heptan-4-ol: *M. Hanack, H.-J. Schneider*, Justus Liebigs Ann. Chem. *686*, 8 (1965).

[7] *(4)*, m.p. 80—100 °C (capillary); IR (KBr): ν(C H) = 2800—3000 cm^{-1}; ^{1}H-NMR (60 MHz, CCl_4, TMS ext.): δ = 1.20 (s, 3H, CH_3), 1.20—2.20 (m, 20H), 3.06 (s, 3H, OCH_3); ^{13}C-NMR (25.2 MHz, $CDCl_3$): δ = 16.90, 18.61, 21.78, 22.07, 22.46, 22.53, 23.98, 27.32, 29.17, 33.10, 36.29 ($C_{sec.}$, CH_3), 50.69 (OCH_3), 57.34, 57.78, 58.82 (C-5, 8, 11), 65.07, 65.77 (C-2, 14), 92.40 (C-1); MS: 258 (M^+, 9%), 230 ($M^+ - C_2H_4$, 100%).

[8] *(5)*, m.p. 252—256 °C (capillary); IR (CCl_4): ν(O H) = 3618, ν(C H) = 2800—3000 cm^{-1}; ^{1}H-NMR (60 MHz, $CDCl_3$, $CHCl_3$ int.): δ = 0.80—2.30 (m, 21H, covering a s), 1.40 (s, 3H, CH_3); ^{13}C-NMR (25.2 MHz, $CDCl_3$): δ = 16.18, 18.36, 21.83, 21.98, 22.42, 27.27, 29.10, 30.47, 32.40, 40.36 ($C_{sec.}$, CH_3), 57.44, 57.49, 58.77 (C-5, 8, 11), 64.87, 66.07 (C-2, 14), 88.52 (C-1); on increasing the resolution to 0.10 Hz the signal at δ = 22.42 is resolved into two signals of equal intensity with a frequency difference of 0.17 Hz; MS: 244 (M^+, 4%), 216 ($M^+ - C_2H_4$, 88%); 3,5-dinitrobenzoate: m.p. 132—135 °C.

[9] The 1-methylcyclobutyl cation obtained as partial structure in *(7)*—*(11)* is > 2 kcal/mol more stable than the 1-methylcyclopropylmethyl cation obtained in *(6)*—*(10)*: *R. P. Kirchen, T. S. Sorensen*, J. Am. Chem. Soc. *99*, 6687 (1977).

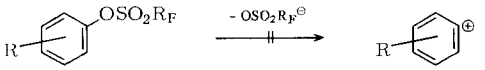
[10] *(12)*, m.p. 240—244 °C (capillary); IR (KBr): ν(C H) = 3077, 3000, 2937, 2820 cm^{-1}; ^{1}H-NMR (60 MHz, $CDCl_3$, $CHCl_3$ int.): δ = −0.50 to 1.00 (m, 16H, cyclopropane-CH_2), 1.12 (s, 3H, CH_3), 1.25—1.80 (m, 4H, cyclobutane-CH_2), 3.20 (s, 3H, OCH_3); ^{13}C-NMR (25.2 MHz, $CDCl_3$): δ = 4.49, 5.17, 5.73, 6.74, 8.14, 8.57, 8.81, 11.57 (cyclopropane-$C_{sec.}$), 20.77, 24.94, 25.12 (cyclobutane-$C_{sec.}$, CH_3), 22.15, 24.42, 24.56, 26.06 (C_{spiro}), 48.36 (CCH_3), 52.24 (OCH_3), 81.51 ($COCH_3$); MS: 258 (M^+, 19%), 243 (20%), 230 (76%), 215 (92%), 202 (100%).

Formation of Phenyl Cations in the Solvolysis of a Dienynyl Trifluoromethanesulfonate[**]

By *Michael Hanack* and *Ulrich Michel*[*]

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

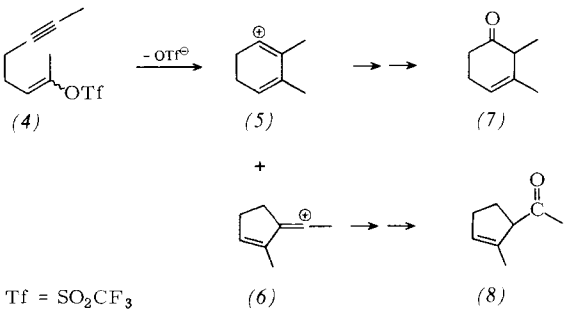
Phenyl cations *(3)* can not be generated by solvolysis of aryl esters even with use of the super-leaving groups triflate (trifluoromethanesulfonate) and nonaflate (nonafluorobutanesulfonate); in nucleophilic solvents, aryl triflates *(1)* and aryl nonaflates *(2)* react only with cleavage of the O—S bond[1].



(1), $R_F = CF_3$
(2), $R_F = C_4F_9$ *(3)*

It has been shown theoretically that the phenyl cation is respectively 29 kcal/mol and 4 kcal/mol more stable than the methyl and the vinyl cation, but 11 kcal/mol and 18 kcal/mol less stable than the ethyl and the 1-methylvinyl cation[2]. An experimentally convincing demonstration of the formation of phenyl cations *(3)* has been achieved in the diazotization of aryldiazonium salts[3].

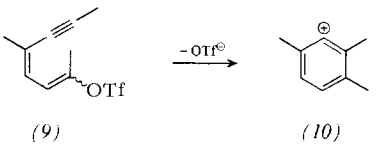
We report here on the first attempt to generate phenyl cations in a completely new way. As we have already found in earlier work, vinyl cations generated by solvolysis can react with participation of a triple bond. Thus the solvolysis of 1-methyl-1-hepten-5-ynyl triflate *(4)* in aqueous trifluoroethanol gave the ketones *(7)* and *(8)* by substitution of the cyclic vinyl cations *(5)* and *(6)*, respectively[4].



(4) *(5)* *(7)* *(6)* *(8)*

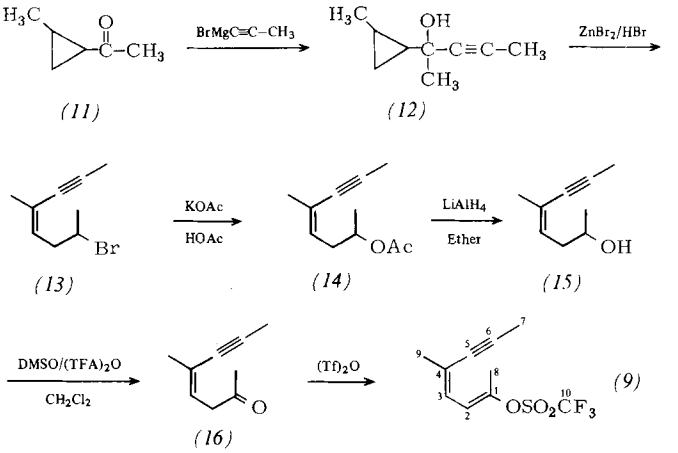
Tf = SO_2CF_3

We tried to solvolyze a dienynyl triflate corresponding to *(4)* in order to check whether it cyclizes to aromatic compounds. If this should be the case, a phenyl cation could be postulated as intermediate.



(9) *(10)*

For the dienynyl triflate a *cis*-substituted $C^3{=}C^4$ double bond is essential. As dienyne derivative we chose 1,4-dimethyl-1,3-heptadien-5-ynyl triflate *(9)*, which is readily accessible in a comparatively easy way[5] (see Scheme 1).



(11) *(12)* *(13)* *(14)* *(15)* *(16)* *(9)*

Scheme 1. Synthesis of *(9)* [6]. All intermediates have been unequivocally characterized. DMSO: dimethyl sulfoxide; $(TFA)_2O$: trifluoroacetic anhydride; $(Tf)_2O$: trifluoromethanesulfonic anhydride.

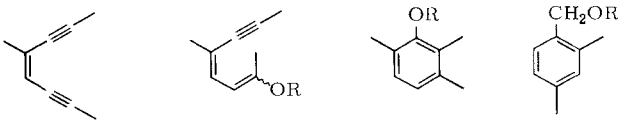
The dienynyl triflate *(9)* was solvolyzed in solvents of various ionic strength and nucleophilicity; the composition of the solvolysis products was determined by capillary gas chromatography, by ^1H- and ^{13}C-NMR spectroscopy of the separated products, and by comparison with authentic samples (Table 1).

Table 1. Solvolysis products of *(9)* in various solvents (relative yields).

Solvent/Buffer	T [°C]	t	*(17)* [%]	*(18)*	[%]	*(19)*	[%]	*(20)*	[%]	Unknown [%]
Anhydrous trifluoroethanol/Na_2CO_3	110	2 d	39	*(18a)*	10	*(19a)*	9	*(20a)*	23	19
Acetone/water/Na_2CO_3	100	3 d	66	*(18b)*	2 [a]	*(19b)*	7	*(20b)*	11	9 [b]
Acetone/water/pyridine	100	3 d	79	*(18b)*	1 [a]	*(19b)*	2	*(20b)*	4	9 [b]
Anhydrous ethanol/Na_2CO_3	100	10 d	70			*(19c)*	1	*(20c)*	9	20

[a] Isolated as ketone *(16)*. [b] In addition 5% of *(15)* is formed.

The products listed in Table 1 are characteristic for the solvolysis of *(9)* with formation of a vinyl cation; this can react *via* elimination to give the diyne *(17)* or by substitution with the solvent to give the ether *(18a)* or *via* the enol *(18b)* to give the ketone *(16)*. The formation of the phenol *(19b)* or of the phenyl ethers *(19a)* and *(19c)* indicates participation of the triple bond during the solvolysis: the phenyl cation *(10)* is



(17) *(18)* *(19)* *(20)*

(a), R = CH_2CF_3; *(b)*, R = H; *(c)*, R = C_2H_5

[*] Prof. Dr. M. Hanack, Dipl.-Chem. U. Michel
Institut für Organische Chemie der Universität
Lehrstuhl für Organische Chemie II
Auf der Morgenstelle 18, D-7400 Tübingen (Germany)

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

formed as intermediate; its substitution by solvent leads to *(19a)*, *(19b)*, or *(19c)*. The composition of the product reflects the typical solvent effects for a solvolysis reaction. In trifluoroethanol, a solvent of high ionic strength, the highest portions of cyclization products, in acetone/water and ethanol higher portions of elimination and substitution products are found.

The reaction path leading to formation of the benzyl derivatives *(20)* is still unclear, but there are all the indications of this reaction sequence also involving rearrangements and reactions with participation of the triple bond.

Received: September 10, 1979 [Z 319 IE]
German version: Angew. Chem. *91*, 928 (1979)

CAS Registry numbers:
(4), 71870-47-8; *(5)*, 71870-48-9; *(6)*, 71870-49-0; *(7)*, 62791-17-7; *(8)*, 1767-84-6; *(9)*, 71870-50-3; *(10)*, 71870-51-4; *(11)*, 930-56-3; *(12)*, 71870-52-5; *(13)*, 71870-53-6; *(14)*, 71870-54-7; *(15)*, 71870-55-8; *(16)*, 71870-56-9; *(17)*, 71870-57-0; *(18a)*, 71870-58-1; *(19a)*, 71870-59-2; *(19b)*, 2416-94-6; *(19c)*, 71870-60-5; *(20a)*, 71870-61-6; *(20b)*, 16308-92-2; *(20c)*, 71870-62-7

[1] *L. R. Subramanian, M. Hanack, L. W. K. Chang, M. A. Imhoff, P. v. R. Schleyer, F. Effenberger, W. Kurtz, P. J. Stang, T. E. Dueber*, J. Org. Chem. *41*, 4099 (1976).

[2] *P. J. Stang, Z. Rappoport, M. Hanack, L. R. Subramanian:* Vinyl Cations. Academic Press, San Francisco 1979, Chap. 9; *Y. Apeloig, P. v. R. Schleyer* in *R. A. Moss, M. Jones, Jr.:* Reactive Intermediates. Wiley-Interscience, New York, in press.

[3] *C. G. Swain, J. E. Sheats, K. G. Harbison*, J. Am. Chem. Soc. *97*, 796 (1975); *R. G. Bergstrom, R. G. M. Landells, G. H. Wahl, Jr., H. Zollinger, ibid. 98*, 3301 (1976).

[4] *M. J. Chandy, M. Hanack*, Tetrahedron Lett. *1975*, 4515.

[5] Cf. also *C. Descoins, D. Samain*, Tetrahedron Lett. *1976*, 745.

[6] *(9)*: ^{1}H-NMR ($CDCl_3$): $\delta = 1.93$ (s, 3H, 9-H), 2.03 (s, 3H, 7-H), 2.15 (s, 3H, 8-H); 6.31 (s, 2H, 2-H, 3-H); ^{1}H-NMR (C_6D_6): $\delta = 1.31$ (s, 3H, 8-H), 1.58 (s, 3H, 9-H), 1.71 (s, 3H, 7-H), 6.23—6.69 (m, 2H, 2-H, 3-H); ^{13}C-NMR 80 MHz ($CDCl_3$): $\delta = 4.4$ (C-7), 19.8 (C-9), 23.8 (C-8), 78.6 (C-5), 93.6 (C-6), 94.6, 110.5, 126.4, 142.3 (C-10), 119.3 (C-3), 124.3 (C-4), 125.1 (C-2), 144.5 (C-1); IR (film): 1150, 1210, 1245 s ($\nu(SO_2)$, $\nu(SO_2$ O)), 1415 s ($\nu(CF_3)$), 1650 vw (ν(C=C)), 2010 w (ν(C—C)).

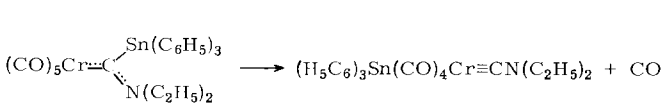
Spontaneous Rearrangement of a Carbene- to a Carbyne Complex: C,Cr Migration of a $Sn(C_6H_5)_3$ Group[1]

By *Ernst Otto Fischer, Helmut Fischer, Ulrich Schubert*, and *Richard B. A. Pardy*[*]

Dedicated to Professor Kurt Issleib on the occasion of his 60th birthday

We recently reported the synthesis of pentacarbonyl[diethylamino(triphenylstannyl)carbene]chromium(0) *(1)*, the first carbene complex in which a main group metal is bound to the carbene carbon[2], by reaction of pentacarbonyl(diethylaminocarbyne)chromium tetrafluoroborate with triphenylstannylpotassium.

We have now found that *(1)* rearranges spontaneously at room temperature, both in the solid state as well as in solution, with loss of CO to give *trans*-tetracarbonyl(diethylaminocarbyne)triphenylstannylchromium *(2)*.



(1) *(2)*

[*] Prof. Dr. E. O. Fischer, Dr. H. Fischer, Dr. U. Schubert, Dr. R. B. A. Pardy [**]
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Royal Society fellow. Permanent address: Canol House, School Lane, Cutnall Green, Nr. Droitwich (England)

The yellow crystalline product *(2)*, which is stable under nitrogen at room temperature, is readily soluble in polar solvents and moderately soluble in apolar solvents. This new type of SnCr compound *(2)* was identified by elemental analysis, mass spectrometry, vibration spectroscopy, and X-ray structure analysis[3]. The IR spectrum of *(2)* shows four absorptions in the ν_{CO} region: 2045 m, 1982 s, 1963 vs, 1952 s cm^{-1} (in octane); thus, as in the crystal (cf. Fig. 1), there is also marked perturbation of the local C_{4v} symmetry of the metal carbonyl moiety in solution.

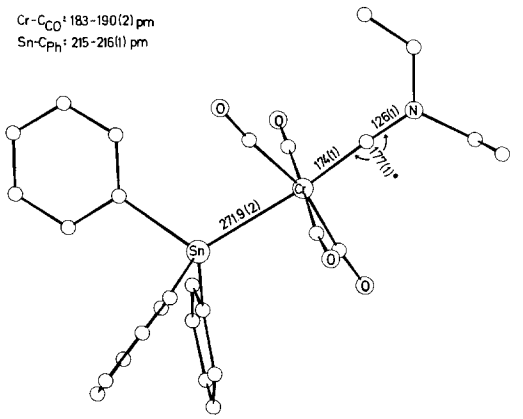


Fig. 1. Molecular structure of the carbyne complex *(2)* in the crystal.

The quantitative formation of *(2)* from *(1)* follows a first order rate law:

$$-d[(1)]/dt = k[(1)]$$

and the rate constants are almost independent of the polarity of the solvent, *e.g.*

$k = 0.85 \times 10^{-3}\ s^{-1}$ in *n*-octane ($\varepsilon_{20\,°C} = 1.95$)
$k = 1.00 \times 10^{-3}\ s^{-1}$ in nitromethane ($\varepsilon_{20\,°C} = 35.7$)

(each at 28.6 °C), thus ruling out a mechanism involving participation of ions.

Corresponding rearrangements have previously been observed in the case of carbene complexes of the type $(CO)_5CrC[N(C_2H_5)_2]X$ in solution, with X = Cl, Br and I, and in substance with X = Br[4], but not with X = F, CN, and NCS. The reaction now discovered by us, namely *(1)*→*(2)*, shows that presence of a lone pair on the migrating heteroatom is not necessary.

The finding that the bond between the carbene carbon atom and the halogen (X = Cl[5], Br[6]) or the tin atom[2] in the corresponding carbene complexes is longer than one would expect would seem to be directly connected with the feasibility of rearrangement to a carbyne complex.

Received: August 15, 1979 [Z 320 IE]
German version: Angew. Chem. *91*, 929 (1979)

CAS Registry numbers:
(1), 71886-77-6; *(2)*, 71849-76-8

[1] Transition Metal-Carbyne Complexes, Part 55.—Part 54: *E. O. Fischer, F. J. Gammel, J. O. Besenhard, A. Frank, D. Neugebauer*, J. Organomet. Chem., in press.

[2] *E. O. Fischer, R. B. A. Pardy, U. Schubert*, J. Organomet. Chem., in press.

[3] $C_{27}H_{25}CrNO_4Sn$; −10 °C; unit cell: $a = 945.1(8)$, $b = 1701(3)$, $c = 1790(2)$ pm, $\beta = 111.71(7)°$, $V = 2714 \times 10^6$ pm^3, $\rho_{calc} = 1.50$ g/cm^3; space group $P2_1/c$ ($Z = 4$). Syntex $P2_1$/XTL, $2° \leq 2\theta \leq 45°$, $\lambda = 71.069$ pm (graphite monochromator): 2460 structural factors ($F_0 \geq 4.5\,\sigma(F_0)$), $R = 0.070$.

[4] *H. Fischer, A. Motsch, W. Kleine*, Angew. Chem. *90*, 914 (1978); Angew. Chem. Int. Ed. Engl. *17*, 842 (1978).

[5] *G. Huttner, A. Frank, E. O. Fischer, W. Kleine*, J. Organomet. Chem. *141*, C17 (1977).

[6] *H. Fischer, A. Motsch, D. Neugebauer*, unpublished.

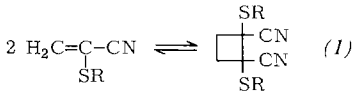
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1111-0871 $ 02.50/0*

Influence of 1,2-Functionalization with —C≡N, —CH=NR, or —CH=O on the Stability of the Cyclobutane System

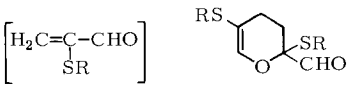
By *Karl-Dietrich Gundermann* and *Paul-Josef Hnida*[*]

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

1,2-Bis(alkylthio)- and 1,2-bis(arylthio)-1,2-cyclobutanedicarbonitriles *(1)* are readily formed by spontaneous dimerization of the corresponding acrylonitriles[1]. The dimerization is an equilibrium reaction; at 100 °C about 50% of the monomer is present[1b]. In order to check the influence of substituents on the stability of the cyclobutane system we have already attempted the synthesis of α-(alkylthio)acroleins *(2)* as starting substances for 1,2-dicarbaldehydes of type *(6)* corresponding to *(1)* on a previous occasion. All these attempts, however, led to the Diels-Alder dimers *(3)*[1a,2] instead of *(2)* [or *(6)*].



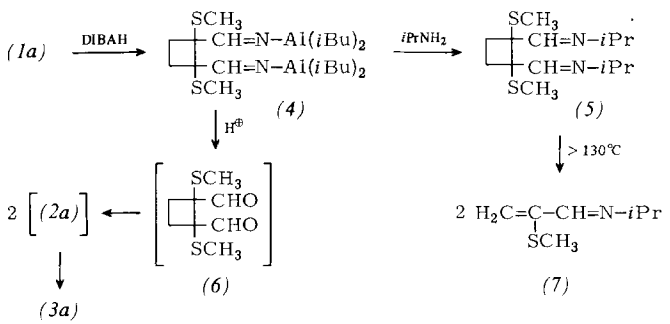
(1)



(2) *(3)*

The partial reduction of dinitriles *(1)* with diisobutylaluminum hydride (DIBAH) to *(4)* followed by hydrolysis ought to afford access to *(6)*, for reactions of this type have already been carried out successfully below 0 °C.

We have now found that reaction of *(1a)* with DIBAH in toluene at −70 °C leads to the aluminum compound *(4)*, which on careful treatment with isopropylamine affords the double Schiff base *(5)* in *ca.* 80% yield. Proof of the intact cyclobutane ring in *(5)* is provided by the AA'BB' signal of the —CH_2CH_2— group in the ^{1}H-NMR spectrum. *(5)* converts into the monomer *(7)* only above 130 °C, and apparently irreversibly.



(a), R = CH_3

On the other hand, acid hydrolysis of the product *(4)* obtained from *(1a)* and DIBAH leads, *inter alia*, to the dihydropyran derivative *(3a)* in *ca.* 30% yield. We conclude therefore that 1,2-bis(alkylthio)-1,2-cyclobutanecarbaldehydes of type *(6)* are apparently thermodynamically very unstable and readily form the "stable" dimers of type *(3)*—probably *via* the monomers *(2)*.

[*] Prof. Dr. K.-D. Gundermann, Dipl.-Chem. P.-J. Hnida
Organisch-chemisches Institut der Technischen Universität Clausthal
Leibnizstrasse 6, D-3392 Clausthal-Zellerfeld (Germany)

Experimental

Synthesis of *(5)*: A stirred solution of *cis,trans-(1a)*[3] (45.3 g) in toluene (1 l) under N_2 is treated within 45—60 min with 400 ml of a 20% solution of DIBAH in toluene. Stirring is continued for 2 h at −75 °C before adding 300 ml of anhydrous isopropylamine to the mixture. After a further 60 h at −75 °C 26 g of water is added dropwise and the temperature not allowed to exceed 20 °C. After removal of solvent *in vacuo* the residue is extracted with ether. Evaporation of the extract to dryness affords 77—81% *(5)*, m.p. 65 °C (from ethanol); IR (KBr): 1640 cm^{-1} (ν(C=N)); ^{1}H-NMR ($CDCl_3$): δ = 2.2 (mc, —CH_2CH_2—).

(3a) from *(1a)*: A 20% solution of DIBAH in toluene (90 ml) is added dropwise at −30 °C under N_2 to a stirred solution of *cis,trans-(1a)*[3] (10.2 g) in anhydrous toluene (250 ml). After 80 minutes' stirring, 400 ml of 5% sulfuric acid is added, the organic phase separated off, and the aqueous phase extracted several times with ether. The organic phase and the combined ether phases are washed with $NaHCO_3$ solution, with water, and then dried over sodium sulfate and fractionally distilled; yield *ca.* 3.0 g *(3a)*, b.p. 109 °C/0.6 torr; semicarbazone 149 °C (from ethyl acetate; IR (film): 1620 (ν(C=C)), 1730 cm^{-1} (ν(C=O)); ^{1}H-NMR ($CDCl_3$): δ = 6.54 (t, —CH—).

Received: July 31, 1979 [Z 322 IE]
German version: Angew. Chem. *91*, 930 (1979)

[1] a) *K.-D. Gundermann*, Intra-Sci. Chem. Rep. *6*, 91 (1972); b) *K.-D. Gundermann, R. Huchting*, Chem. Ber. *92*, 415 (1959).
[2] *P.-J. Hnida*, Dissertation, Technische Universität Clausthal 1979.
[3] *K.-D. Gundermann, A. Lösler*, Justus Liebigs Ann. Chem. *758*, 155 (1972).

The First 2,3,5,6-Tetraphosphabicyclo[2.2.0]hexane[1]

By *Rolf Appel, Volker Barth, Mechthild Halstenberg, Gottfried Huttner*, and *Joachim von Seyerl*[*]

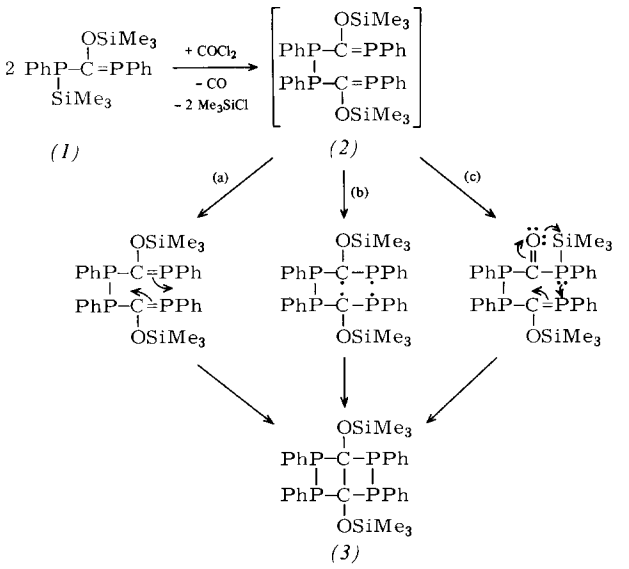
Dedicated to Professor Kurt Issleib on the occasion of his 60th birthday

We recently reported on the stepwise course of the reaction of phosgene with phenylbis(trimethylsilyl)phosphane in which the (phosphinomethylene)phosphane *(1)* and a secondary product of unknown structure but having the composition $[(PhP)_2(COSiMe_3)]_2$ are formed[1]. ^{31}P-NMR data[2] are not consistent with the assumption that *(1)* undergoes further reaction with phosgene with cleavage of a silyl group and P—P coupling to give *(2)*: Although the spectrum shows a characteristic fine structure for an AA'BB' spin system, the signal at δ = 164 for phosphorus of coordination 2 has disappeared.

By X-ray structure analysis[3] we have been able to identify this secondary product, which melts at 148—150 °C, as 1,4-bis(trimethylsiloxy)-2,3,5,6-tetraphenyl-2,3,5,6-tetraphosphabicyclo[2.2.0]hexane *(3)*. The non-equivalence of the AA' and BB' groups[2]—not apparent from formula *(3)*—is caused by strong twisting of the molecule: A molecular model or stereoscopic viewing of Figure 1 shows much more clearly than any two-dimensional representation of the molecule that the phosphorus atoms P1 and P1' have a different

[*] Prof. Dr. R. Appel, Dipl.-Chem. V. Barth, Dr. M. Halstenberg
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)
Prof. Dr. G. Huttner, Dipl.-Chem. J. von Seyerl
Lehrstuhl für Synthetische Anorganische Chemie der Universität
Postfach 7733, D-7750 Konstanz (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1111-0872 $ 02.50/0



chemical environment from that of P2 and P2′. Despite the fact that all P-atoms bear similar substituents the distances between the atoms not bound to each other, *viz.* P1, P1′ and P2, P2′, differ markedly.

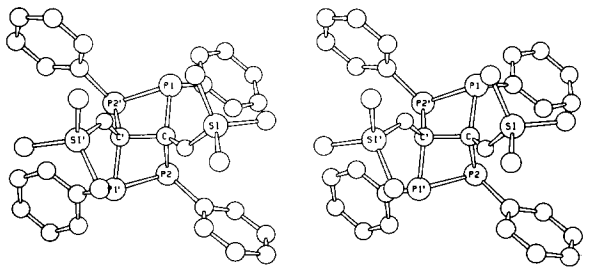
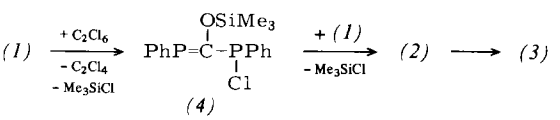


Fig. 1. Stereodiagram of the molecular structure of *(3)* in the crystal.

Distances [pm]		Angles [°]	
Si O	166.0(4)	C O Si	133.9(4)
O C	140.0(7)	P1 C P2	117.2(3)
C P1	188.7(6)	P1 C C′	96.8(4)
C P2	195.0(6)	P2 C C′	93.8(4)
C C′	157.0(9)	P1 C O	119.3(4)
P1 P2′	222.8(2)	P2 C O	112.1(4)
P2···P2′	317.4(3)	C′ C O	113.3(5)
P1···P1′	416.0(3)	C P1 P2′	77.3(2)
		C P1 Ph	108.6(3)
		P2 P1′ Ph	106.7(2)
		C P2 P1′	76.4(2)
		C P2 Ph	102.4(3)
		P1 P2′ Ph	104.3(2)

Spectroscopic evidence for the intermediary existence of *(2)* is still lacking. The postulated reaction course—spontaneous intramolecular [2+2]-cycloaddition of *(2)* as pericyclic (a) free-radical (b) or multistep process (c)—is supported by isolation of an intermediate analogous to *(2)* in the reaction of phenylbis(trimethylsilyl)phosphane with phenyl isocyanide dichloride, an aza analog of phosgene[4] and by an independent synthesis of *(3)* from *(1)* and hexachloroethane.



In analogy to the formation of tetraorganyldiphosphanes from trimethylsilyl-substituted organylphosphanes and C_2Cl_6[5], it is assumed that the intermediate *(4)* reacts with *(1)* with P P-coupling.

Received: July 2, 1979 [Z 323a IE]
German version: Angew. Chem. *91*, 935 (1979)

[1] Part 18 of Phosphorus-Carbon-Halogen Compounds.—Part 17: *R. Appel, V. Barth*, Angew. Chem. *91*, 497 (1979); Angew. Chem. Int. Ed. Engl. *18*, 469 (1979).

[2] $^{31}P\{^1H\}$-NMR (CD_2Cl_2, H_3PO_4 ext.): $\delta = +22.5$, -24.6 [multiplet of AA′BB′-type with $J(AA') = 101.6$, $J(AB) = 98.8$, $J(AB') = 0.8$, $J(BB') = 10.3$ Hz]; the observed spectrum is identical to one simulated by "itercall" (Bruker).

[3] *(3)* crystallizes monoclinically, space group C2/c, with the lattice constants $a = 2403.7(30)$, $b = 912.2(6)$, $c = 1620.6(20)$ pm, $\beta = 112.14(9)°$, $V = 3309.7 \times 10^6$ pm^3; $Z = 4$; $\rho_{calc} = 1.27$/g cm^3. 1274 independent reflections were measured (Syntex P21, ω scan, $T = 173$ K); structure solved by conventional methods (Syntex XTL), refinement to $R_1 = 0.067$.

[4] *R. Appel, V. Barth, F. Knoll, I. Ruppert*, Angew. Chem. *91*, 936 (1979); Angew. Chem. Int. Ed. Engl. *18*, 873 (1979).

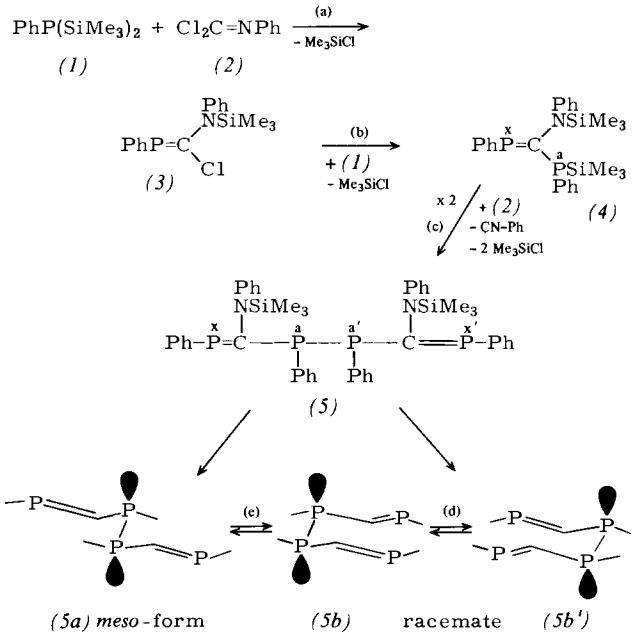
[5] *R. Appel, K. Geisler, H. F. Schöler*, Chem. Ber. *110*, 376 (1977).

The First 1,3,4,6-Tetraphospha-1,5-hexadiene, a Molecule with Fluxional Bonds (Identical Tetraphospha Cope Rearrangement) and Configurational Isomerism[1]

By *Rolf Appel, Volker Barth, Fritz Knoll*, and *Ingo Ruppert*[*]

Dedicated to Professor Kurt Issleib on the occasion of his 60th birthday

In continuation of our investigations on the reactions of silylphosphanes with halogen-carbon compounds we have now examined the reaction of isocyanide dihalides such as *(2)*, as aza analogs of phosgene, with phenylbis(trimethylsilyl)phosphane *(1)*. By replacing the oxygen by the imino function we had anticipated a stabilization and hence possible isolation of the postulated reactive intermediates *(3)* and *(5)*, which could not be detected in the reaction with phosgene[2].



As expected *(1)* reacts with *(2)* in *n*-pentane in the molar ratio 2:1 *via* double condensation and a 1,3 silyl shift to give the (phosphinomethylene)phosphane *(4)*, which could be

[*] Prof. Dr. R. Appel, Dipl.-Chem. V. Barth, Dr. F. Knoll, Dr. I. Ruppert Anorganisch-chemisches Institut der Universität Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

identified by means of its distinctive AX-type ^{31}P-NMR spectrum; however, it has not yet been isolated in analytically pure form. On NMR investigation of the reaction in benzene an additional ^{31}P-signal appeared in the spectrum very close to the X-doublet of *(4)* at $\delta = 216$, which gradually disappeared again and which we assign to the intermediate *(3)*.

Further reaction with isocyanide dichloride *(2)* leads to elimination of phenyl isocyanide and precipitation of a yellow solid (m.p. 135 °C). Correct elemental analysis, cryoscopic molecular weight determination, and the sharp AA'XX'-^{31}P$\{^1$H$\}$ spectrum of *(5a)* at 30 °C shown in Figure 1—especially the PP coupling parameters and the characteristic downfield shift of the methylenephosphane (X) component (Table 1)—confirm the constitution of a tetraphosphahexadiene *(5)*.

Table 1. ^{31}P$\{^1$H$\}$-NMR data of the methylenephosphanes (Varian FT80A, 32.4 MHz, H_3PO_4 ext.).

(4) (C_6D_6): $\delta = -39.0$ [d, $^2J(P^xP^a) = 78.9$ Hz, P^a], 213.8 [d, $^2J(P^aP^x) = 78.9$ Hz, P^x]

(5a) (CD_2Cl_2, room temp.): $\delta = -12.3$ [P^a], 258.0 [P^x]; AA'XX' spectrum [7] with $^1J(P^aP^{a'}) = 112.5$, $^2J(P^aP^x) = 157.4$, $^3J(P^aP^{x'}) = 24.6$, $^5J(P^xP^{x'}) = 38.6$ Hz (notation: see scheme)

(5b) (CD_2Cl_2, -10 °C coalescence temp.): $\delta = 115.7$ (maximum of the exchange peaks); (CD_2Cl_2, -70 °C): $\delta = -3.2$ [P^a], 234.6 [P^x]; AA'XX' spectrum [7] with $^1J(P^aP^{a'}) = 150.9$, $^2J(P^aP^x) = 136.6$, $^3J(P^aP^{x'}) = 56.4$, $^5J(P^xP^{x'}) = 0.0$ Hz

Since analysis showed *(5)* to be homogeneous the additional exchange signal observed at room temperature must be assigned to a species *(5b)* having the same composition. Its individualization at -70 °C to a further AA'XX' multiplet pattern (Fig. 1) shows that *(5b)* is a diastereomeric tetraphosphahexadiene. Since its diphosphane (A)- and methylenephosphane (X)-signal groupings coalesce centrally and reversibly as a function of the recording temperature, we assume that *(5b)* experiences an identical rearrangement—independently of *(5a)*[3].

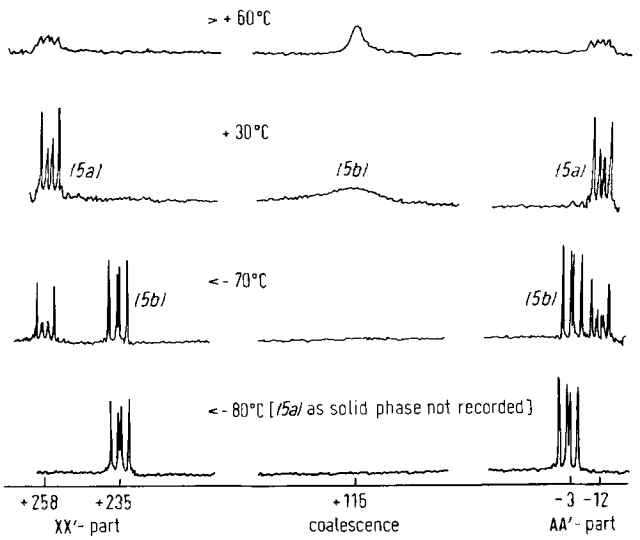


Fig. 1. Temperature dependent ^{31}P$\{^1$H$\}$-NMR spectrum of *(5)*; coupling parameters, see Table 1.

The equilibrium (d) would represent the first sigmatropic [3,3]-shift with P—P bond rupture, P—P linkage and migration of phosphorus-carbon p_π—p_π bonds; thus it would fully correspond to the degenerate Cope rearrangement in the carba-analogous 1,5-hexadiene system[4].

Diphosphanes with the substitution pattern $(XYP)_2$ are usually obtained as a 1:1 mixture of the *meso* form and racemate, which are distinguishable ^{31}P-NMR spectroscopically[5]. The oxidative coupling step *(4)*→*(5)* [eq. (c)] also leads to a statistically equimolar mixture of the diastereomers *(5a)* and *(5b)*. *(5a)* slowly crystallizes out below -80 °C (cf. Fig. 1) and can be separated by low-temperature filtration. Both the filtrate enriched in *(5b)*, and *(5a)* redissolved below -80 °C, rapidly equilibrate again above -70 °C to the racemate/*meso* form mixture [Equilibrium (e)]. Attempts with chiral shift reagents to identify *(5a)* as *meso* form and *(5b)* as racemate have proven unsuccessful. However, the rapid equilibration (d) of *(5b)* at room temperature, a temperature at which *(5a)* remains unchanged, would suggest—in analogy to the stereochemical requirements of the Cope rearrangement—a reaction starting from the conformation *(5b/5b')*, which is realizable only in the racemate (see scheme). With the same preferred *trans* location of the lone pairs the required proximity of the reactive P—C centers is not reached in the *meso* form. Consequently, this diastereomer only shows reversible line-broadening at a much higher temperature (Fig. 1, 60 °C); on raising the temperature further this is accompanied by an irreversible decomposition.

This finding would indicate a further more energy-demanding rearrangement process, *e.g.* following 180° rotation about the P—P axis in *(5a)*[6]. An unequivocal assignment of the diastereomers and simultaneous elucidation of the arrangement of the (*E,Z*)-substituents at the C—P bond is expected from an X-ray structure analysis of a crystal fraction which, according to low-temperature ^{31}P-NMR analysis, contains only the *(5a)*-form.

The marked analogy between the reaction of methylene*phosphanes* and corresponding alkene systems would suggest that the P—C bond does not have the known ylide character of methylene*phosphoranes* but in this connection is rather to be compared with the olefinic double bond.

Received: July 2, 1979 [Z 323b IE]
German version: Angew. Chem. *91*, 936 (1979)

CAS Registry numbers:
(1), 24103-44-4; *(2)*, 622-44-6; *(3)*, 71901-94-5; *(4)*, 71887-45-1; *(5a)*, 71887-46-2; *(5b)*, 71929-10-7

[1] Part 19 of Phosphorus-Carbon-Halogen Compounds.—Part 18: *R. Appel, V. Barth, M. Halstenberg, G. Huttner, J. von Seyerl*, Angew. Chem. *91*, 935 (1979); Angew. Chem. Int. Ed. Engl. *18*, 872 (1979).

[2] *R. Appel, V. Barth*, Angew. Chem. *91*, 497 (1979); Angew. Chem. Int. Ed. Engl. *18*, 469 (1979).

[3] The activation energy of *ca.* 10 kcal/mol, as determined by the coalescence method, is much lower than that found for other (hetero) Cope rearrangements.

[4] *J. J. Gajewski, N. D. Conrad*, J. Am. Chem. Soc. *100*, 6268 (1978); and references cited therein.

[5] Review: *J. B. Lambert, G. F. Jackson, D. C. Mueller*, J. Am. Chem. Soc. *92*, 3093 (1970).

[6] Cf. the discussion for a diaza Cope system by *E. Goldschmitt, F. Vögtle*, Chem. Exp. Didakt. *1*, 335 (1975).

[7] On the basis of this parameter the experimental spectra are identical with the simulated ("itercall", Bruker) spectra.

Tetracarbanilanilidodichromium(II): A Clue to the Understanding of the CrCr Quadruple Bond[**]

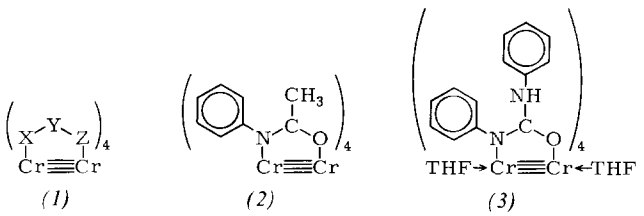
By *F. Albert Cotton, William H. Ilsley,* and *Wolfgang Kaim*[*]

Numerous complexes of the general type *(1)* have been prepared and investigated crystallographically since the

[*] Prof. Dr. F. A. Cotton, Dr. W. H. Ilsley, Dr. W. Kaim
Department of Chemistry, Texas A & M University
College Station, Texas 77843 (USA)

[**] This work was supported by the Robert A. Welch Foundation.—*W. K.* acknowledges a Liebig Stipend from the Verband der Chemischen Industrie, Frankfurt am Main.

structural characterization of a CrCr quadruple bond in $Cr_2(O_2CCH_3)_4(H_2O)_2$[1]. The results obtained so far allow a strict classification of the compounds *(1)* into two distinctly different groups: Complexes with four η^2-carboxylato ligands, $Cr_2(O_2CR)_4$, have Cr–Cr-bond lengths ranging from 2.283(2) Å to 2.541(1) Å[2]. The metal-metal distance is somewhat shorter in $[Cr_2(CO_3)_4(H_2O)_2]^{4-}$, *viz.* 2.214(1) Å[2c]. *All* compounds of this kind either contain strongly coordinated axial ligands, or they display a chain structure with short *inter*molecular Cr···O distances[2].—All the other complexes with the general structure *(1)* contain "supershort" (<1.90 Å) CrCr bonds; the bridge ligand type varies from arene[3] and heteroarene[4] to ylide[5] and carboxamide anions[6]. Molecules of this type do not exhibit any axial coordination.



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

The short Cr–Cr distance of 1.873(4) Å in tetraacetanilidodichromium *(2)*[6] has prompted the hypothesis, that the presence or absence of axial ligands *alone* might be responsible for the enormous variability of the CrCr bond length in Cr_2^{4+} complexes[6]. We have, therefore, increased our efforts to prepare and investigate crystallographically compounds with ligands similar to carboxylates.

We report here on the synthesis and X-ray structure analysis of tetracarbanilanilidodichromium(II), which is formed in the reaction of carbanilanilidolithium with dichromium tetracetate in tetrahydrofuran (THF). Crystals were obtained by diffusion (THF/*n*-hexane). Figure 1 shows the molecular structure of the $Cr_2[PhNC(NHPh)O]_4(THF)_2$ unit *(3)*[7].

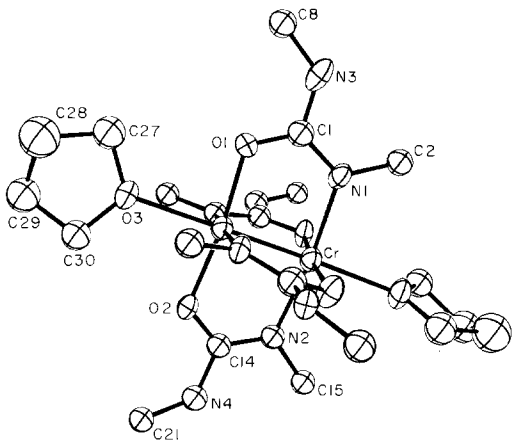


Fig. 1. Structure of $Cr_2[PhNC(NHPh)O]_4 \cdot 2THF$ *(3)* in the crystal. For clarity only the carbon of attachment of each phenyl group is shown.

The crucial difference between *(3)* and the otherwise very similar compound *(2)* lies in the influence of two relatively tightly bound THF molecules in the axial positions of *(3)*; the Cr···O'(THF) distance is 2.350(5) Å. This combination of coordinated solvent molecules increases the Cr–Cr-distance by 0.37 Å, from 1.873(4) Å in *(2)* to 2.246(2) Å in *(3)*.

Other important bond lengths and angles are: Cr–O 1.993(6), Cr–N 2.093(7) Å; Cr–Cr–O'(THF) 178.2(2), Cr–Cr–O 93.8(2), Cr–Cr–N 86.5(2)°. Comparison with *(2)*[6] indicates weaker bonding to the bridging ligands in *(3)*.

The enormous lengthening of the CrCr quadruple bond in *(3)* with respect to *(2)*, despite an essentially similar ligand type, shows that axial coordination is, (or, at least, can be) the major determining factor for the length (and strength) of the Cr–Cr bond. The somewhat shorter distance in *(3)* compared to the values for typical carboxylates ($d_{CrCr} \approx 2.35$ Å)[2] may be caused by the stronger basicity of the carboxanilide anion. Further investigations as well as theoretical studies[8] are necessary in order to distinguish the effects of axial and bridging ligands, and thus to understand the mechanisms of the variability of the chromium-chromium quadruple bond.

Received: August 13, 1979 [Z 324 IE]
German version: Angew. Chem. *91*, 937 (1979)

CAS Registry number:
(3), 71888-46-5

[1] *F. A. Cotton, B. G. DeBoer, M. D. LaPrade, J. R. Pipal, D. A. Ucko*, J. Am. Chem. Soc. *92*, 2926 (1970); Acta Crystallogr. *B 27*, 1664 (1971). The formally similar tetraallyl complex has a different structure: *G. Albrecht, D. Stock*, Z. Chem. *7*, 321 (1967); *T. Aoki et al.*, Bull. Chem. Soc. Jpn. *42*, 545 (1969).

[2] a) *F. A. Cotton, M. W. Extine, G. W. Rice*, Inorg. Chem. *17*, 176 (1978); b) *F. A. Cotton, G. W. Rice, ibid. 17*, 688 (1978); c) *ibid. 17*, 2004 (1978).

[3] *F. A. Cotton, S. Koch, M. Millar*, J. Am. Chem. Soc. *99*, 7372 (1977).

[4] *F. A. Cotton, P. E. Fanwick, R. H. Niswander, J. C. Sekutowski*, J. Am. Chem. Soc. *100*, 4725 (1978).

[5] *F. A. Cotton, B. E. Hanson, G. W. Rice*, Angew. Chem. *90*, 1015 (1978); Angew. Chem. Int. Ed. Engl. *17*, 953 (1978).

[6] *A. Bino, F. A. Cotton, W. Kaim*, J. Am. Chem. Soc. *101*, 2506 (1979).

[7] The red-brown crystals have the composition $Cr_2[PhNC(NHPh)O]_4 \cdot 2THF \cdot C_6H_{14}$; the *n*-hexane molecules occupy free spaces in the crystal lattice. This compound crystallizes in the space group Pccn; $a = 24.813(5)$ Å, $b = 13.408(3)$ Å, $c = 18.631(3)$ Å, $Z = 4$. The structure has been refined to conventional discrepancy indices of $R_1 = 0.0828$ and $R_2 = 0.1040$ using 1811 reflections having $I > 3\sigma(I)$.

[8] Cf. *M. Benard, A. Viellard*, Nouv. J. Chim. *1*, 97 (1977); *F. A. Cotton, G. G. Stanley*, Inorg. Chem. *16*, 2668 (1977); *M. Benard*, J. Am. Chem. Soc. *100*, 2354 (1978).

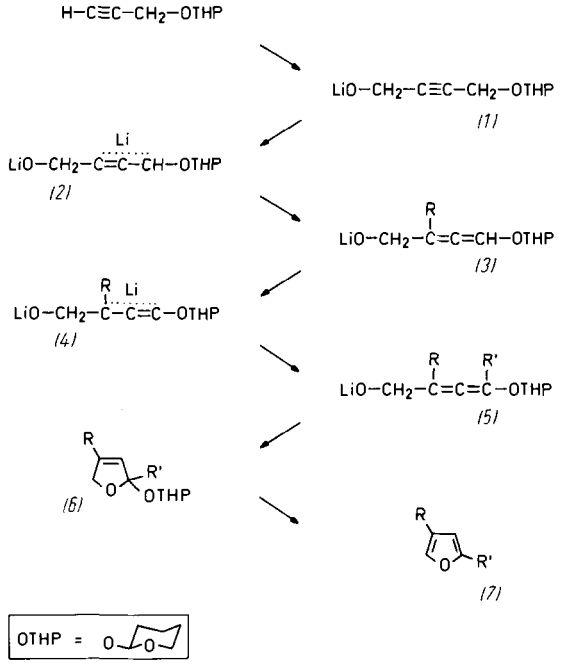
Metalated 2-Alkynyl- and 1,2-Alkadienyl 2-Tetrahydropyranyl Ethers: Versatile Building Blocks for Furan Syntheses[**]

By *Manfred Stähle* and *Manfred Schlosser*[*]

tert-Butyllithium metalates lithium 4-(2-tetrahydropyranyloxy)-2-butynolate *(1)* quantitatively to give the allenyllithium compound *(2)*. No side-reactions take place: neither the generally possible[1] hydrogen/metal exchange at the alcoholate group, nor the equally well known addition[2] of the organometallic compound to the triple bond is observed. The velocity and the uniform outcome of the reaction underlines once again the activating influence of an acetal group[3,4]. Methanol protonates *(2)* to afford the 4-(2-tetrahydropyranyloxy)-2,3-butadienolate (*(3)*: R = H); reaction with hexyl iodide or benzyl chloride yields the 2-alkylated derivatives (*(3)*: R = C_6H_{13}, $CH_2C_6H_5$). Further treatment with *tert*-butyllithium generates new allenyllithium compounds *(4)* which react with alkyl halides to give 4-alkylated 4-(2-tetrahydropyranyloxy)-2,3-butadienolates (*(5)*: R = C_6H_{13}; R′ = CH_3, $CH_2CH{=}CHCH_3$). The allenyl ethers *(3)* and *(5)* may be hydrolyzed with dilute acids and cyclized—presumably *via* a 2-(2-tetrapyranyloxy)-2,5-dihydrofuran *(6)* intermediate—to produce mono- and dialkylated furans (*(7a)*: R = C_6H_{13}, R′ = H, 67%; *(7b)*: R = $CH_2C_6H_5$, R′ = H, 39%;

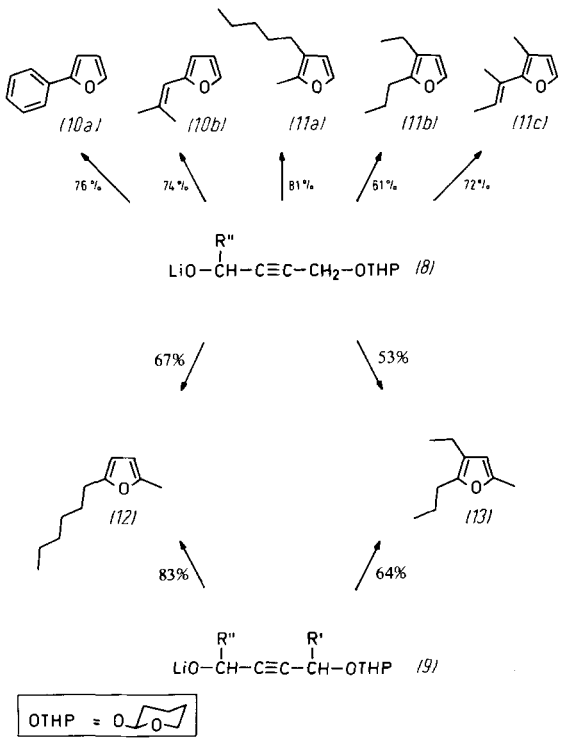
[*] Prof. Dr. M. Schlosser, Chem. techn. M. Stähle
Institut de Chimie Organique de l'Université
Rue de la Barre 2, CH-1005 Lausanne (Switzerland)

[**] This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project 2.693.0.76 and 2.188.0.78).



(7c): $R = C_6H_{13}$, $R' = CH_3$, 55%; *(7d)*: $R = C_6H_{13}$, $R' = CH_2CH{=}CHCH_3$, 15%). If desired, the alcoholates *(3)* and *(5)* may be neutralized and the alcohols, though fairly labile, isolated. More advantageously, however, the entire multistep reaction sequence, is performed as a one-pot reaction, starting off with the preparation of *(1)* from 2-propynyl(2-tetrahydropyranyl) ether, butyllithium, and formaldehyde.

In the same way it was possible to convert the singly and doubly branched tetrahydropyranyloxybutynolates *(8)* [$R'' = C_6H_5$, $CH{=}C(CH_3)_2$, CH_3, C_3H_7, (Z)-$(CH_3){=}CHCH_3$] and *(9)* [$R' = CH_3$; $R'' = C_3H_7$, C_6H_{13}] into 2-mono-, and 2,3- and 2,5-di- as well as 2,3,5-trisubstituted furans *(10)*—*(13)*. The structure and purity of all the furans are confirmed by NMR spectra and elemental analysis[8].



We are aware of only one example related to this new synthetic access to furans: After metalation, 2-octynyl 2-tetrahydropyranyl ether reacts with benzaldehyde to yield a product mixture, which upon treatment with acid gives rise to some 3-pentyl-2-phenylfuran[5].

Received: August 20, 1979 [Z 325 IE]
German version: Angew. Chem. *91*, 938 (1979)

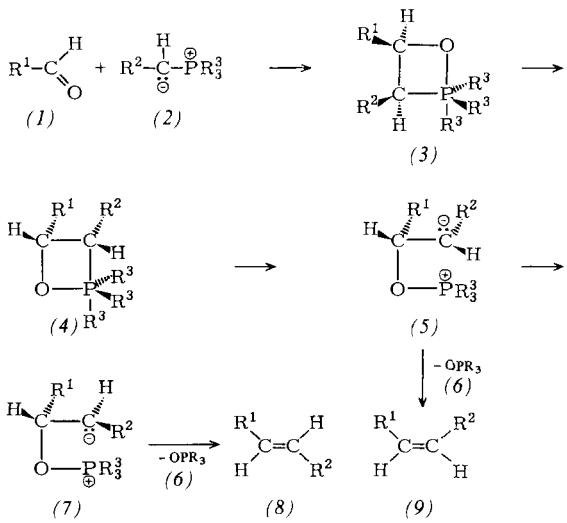
CAS Registry numbers:
(1), 71887-84-8; *(2)*, 71887-85-9; *(3)*, (R = H), 71887-86-0; *(3)*, ($R = C_6H_{13}$), 71887-87-1; *(3)*, ($R = CH_2C_6H_5$, 71887-88-2; *(4)*, ($R = C_6H_{13}$, 71887-89-3; *(5)*, ($R = C_6H_{13}$; $R' = CH_3$), 71887-90-6; *(5)*, ($R = C_6H_{13}$; $R' = CH_2$-CH = CH-CH_3), 71887-91-7; *(7a)*, 71887-92-8; *(7b)*, 62495-31-2; *(7c)*, 71887-93-9; *(7d)*, 71887-94-0; *(8)*, ($R'' = C_6H_5$), 71887-95-1; *(8)*, [$R'' = CH = C(CH_3)_2$], 71887-96-2; *(8)*, ($R'' = CH_3$), 71887-97-3; *(8)*, ($R'' = C_3H_1$), 71887-98-4; *(8)*, [R" = Z-C(CH$_3$) = CHCH], 71887-99-5; *(9)*, ($R' = CH_3$; $R'' = C_3H_7$, 71901-96-7; *(9)*, ($R' = CH_3$; $R'' = C_6H_{13}$), 71901-97-8; *(10a)*, 17113-33-6; *(10b)*, 10504-11-7; *(11a)*, 71888-00-1; *(11b)*, 71888-01-2; *(11c)*, 71888-02-3; *(12)*, 5312-82-3; *(13)*, 71888-03-4; 2-propynyl 2-tetrahydropyranyl ether, 6089-04-9; formaldehyde, 50-00-0

[1] *D. R. Dimmel, S. B. Gharpure*, J. Am. Chem. Soc. *93*, 3991 (1971).
[2] *L. I. Olsson, A. Claesson*, Tetrahedron Lett. *1974*, 2161.
[3] Cf. *J. Hartmann, M. Stähle, M. Schlosser*, Synthesis *1974*, 888.
[4] Cf. the first metalation of a 2-alkynyl tetrahydropyranyl ether [5], 2-alkynyl methyl ether [6] and 1,2-alkadienyl methyl ether [7].
[5] *F. Mercier, R. Epszstein, S. Holand*, Bull. Soc. Chim. Fr. *1972*, 690.
[6] *R. Mantione*, C. R. Acad. Sci., Ser. C *268*, 997 (1969).
[7] *S. Hoff, L. Brandsma, J. F. Arens*, Rec. Trav. Chim. Pays-Bas *87*, 916 (1968); *88*, 609 (1969).
[8] Detailed procedures will appear later in Helv. Chim. Acta.

Structure of the Primary Adduct of a Phosphorus Ylide and Fluorenone

By *Hans Jürgen Bestmann, Kurt Roth, Eberhard Wilhelm, Reinhild Böhme*, and *Hans Burzlaff*[*]

From our investigations on the mechanism of the Wittig reaction[1] it follows that reaction of aldehydes *(1)* with phosphorus ylides *(2)* affords oxaphosphetanes *(3)* in which the substituents R^1 and R^2 on the four-membered ring are arranged in the *Z* position and, according to the rules on the entry and exit of nucleophiles in the mutual interconversion of tetra- and pentacoordinated phosphorus, the oxygen atom occupies an apical position[2]. Accordingly, decomposition into phosphane oxide and olefin requires a ligand rearrange-



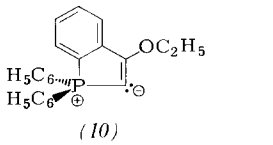
[*] Prof. Dr. H. J. Bestmann, Dipl.-Chem. K. Roth, Dr. E. Wilhelm
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestr. 42, D-8520 Erlangen (Germany)
Prof. Dr. H. Burzlaff, Dr. R. Böhme
Institut für Angewandte Physik (Kristallographie) der Universität
Loewenichstr. 22, D-8520 Erlangen (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1111-0876 $ 02.50/0

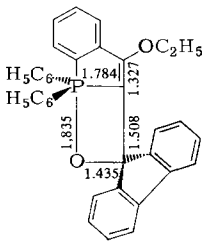
ment process in the trigonal-bipyramidal structure *(3)*, which brings the rupturing C—P bond into the apical position. We postulate that bond rupture occurs during or just after formation of *(4)*; a betaine *(5)* is formed.

The stereochemistry of the olefin being formed is determined by the electronic character of the residue R^2 on the original ylide and of the stationary ligands R^3. If R^2 is an electron donor and the ligands R^3 are phenyl groups a very rapid elimination from *(5)* of the triphenylphosphane oxide *(6)*, $R = C_6H_5$, takes place and *Z*-olefins *(9)* are obtained with high stereoselectivity. If R^2 is an electron acceptor the lifetime of *(5)* is increased. Rotation is possible, resulting in the thermodynamically more stable conformation *(7)*, from which the *E*-olefins *(8)* are formed with cleavage of *(6)*, $R = C_6H_5$. Substituents R^3 with donor character (*e.g.* alkyl or cycloalkyl groups) retard the phosphane oxide cleavage, and the probability of the conformational change *(5)*→*(7)* becomes greater. As a result, a sharp increase in *E*-olefin formation is observed on going from $R^3 = C_6H_5$ to R^3 = alkyl or cycloalkyl[1].

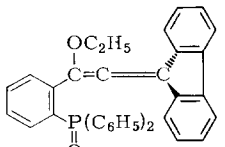
Reaction of the cyclic phosphaallene ylide *(10)*[3] with carbonyl compounds affords stable crystalline primary products, to which, on the basis of the mechanistic postulates discussed above, we assign a trigonal-bipyramidal structure *(3)*[3]. The X-ray structure analysis[4] of the adduct obtained from fluorenone and *(10)* now confirms this assignment.



(10)



(11)



(12)

The atoms bound directly to phosphorus in *(11)* form a distorted trigonal bipyramid (Fig. 1), in which the sum of the equatorial angles is 358.3°. P, O1, C1 and C2 lie in a plane at the corners of a distorted rhombus. The five-membered ring formed by the atoms P, C2, C3, C4, and C9 is likewise planar. The P—O bond, having a length of 183.5 pm, is markedly shorter than the corresponding bond in the adduct obtained from hexaphenylcarbodiphosphorane and hexafluoroacetone (201 pm)[5].

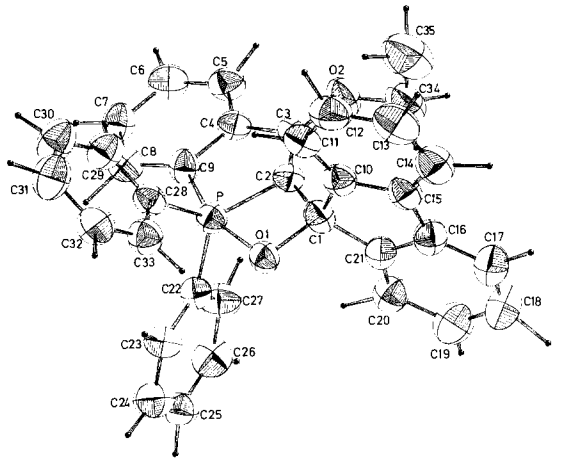


Fig. 1. ORTEP diagram of the molecular structure of *(11)* in the crystal.

Having now confirmed the structure of *(11)*, we regard the finding that *(11)* on the one hand is converted into the allene *(12)* and on the other splits off fluorenone only on heating above the melting point[3] as indirect proof for the ligand rearrangement process *(3)*→*(4)* in the course of the Wittig reaction; the rigidity of the molecule precludes such a rearrangement in the case of *(11)*.

Received: July 13, 1979 [Z 327 IE]
German version: Angew. Chem. *91*, 945 (1979)

CAS Registry numbers:
(10), 64627-00-5; *(11)*, 64627-09-4; *(12)*, 64627-07-2; fluorenone, 486-25-9

[1] *H. J. Bestmann*, Actes 1er Congr. Int. Comp. Phosphorés, Rabat, Oct. 1977, p. 519; Pure Appl. Chem. *51*, 515 (1979); *H. J. Bestmann, W. Downey, K. Geibel, I. Ugi, D. Marquarding, R. Kamel*, unpublished results.

[2] Cf. also *D. Marquarding, F. Ramirez, I. Ugi, P. Gillespie*, Angew. Chem. *85*, 99 (1973); Angew. Chem. Int. Ed. Engl. *12*, 91 (1973).

[3] *H. J. Bestmann, K. Roth, R. W. Saalfrank*, Angew. Chem. *89*, 915 (1977); Angew. Chem. Int. Ed. Engl. *16*, 877 (1977).

[4] $C_{35}H_{27}O_2P$, colorless monoclinic crystals (from benzene/cyclohexane), space group $P2_1$-C_2^2, $a = 994.4$, $b = 1410.8$, $c = 1036.7$ pm, $\beta = 114.7°$, $Z = 2$; 1922 structure factors, $R = 0.063$. We thank Dr. *G. Liehr* for the diffraction measurements.

[5] *G. Chioccola, J. J. Daly*, J. Chem. Soc. *A 1968*, 568.

Phosphadiarsiranes[**]

By *Marianne Baudler* and *Dietrich Habermann*[*]

Dedicated to Professor Kurt Issleib on the occasion of his 60th birthday

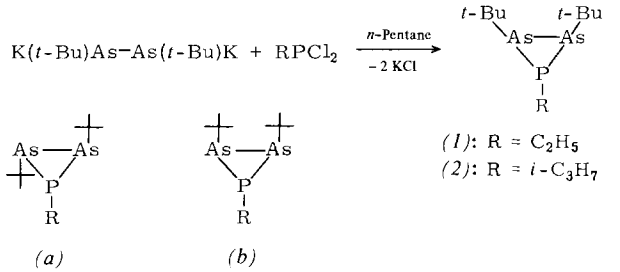
Monocyclic three-membered ring compounds containing phosphorus are presently the subject of numerous studies in preparative phosphorus chemistry[1,2]. Cyclotriphosphanes $(RP)_3$[3], diphosphiranes $(RP)_2CR'_2$[4], diphosphasiliranes $(RP)_2SiR'_2$[5] and diphosphaboriranes $(RP)_2BNR'_2$[6] have already been synthesized and isolated. We now report on the first phosphadiarsiranes $(RAs)_2PR'$—thus demonstrating that three-membered heterocycles containing elements of the 4th period can also be stable enough for preparative isolation.

In the [2 + 1]-cyclocondensation of a 1,2-dialkali metal 1,2-diorganyldiarsenide with a dihaloorganylphosphane an oligomerization of the initially formed phosphadiarsirane to more stable larger ring systems was to be reckoned with. Such rearrangement reactions are favored by nucleophilic reaction partners, polar solvents and elevated reaction temperatures[3-6]. Yet metastable primary products can very often be kinetically stabilized by bulky substituents. With these points in mind 1,2-dipotassium 1,2-di-*tert*-butyldiarsenide was allowed to react with ethyl- and isopropyldichlorophosphane under mild conditions in a heterogeneous reaction.

The main products were found by ^{31}P-NMR spectroscopy to be the phosphadiarsiranes *(1)* and *(2)*, respectively. Both compounds were each present as a mixture of the diastereomers *(a)* and *(b)*, of which the isomer *(a)* with *trans*-oriented *tert*-butyl groups is the most stable. Some other compounds formed included the four-membered heterocycles $(t\text{-BuAs})_3PR$ [*(3)*: $R = C_2H_5$ and *(4)*: $R = i\text{-}C_3H_7$],

[*] Prof. Dr. M. Baudler, Dipl.-Chem. D. Habermann
Institut für Anorganische Chemie der Universität
Greinstrasse 6, D-5000 Köln 41 (Germany)

[**] Contributions to the Chemistry of Phosphorus, Part 92. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 91: *M. Baudler, H. Ternberger, W. Faber, J. Hahn*, Z. Naturforsch., Teil *B*, in press.



(t-BuAs)$_2$(PR)$_2$ [*(5)* and *(6)*], [(t-BuAs)(PR)]$_2$ [*(7)* and *(8)*], and t-BuAs(PR)$_3$ [*(9)* and *(10)*], respectively, in each of which the substituents of neighboring ring atoms are *trans* oriented (cf. Table 1). In addition small amounts of the diphosphaarsiranes t-BuAs(PR)$_2$[7] were detectable. In a later stage of the reaction increasing amounts of five- and six-membered ring compounds are also formed.

Table 1. ^{31}P-NMR data of the compounds *(1)*—*(10)* [a].

(1a):	$\delta = -117.2$	*(1b)*:	$\delta = -118.3$
(2a):	$\delta = -81.2$	*(2b)*:	$\delta = -91.9$
(3):	$\delta = -87.0$	*(4)*:	$\delta = -67.7$
(5):	$\delta = -77.1$	*(6)*:	$\delta = -61.7$
(7):	$\delta = -84.0$	*(8)*:	$\delta = -72.7$
(9):	$\delta_A = -66.4$, $\delta_{B_2} = -77.7$; $J_{AB} = 124.7$ Hz		
(10):	$\delta_A = -54.4$, $\delta_{B_2} = -68.6$; $J_{AB} = 135.0$ Hz		

[a] All measurements in *n*-pentane; δ-values with negative sign for upfield shift.

Whereas the phosphadiarsirane *(1)* oligomerizes at a considerable rate even at −78 °C and cannot be isolated without decomposition, compound *(2)* is essentially thermally more stable owing to the effective shielding of the three-membered ring by the isopropyl group on the phosphorus. In this case the [2+1]-cyclocondensation can be carried out at 0 °C; the product *(2)* is obtainable as the pure isomer *(a)* by molecular distillation and low-temperature crystallization.

At room temperature *(2)* is a colorless, air-sensitive liquid which turns pale yellow on prolonged exposure to light. The composition of the compound is confirmed by elemental analysis (As, P, C, H) and its mass spectrum (field ionization, M^+: $m/e = 338$). An undecoupled ^{31}P-NMR spectrum shows an unresolved multiplet at $\delta = -81$ with a halfwidth of *ca.* 50 Hz, so no P—H bonds can be present. Strong ring-vibration bands are observed between 400 and 200 cm^{-1} in the IR and Raman spectra. The ^{1}H{^{31}P}-NMR spectrum confirms the assignment of the isomers.

Procedure

(2): A solution of freshly distilled dichloro(isopropyl)phosphane (2.56 g, 17.7 mmol, substoichiometric amount) in *n*-pentane (100 ml) is added dropwise within 5 h to a vigorously stirred suspension of 1,2-dipotassium 1,2-di-*tert*-butyldiarsenide[8] (10.7 g, 31 mmol) in pentane (100 ml) at 0 °C. Stirring is continued for a further 1 h; thereafter no more i-PrPCl$_2$ can be detected by ^{31}P-NMR spectroscopy, and *ca.* 40% of the phosphorus content is present as *(2)*. The precipitate is filtered off rapidly in the cold and washed twice with 20 ml of pentane. The combined filtrate and washings are evaporated down at 0 °C (oil-pump vacuum) until all solvent has been removed. The residue, an orange-yellow oil and a light yellow solid, is distilled at 10^{-4} torr over a sloping recovery bend (oil-bath preheated to 110 °C, receiver cooled with liquid nitrogen). The fraction distilling over up to a bath temperature of 140 °C is redistilled in the same way. On dissolution of the pale yellow, oily crude product (1.5 g) in *n*-pentane (1.5 ml) and cooling to −78 °C white crystals are obtained; these are recrystallized in the same way three times. Yield 0.8 g (13.4%) *(2)*; purity 99.8% (^{31}P-NMR).

Received: September 17, 1979 [Z 328 IE]
German version: Angew. Chem. *91*, 939 (1979)

CAS Registry numbers:
(1a), 71888-11-4; *(1b)*, 71927-81-2; *(2a)*, 71888-12-5; *(2b)* 71927-88-3; *(3)*, 71888-13-6; *(4)*, 71888-14-7; *(5)*, 71888-15-8; *(6)*, 71888-16-9; *(7)*, 71888-17-0; *(8)*, 71888-18-1; *(9)*, 71888-19-2; *(10)*, 71888-20-5; K(*tert*Bu)As-As(*tert*Bu)K, 37791-66-5; (*iso*C$_3$H$_7$)PCl$_2$, 25235-15-8

[1] See *H. Quast*, Nachr. Chem. Tech. Lab. *27*, 120 (1979).
[2] *M. Baudler*, Plenary lecture Int. Conf. Phosphorus Chem. in Halle, September 17, 1979; J. Pure Appl. Chem., in press.
[3] *M. Baudler, J. Hahn, H. Dietsch, G. Fürstenberg*, Z. Naturforsch. *B 31*, 1305 (1976); *M. Baudler, Ch. Gruner, ibid. B 31*, 1311 (1976); *M. Baudler, Ch. Pinner, Ch. Gruner, J. Hellmann, M. Schwamborn, B. Kloth, ibid. B 32*, 1244 (1977); *M. Baudler, W. Driehsen, S. Klautke*, Z. Anorg. Allg. Chem., in press.
[4] *M. Baudler, F. Saykowski*, Z. Naturforsch. *B 33*, 1208 (1978).
[5] *M. Baudler, H. Jongebloed*, Z. Anorg. Allg. Chem., in press; *K.-F. Tebbe, ibid.*, in press.
[6] *M. Baudler, A. Marx, J. Hahn*, Z. Naturforsch. *B 33*, 355 (1978); *M. Baudler, A. Marx, ibid.*, in press.
[7] *M. Baudler, S. Klautke, K. Förster*, unpublished results.
[8] Prepared according to *A. Tzschach, V. Kiesel* [J. Prakt. Chem. *313*, 259 (1971)] but in benzene/hexane (1:1); the salt is thus obtained free of solvent.

N-Nitroso Sugar Amino Acids[**]

By *Kurt Heyns, Siyka Röper, Harald Röper*, and *Bernd Meyer*[*]

Aldoses and ketoses react with amino acids to give sugar amino acids of type *(1)* and *(3)*, respectively; these are key substances of non-enzymating browning (Maillard reaction)[1].

We have now succeeded in preparing the *N*-nitroso glucose amino acids *(2a—c)* and *N*-nitroso fructose amino acids *(4a—d)* by reaction of the glucose amino acids *(1a—c)* and fructose amino acids *(3a—d)* with sodium nitrite (pH = 3, 0 °C) and in characterizing them (see Table 1).

The surprisingly easy and quantitative nitrosation of the substrates *(1)* and *(2)* poses several questions: what role does this reaction play on heating "natural" nitrite-containing Maillard systems, *e.g.* cured meat products? To what extent and under which conditions are *N*-nitroso sugar amino acids formed on heating such systems, and do these compounds exhibit mutagenic and/or carcinogenic action. Could the ingestion of *N*-nitroso compounds with food or their endogenic formation from sugar amino acids and nitrite in the stomach lead to cancer?

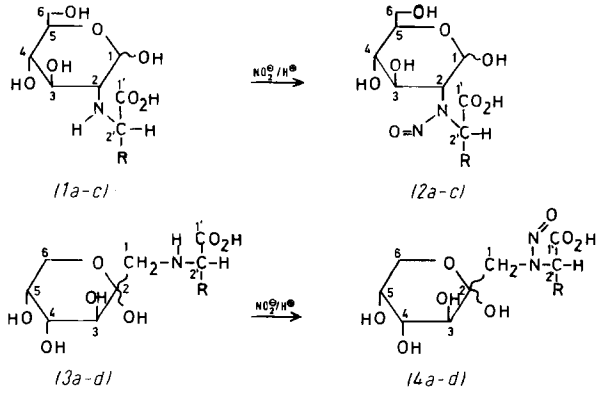
The *N*-nitroso derivative *(2a)*, like the parent compound *(1a)*, shows no mutagenic action in the Ames test; *(3b)* and *(4b)* are still under investigation[3].

N-nitrosation is very clearly recognizable in the ^{13}C-NMR spectrum. In contrast with the spectrum of *(1a)*, that of *(2a)* shows downfield shifts of $\Delta\delta = 9.4$ for C-2, ≈ 3.7 for C-3, 3.3 for C-1 and 1.5 for C-2′[2,4].

[*] Prof. Dr. K. Heyns [†], Dipl.-Chem. S. Röper, Dr. H. Röper [†], Dipl.-Chem. B. Meyer
Institut für Organische Chemie und Biochemie der Universität
Martin-Luther-King-Platz 6, D-2000 Hamburg 13 (Germany)

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

[†] Authors to whom correspondence should be addressed.



(1a-c) (2a-c) (3a-d) (4a-d)

spectrometric differentiation of *N*-nitroso fructose amino acids *(4)* from the *N*-nitroso glucose amino acids *(2)*.

General procedure

1 mmol of the D-glucose amino acids *(1a—c)*[7a,b] or D-fructose amino acids *(3a—d)*[7b,c] was dissolved in 5 ml water. The stirred solution was adjusted to pH = 3 with dilute HCl, cooled with ice, and treated with a solution of $NaNO_2$ (1.5 mmol) in H_2O (2 ml). Thin-layer chromatography after 6 min to 5 h showed that quantitative reaction to *(2a—c)* or *(4a—d)*, respectively, had taken place (Al foil, silica gel 60/F_{254} (Merck), solvent: $CHCl_3$/MeOH/conc. NH_4OH = 3/3/1 (v/v/v), detection of the substances by UV fluorescence,

Table 1. Selected data of the sugar amino acids of type *(1)* and *(3)* and of the *N*-nitroso-sugar amino acids of type *(2)* and *(4)* [2]. All products of type *(3)* and *(4)* gave correct elemental analyses.

			^{1}H-NMR [a] α-Anomer		^{1}H-NMR [a] β-Anomer		IR [b]	$[\alpha]_D^{20}$ [°] (*c* in H_2O)	MS [d] [6]	
	R		δH-2	δH-2′	δH-2	δH-2′	$\tilde{\nu}_{N\ NO}$ [cm^{-1}]		$M-CH_3$	$M-NO$
Glu-Gly	H	*(1a)*	3.23	3.62/3.64	2.97	3.63	—			
NO-Glu-Gly	H	*(2a)*	4.72	4.38/4.12	4.35	4.09/4.20	1370	+22.8 (0.95)	4.77%	4.42%
Glu-D-Ala	CH_3	*(1b)*	3.22	3.77	2.91	4.07	—			
NO-Glu-D-Ala	CH_3	*(2b)* [c]	4.56	4.76	4.30	4.25	1385	+42.0 (0.48)	1.46%	0.57%
Glu-L-Asp	CH_2CO_2H	*(1c)*	3.26	4.16	3.04	4.27	—			
NO-Glu-L-Asp	CH_2CO_2H	*(2c)* [c]	≈4.65	5.28	4.37	4.92	1385	−35.2 (0.61)	0.49%	1.0%

			^{1}H-NMR [a, e] α-Anomer		^{1}H-NMR [a, e] β-Anomer		IR [b]	$[\alpha]_D^{20}$ [°] (*c* in H_2O)	MS [d] [6]
	R		δH-1A/H-1B	δH-2′	δH-1A/H-1B	δH-2′	$\tilde{\nu}_{N\ NO}$ [cm^{-1}]		$M-CH_3$
Fru-Gly	H	*(3a)*	—	—	3.18/3.24	3.56	—		
NO-Fru-Gly	H	*(4a)*	4.18/4.64	4.06/4.25	—	4.70/4.85	1380	−63.3 (0.91)	1.08%
Fru-L-Ala	CH_3	*(3b)*	—	—	3.16/3.19	3.64	—		
NO-Fru-L-Ala	CH_3	*(4b)* [c]	4.29/4.55	4.88	4.23/—	4.59	1370	−62.0 (0.81)	0.61%
Fru-L-Phe	CH_2Ph	*(3c)*	—	—	3.11/3.16	3.87	—		
NO-Fru-L-Phe	CH_2Ph	*(4c)*	4.08/—	4.62	—	—	1380	−108.0 (0.68)	0.79%
Fru-L-Val	$CH(CH_3)_2$	*(3d)*	—	—	3.16/3.19	3.51	—		
NO-Fru-L-Val	$CH(CH_3)_2$	*(4d)* [c]	4.39/—	4.24	4.35/—	4.19	1375	−68.5 (0.5)	2.01%

[a] 270 MHz, *c* = 3—7% in D_2O, internal standard 0.5% acetone (δ = 2.09). [b] KBr pellet 1%. [c] The *syn*- and *anti*-forms are also detectable by NMR spectroscopy. [d] EI spectra of the trimethylsilyl derivatives. [e] The anomers were assigned on the basis of the chemical shift of H-4.

A large downfield shift of Δδ = 1.3—1.5 is observed for H-2 in the ^{1}H-NMR spectra of the *N*-nitroso-D-glucose amino acids *(2a—c)* compared with the spectra of *(1a—c)*. In the case of H-2′ the shift is somewhat smaller. Comparable circumstances are found in the case of the *N*-nitroso-D-fructose amino acids *(4a—d)* with Δδ ≈ 1.1 for H-1A and H-1B, and 0.6—0.8 for H-2′. The remaining protons of the products *(2a—c)* and *(4a—d)* show only slight shifts in comparison with those of the substrates.

As expected, in acidic media the *N*-nitroso derivatives anomerize more rapidly than the substrates, so that anomeric mixtures are present in all cases after nitrosation.

EI mass spectra[5] of the pentakis(trimethylsilyl) derivatives of the substrates and products have been recorded. The EI mass spectra of persilylated *(1a—c)* and *(3a—d)* show molecular ions with ≈2% and ions $M-15(CH_3)$ with ≈8% relative intensity. The EI mass spectra of the persilylated products *(2a—c)* show fragments in the upper mass region at $M-15(CH_3)$ and $M-30(NO)$; in the case of the persilylated products *(4a—d)* only the fragment at $M-15(CH_3)$ is found in this region (Table 1). Cleavage of $H_2CN(NO)CHRCOOSiMe_3$ radicals from the molecular ions leads to the appearance of characteristic sugar fragments in the spectra at *m/e* = 437 [35.6—17.9%][6]. This ion can be used for the mass Griess reagent[8] and color reaction with naphthoresorcinol solution. The products have R_f values about 0.1—0.2 greater than the substrates). The reaction solutions were evaporated to dryness *in vacuo* at 30 °C and extracted with anhydrous pyridine. After removal of pyridine the pure *N*-nitroso compounds are obtained as syrups (see Table 1).

Received: June 18, 1979 [Z 329 IE]
Supplemented: September 21, 1979
German version: Angew. Chem. *91*, 940 (1979)

CAS Registry numbers:
α-*(1a)*, 71887-65-5; β-*(1a)*, 71887-66-6; α-*(1b)*, 71887-67-7; β-*(1b)*,71887-68-8; α-*(1c)*, 71887-69-9; β-*(1c)*, 71887-70-2; α-*(2a)*, 71887-71-3; β-*(2a)*, 71887-72-4; α-*(2b)*, 71887-73-5; β-*(2b)*, 71887-74-6; α-*(2c)*, 71901-95-6; β-*(2c)*, 71887-75-7; β-*(3a)*, 60644-20-4; β-*(3b)*, 71887-76-8; β-*(3c)*, 71887-77-9; β-*(3d)*, 60644-21-5; α-*(4a)*, 71901-45-6; β-*(4a)*, 71887-78-0; α-*(4b)*, 71887-79-1; β-*(4b)*, 71887-80-4; α-(4c), 71887-81-5-; α-*(4d)*, 71887-82-6; β-*(4d)*, 71887-83-7;

[1] *J. E. Hodge*, J. Agric. Food Chem. *1*, 928 (1953); *G. P. Ellis*, Adv. Carbohyd. Res. *14*, 63 (1959); *K. Heyns, H. Paulsen* in: Veränderungen der Nahrung durch industrielle und haushaltsmässige Verarbeitung. Steinkopff, Darmstadt 1960; *T. M. Reynolds*, Adv. Food Res. *12*, 1 (1963); *14*, 167 (1965).
[2] *S. Röper*, planned Dissertation, Universität Hamburg 1980.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 *0570-0833/79/1111-0879 $ 02.50/0*

[3] We thank Dr. *B. Pool*, Deutsches Krebsforschungszentrum, Heidelberg, for carrying out the Ames tests.
[4] *P. S. Pregosin, E. W. Randall*, Chem. Commun. *1971*, 399.
[5] We thank Prof. Dr. *W. König* and Dipl.-Chem. *D. Bloss* for recording the mass spectra.
[6] Rel. int. in % referred to $m/e = 73$ ($SiMe_3^+$) = 100%.
[7] a) *K. Heyns, H. Breuer, H. Paulsen*, Chem. Ber. *90*, 1374 (1957); b) *K. Heyns, H. Breuer, ibid. 91*, 2750 (1958); c) *K. Heyns, H. Paulsen*, Justus Liebigs Ann. Chem. *622*, 160 (1959).
[8] *R. Preussmann, G. Neurath, G. Wulf-Lorentzen, D. Daiber, H. Hengy*, Z. Anal. Chem. *202*, 187 (1964).

Diarylsulfur(VI) Oxide Difluoride by Direct Fluorination of Sulfoxides[**]

By *Ingo Ruppert*[*]

Dedicated to Professor Kurt Issleib on the occasion of his 60th birthday

All attempts to directly halogenate diorganyl sulfoxides have so far failed. Even on reaction with XeF_2 no diorganosulfur(VI) oxide fluorides could be trapped[1]. Fluorine, on the other hand, adds the diaryl sulfoxides *(1a, b)* smoothly under the gentle conditions of liquid phase fluorination (dilution of substrate and fluorine). The difluorides *(2a, b)* that are formed can be filtered off in high yields; their constitution is confirmed by elemental analysis and by mass[2] and NMR spectroscopic findings (Table 1).

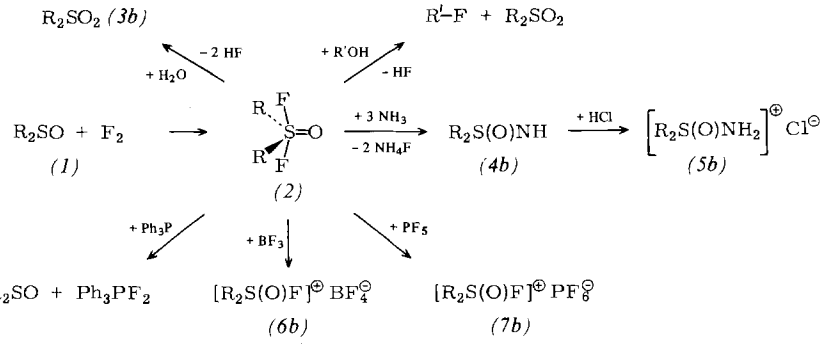
Thus, for the first time we have ready access to such aryl derivatives of sulfur oxide fluoride, which cannot be obtained by arylation of SOF_4. The halogenation with fluorine has the advantage—apart from the favorable price of the reagent—that *(2a, b)* are formed without difficultly separable coupling products.

Competing CH-substitution or cleavage of the aryl moiety could be largely suppressed. The ^{19}F-NMR spectrum of the concentrated $CFCl_3$ filtrate, however, showed besides further *(2a)* also traces of the cleavage products $PhS(O)F$[3] and $PhS(O)F_3$; the latter cleavage product could be identified by its significant AB_2 coupling pattern[4] of chemically nonequivalent fluorine atoms, although comparable monoorgano-derivatives of SOF_4 are unknown.

Further investigations were carried out with *p*-fluoro-substituted *(2b)*, since incorporation of this fluorine probe facilitates monitoring of the reaction by the sensitive technique of ^{19}F-NMR spectroscopy with simultaneous recording of educt and product(s)[6].

The substitution behavior of the diarylsulfur oxide difluorides *(2)* is determined by the preferred formation of the sulfone coordination. Hydrolysis of *(2b)*, which is highly sensitive to moisture and can be handled only under dried protective gas, proceeds uniformly to the sulfone *(3b)*[7]. With alcohols, initial substitution is followed by elimination of the organyl group bound to the oxygen as alkyl fluoride. The driving force of this thia(VI)-analogous "Arbusov elimination" could be formation of the thermodynamically most favorable sulfone. Finally, ammonolysis leads to *(4b)*, the monoaza-analog of the sulfone. *(4b)* is hydrochlorinated to the analytically pure chloride *(5b)*.

Bonding comparable with that in the preferred sulfone arrangement should also be achievable by withdrawal of fluoride from *(2b)*. Indeed, reaction with strong fluoride-acceptors such as BF_3 or PF_5 affords the compounds *(6b)* and *(7b)*, respectively, which contain an oxo cation isoelectronic with the phosphinic fluorides and having pentavalent sulfur and a new fluoroorganic periphery. The $^{13}C\{^1H\}$-NMR spectrum



(a), R = C_6H_5; *(b)*, R = *p*-F–C_6H_4
R' = CH_3, C_2H_5, $C(CH_3)_3$

Table 1. ^{19}F- and $^{13}C\{^1H\}$-NMR spectroscopic data of the diarylsulfur(VI) oxide fluorides and their derivatives [a].

	^{19}F-NMR [b]		$^{13}C\{^1H\}$-NMR [b]			
	S F	Ar F	C-1	C-2 [c]	C-3 [c]	C-4
(2a) [5]	100.7 s		147.6 t (17.0)	124.8 t (4.6)	128.9 s	132.5 s [d]
(2b) [5]	102.0 s	–105.0 ps [e]	143.6 td (18.4, 3.6)	128.5 td (6.8, 9.5)	116.3 d (0, 23.3)	164.8 d (0, 256.3) [d]
(3b)		–104.3 ps	138.1 d (3.5)	130.8 d (10.2)	117.0 d (22.7)	165.1 d (255.6)
(4b)		–106.3 ps	139.5 d (2.9)	130.7 d (9.5)	116.5 d (22.7)	165.4 d (254.9)
(5b)		– 99.2 ps	130.5 d (3.0)	133.6 d (10.7)	119.3 d (23.7)	168.7 d (260.0)
(6b), *(7b)*	35.8 s	– 89.5 ps [f]	122.9 dd (12.0, 2.8)	135.4 dd (1.5, 12.5)	120.5 d (0, 24.5)	171.0 dd (1.5, 266.0)

[a] With exception of *(5b)* (CD_3OD) and *(6b)* (CD_3CN) the ^{19}F- (Varian EM 390, 84.7 MHz, $CFCl_3$ int.) and $^{13}C\{^1H\}$-NMR spectra (Bruker WH 90, 22.6 MHz, TMS int.) of all the compounds were recorded in conc. $CDCl_3$ solution; *(2a)* and *(2b)* were treated with traces of Et_3N to suppress SF exchange. [b] Positive signs refer to downfield shifts (deshielding w.r.t. standard), negative signs to upfield shifts; the δ-value is followed by the multiplicity and the contribution of the (*FS-C*) (quoted first) and/or fluoroarene coupling. [c] Assignment in C-2 and C-3 according to size of fluoroarene coupling and for *(2a) via* the shift increment of the *p*-fluoro-substitution. [d] Broadening of the signal by (*FS-C-4*) interaction. [e] Pseudosinglet with multiplet fine splitting by arene protons. [f] ^{19}F-NMR: $\delta = -149.0$ (s, BF_4^-); -71.5 (d, $J(PF) = 713$ Hz, PF_6^-).

[*] Dr. I. Ruppert
Anorganisch-chemisches Institut der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn 1 (Germany)

[**] Fluorinated Organoelements: Oxidative Liquid-Phase Direct Fluorination, Part 6. – Part 5: *I. Ruppert*, J. Fluorine Chem. 14, 81 (1979); part of Habilitationsschrift, Universität Bonn 1979.

of *(6b)* [and *(7b)*] shows besides the fluoroarene coupling an additional doublet splitting due to the fluorine atom attached to sulfur. This multiplicity, gradation of coupling constants comparable to the neutral compound, and, finally, the expected integration ratio in the ^{19}F-NMR spectrum confirm the salt-like structure of *(6b)* and *(7b)*.

In the reversal of its equation of formation, *(2a, b)* transfers both of its fluorine atoms to triphenylphosphane at room temperature. This reaction—hitherto only observed with SF_4[8a] and its covalent organo derivatives[8b]—is surprising for S^{VI} derivatives, insofar as the SF bond usually becomes stronger with increasing coordination by electronegative ligands and thus with increasing the partial charge of the sulfur atom.

Procedure

All operations must be carried out under strict exclusion of moisture.

Synthesis of *(2a)* and *(2b)*: A stream of fluorine diluted with helium (max. 20 ml F_2 to 100 ml He per min) is passed into a magnetically stirred solution of *(1)* (40 mmol) in anhydrous $CFCl_3$ (250 ml) (quartz flask with Teflon delivery tube and fitted with a frit with, −90 °C circulatory cooling). The gas mixture is additionally precooled by passage through a metal spiral in an EtOH-slush bath (−115 °C) and the reaction solution is kept at 0 °C for *(1a)* and at −78 °C for *(1b)*. The reaction is complete only after addition of a three- to fourfold excess of fluorine. For determining the end-point of the reaction, $^{13}C\{^1H\}$-NMR is recommended in the case of *(2a)* and ^{19}F-NMR in the case of *(2b)*. The suspension is filtered off cold and $CFCl_3$ is removed from the colorless residue *in vacuo* (mercury vapor jet pump); yield: 80—90% finely crystalline, analytically pure *(2a)* (m.p. 79 °C, dec.) or *(2b)* (m.p. 75 °C, dec.).

For ammonolysis and salt formation a stoichiometric amount of precondensed NH_3, NF_3, or PF_5 is added to a solution of freshly prepared *(2b)* (30 mmol) in CH_2Cl_2 (100 ml) in a vacuum system at −78 °C. The magnetically stirred reaction mixture is allowed to warm to room temperature overnight and the volatile components are then removed in a vacuum. The residue consists of *(4b)*, *(6b)*, or *(7b)* slightly contaminated with sulfone *(3b)*. *(4b)*, a light brownish oil, is taken up in ether and treated with HCl gas until precipitation is complete. Filtration affords colorless hydrochloride *(5b)* (73%, m.p. 179 °C, dec.), from which *(4b)* can be recovered again by addition of Et_3N.—Hydrolysis, alcoholysis[9], and defluorination[10] of *(2b)* were monitored ^{19}F-NMR spectroscopically.

Received: March 30, 1979 [Z 330 IE]
Supplemented: June 18, 1979
German version: Angew. Chem. *91*, 941 (1979)

CAS Registry numbers:
(1a),945-51-7; *(1b)*, 395-25-5; *(2a)*, 71888-04-5; *(2b)*,71901-98-9; *(3b)*, 383-29-9; *(4b)*, 71888-05-6; *(5b)*, 71888-06-7; *(6b)*,71888-08-9; *(7b)*, 71888-09-0

[1] The formation of $R_2S(O)F_2$ was however suggested indirectly, owing to the hydrolysis to the sulfone: *M. Zupan, B. Zajc*, J. Chem. Soc. Perkin Trans. 1 *1978*, 965.

[2] The mass spectra of *(2a, b)* superposed by the fragments of the corresponding sulfones confirm the expected molar masses by an intense ($M^+ - 19$(F)) ion.

[3] ^{19}F-NMR: $\delta = +6.3$, confirmed by addition of the authentic compound, prepared according to *F. Seel, R. Budenz, R. D. Flaccus, R. Staab*, J. Fluorine Chem. *12*, 437 (1978).

[4] ^{19}F-NMR: $\delta = +65.5$ (pseudo-t, $^2J(F_{ax}F_{eq}) = 162.4$ Hz, F_{eq}), +100.8 (d, $^2J(F_{eq}F_{ax}) = 162.4$ Hz F_{ax}); indexing assuming a distorted trigonal-bipyramidal sulfur coordination.

[5] Freshly prepared $CHCl_3$ solutions of *(2a, b)* show an exchange signal due to traces of HF as resonance in the SF region, which on handling the solutions in glass gradually becomes equal to the base line of the spectrum with increasing etching of the glass vessel. However by addition of a small amount of Et_3N the SF signal can be fixed at a value with the usual halfwidth and the HF-catalyzed sulfone formation restricted. Complementarily, in the ^{13}C-NMR experiment the triplet splittings of the arene carbon atoms can be recognized; *I. Ruppert, V. Bastian*, Angew. Chem. *90*, 226 (1978); Angew. Chem. Int. Ed. Engl. *17*, 214 (1978).

[6] The gradation of the fluoroarene coupling affords additional help in the assignment of the ^{13}C-signals in C-2 and C-3.

[7] $^{13}C\{^1H\}$- and ^{19}F-NMR spectroscopic comparison with *(3b)* prepared conventionally from *(1b)* and 30% aqueous H_2O_2 in glacial acetic acid.

[8] a) *W. C. Smith*, J. Am. Chem. Soc. *82*, 6176 (1960); b) *I. Ruppert*, Chem. Ber. *112*, 3023 (1979).

[9] ^{19}F-NMR ($CHCl_3$) of alkyl fluorides: MeF: $\delta = -267.9$ (q, J(HF) = 46.5 Hz); EtF: −211.9 (tq, J(HF) = 46.5 Hz, ^3J(H CC F) = 26.5 Hz); tBuF: −130.9 (dec, ^3J(H CC F) = 21.6 Hz).

[10] ^{19}F-NMR ($CHCl_3$) of Ph_3PF_2: $\delta = -40.7$ (d, J(PF) = 663 Hz).

Polar [4+2]- and [4+4]-Photocycloadditions: Effects of Hybridization in Diradicals[**]

By *Gerd Kaupp* and *Heinz-Willi Grüter*[*]

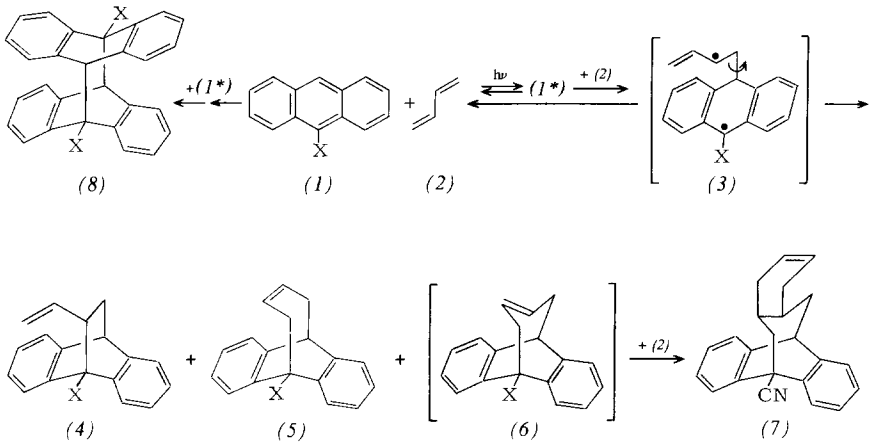
Numerous orbital symmetry postulates (EHT-techniques) for "concerted reactions" had to be modified for polar reactions, using more sophisticated PMO- or CI-theories. Thus, it was "predicted" that photochemical Diels-Alder reactions between excited anthracene (anthracene substituted with acceptor groups) and acceptor- (donor-) dienophiles are "allowed" due to cross-over of orbital levels, while competing [4+4]-reactions are correspondingly "forbidden"[1]. The experimentally supported diradical mechanism operating in singlet reactions of this type[2] leads to different expectations. We report here on the suppression of photochemical [4+2]- and promotion of photochemical [4+4]-reactions by means of polar substituents, exactly as required by the diradical mechanism in the special cases under discussion.

Electronically excited anthracene *(1a*)* is trapped by 1,3-butadiene *(2)* (6 M) giving *(4a)* and *(5a)* in the ratio 20:1[3]. The ratio of [4+2]- to [4+4]-adducts is reversed, however, when electronically excited 9-anthracenecarbonitrile *(1b*)* ($\lambda = 310$—410 nm) reacts with *(2)* (3.2 M in benzene). One obtains *(4b)*, *(5b)* and *(6b)*→*(7)* in the ratio 1:3.2:13.3 [altogether 19%, together with 80% *(8b)*][4].

This striking difference is readily comprehensible upon considering molecular models of the diradical *(3)* (which is inferred by extrapolation), even though the extent of unproductive reverse reaction [*(3)*→*(1)*+*(2)*] cannot be predicted as yet: the formation of the six-membered ring [yielding *(4)*] requires considerable rehybridization at the benzhydrylic radical center of *(3)* out of planarity towards pyramidal geometry, in order to decrease the C—C-distance and to improve the overlap of electrons prior to the initiation of the bonding process. On the other hand the electron overlap is well suited for the formation of eight-membered rings [of *(5)* and *(6)*] (according to molecular models) even with the planar diradical *(3)*. However, the formation of *(5)* first requires an internal rotation within the allylic system [or else reaction of *s-cis-(2)* with *(1*)*] and for reasons of severe strain *(6)* will only be formed, when the planarity of the benzhydrylic radical center as in *(3b)* is stabilized by additional delocalization into the polar cyano group, since this effectively inhibits the competitive formation of *(4b)*. Therefore in the case of the apolar

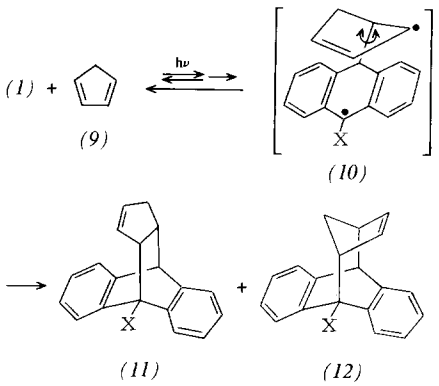
[*] Univ.-Doz. Dr. G. Kaupp, H.-W. Grüter
Chemisches Laboratorium der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)

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



system *(3a)* with less stabilization of the sp^2-geometry (more facile rehybridization) a higher proportion of Diels-Alder addition to *(4)* is to be expected than for the more polar *(3b)*, as is experimentally observed.

Similar effects may be used for control of cyclovinylogous photoadditions with *s-cis*-fixed 1,3-dienes. Thus, the photoreaction of anthracene *(1a)* in cyclopentadiene *(9)* at 0 °C yields the [4+2]- and [4+4]-adducts *(11a)* and *(12a)* in the



(a), X = H; *(b)*, X = CN; *(c)*, X = Cl

ratio 1:1.4[5]. Similarly 9-anthracenecarbonitrile *(1b)* and 9-chloroanthracene *(1c)* react with *(9)* after light absorption with fluorescence quenching (91.5% and 17.5% quenched; 5.0 M *(9)* in benzene) but without discernable exciplex fluorescence[6]. The [4+4]-adducts *(12b)* (79%)[4] and *(12c)* (40%)[4] are formed, but not the [4+2]-adducts *(11b,c)*. Again less geometrical change at the benzhydrylic radical center in *(10)* is required for the initiation of eight-membered ring formation (according to molecular models) than for the at least conceivable six-membered ring formation. Due to additional delocalization into the substituents the rehybridizations are more difficult and this also hinders the formation of rotamers which are well suited for closure to six-membered rings (methylene-H/*peri*-H interaction)[6].

The diradical intermediates *(3b)*, *(10b)*, and *(10c)* are favored sterically and electrostatically. Isomeric [4+2]-adducts, formally derived *via* primary attack of *(2)* or *(9)* on the substituted C-atom of *(1)*, are not found. In the photoreaction of 9-chloroanthracene *(1c)* (0 °C) with *(9)* thermolabile side-products (presumably due to attack on one of the outer rings) are formed, which, upon work-up, regenerate 4% of *(1c)*. Such side reactions are more prominent during photolysis of 9,10-dichloroanthracene dissolved in *(9)* (*ca.* 80% regeneration upon work-up). One obtains 14% of the [4+4]-adduct analogous to *(12)*)[4], but as expected no Diels-Alder adduct of type *(11)*.

The effects of polar substituents on the reactivity of 1,4-diradicals described here (and previously disregarded) promise further applications in preparative photochemistry.

Received: June 28, 1979 [Z 331 IE]
German version: Angew. Chem. *91*, 943 (1979)

CAS Registry numbers:
(1a), 12012-7; *(1b)*, 1210-12-4; *(1c)*, 716-53-0; *(2)*, 106-99-0; *(4a)*, 63840-02-8; *(4b)*, 71871-45-9; *(5a)*, 63840-03-9; *(5b)*, 71871-46-0; *(7a)*, 71885-48-8; *(7b)*, 71871-47-1; *(8b)*, 33998-38-8; *(9)*, 542-92-7; *(11a)*, 38483-18-0; *(12a)*, 38598-70-8; *(12b)*, 71871-48-2; *(12c)*, 71871-49-3; *(12c)*, dichloro analog, 71871-50-6; 9,10-dichloroanthracene, 605-48-1

[1] *N. D. Epiotis, R. L. Yates*, J. Org. Chem. *39*, 3150 (1974); references cited therein.

[2] *G. Kaupp*, Chimia *25*, 230 (1971); Justus Liebigs Ann. Chem. *1973*, 844; for the notion diradical cf. *G. Kaupp, E. Teufel, H. Hopf*, Angew. Chem. *91*, 232 (1979); Angew. Chem. Int. Ed. Engl. *18*, 215 (1979).

[3] *G. Kaupp*, Justus Liebigs Ann. Chem. *1977*, 260; 18% yield together with 69% *(8a)*.

[4] The new compounds *(4b)*, *(5b)*, *(7)*, *(12b)*, and *(12c)* as well as the [4+4]-adduct from 9,10-dichloroanthracene with *(9)* were isolated in crystalline form and characterized spectroscopically (^{1}H-NMR, ^{13}C-NMR, UV, IR) and by elemental analysis.

[5] *G. Kaupp*, Angew. Chem. *84*, 718 (1972); Angew. Chem. Int. Ed. Engl. *11*, 718 (1972); 75% yield together with *(8a)*; 1,3-cyclohexadiene also yields the corresponding [4+2]- (19%) and [4+4]-adducts (54%) (in benzene, ratio 3:7): *G. Kaupp*, The Woodward-Hoffmann-Rules and Thereafter. Universität Freiburg, 1974/75; cf. [3]; the differing data for the [4+2]/[4+4]-ratios of ≤4/96 [*N. C. Yang, J. Libman*, J. Am. Chem. Soc. *94*, 1405 (1972)] or later of 15/85 [*N. C. Yang, R. L. Yates, J. Masnovi, D. M. Shold, W. Chiang*, Pure Appl. Chem. *51*, 173 (1979)] could not be verified.

[6] *G. Kaupp, M. Stark, E. Teufel, H.-W. Grüter*, presented at the Chemiedozenten-Tagung in Darmstadt (Germany), March 29, 1979.

Quantitative Trace Analysis of Thallium in Biological Material[**]

By *Christoph Achenbach, Rolf Ziskoven, Ferdinand Koehler, Ute Bahr*, and *Hans-Rolf Schulten*[*]

Regarding the pharmacokinetics of thallium we now have available the first results[1] obtained by the technique of field desorption mass spectrometry (FD-MS).

[*] Dr. H.-R. Schulten [†], Dipl.-Chem. U. Bahr
Institut für Physikalische Chemie der Universität Bonn
Wegelerstrasse 12, D-5300 Bonn (Germany)

Dr. C. Achenbach, Dr. R. Ziskoven
Physiologisches Institut II der Universität
Bonn (Germany)

Dr. F. Koehler
Institut für Humangenetik der Universität
Bonn (Germany)

[**] Quantitative Field Desorption Mass Spectrometry, Part 18. This work was supported by the Deutsche Forschungsgemeinschaft and the Ministerium für Wissenschaft und Forschung des Landes Nordrhein-Westfalen. Part 17: *U. Bahr, H.-R. Schulten*, J. Labelled Compd. Radiopharm., in press.

[†] Author to whom correspondence should be addressed.

The recent discovery of high levels of thallium pollution in the environment has focused attention on the tetratogenicity (fetus malformation). For detailed investigations in this sector a method is required which enables the quantitative detection of thallium in extremely small tissue samples (embryos, placenta tissues *etc.*) thus permitting correlation of measured values with teratological findings.

FD-MS[2] enables direct detection and quantitative determination of metal cations in biological and environmental samples in the picogram range[3] without a separate charring step. The limit of detection with FD-MS is 10^{-15} g for cesium, 10^{-12} g for lithium and 10^{-11} g for thallium. For quantitative determinations by mass spectrometry, isotope dilution analysis using stable isotopes was chosen. The high specificity of FD-MS makes an involved and time-consuming sample preparation unnecessary, the tissues and cell components of the samples are merely homogenized and centrifuged. The time required for an analysis is only *ca.* 20 min; the amount of sample required is *ca.* 1 mg.

For the measurements a double focusing mass spectrometer (Varian MAT 731) with FD ion source and indirect emitter—heating with a tunable argon ion laser (Spectra Physics, Model 166)—was used. To compensate for statistical deviations in the flow of ions, the electric signals of the ions were accumulated *via* a multichannel analyzer (Tracor Northern NS-570A). On accumulation of electric signals over *ca.* 100 scans the accuracy of the results for pure salt solutions lies below 1%, for metals from complex matrixes between 5 and 10%.

For determination of the distribution of thallium with time in an organism we administered orally 160 mg of thallium per kg body weight to mice. After fixed periods of time the acutely poisoned mice were killed and the thallium concentrations in the heart, liver, kidney and brain were determined by FD-MS (Fig. 1). According to the results it would appear that the brain possesses an inbuilt barrier for thallium, which however breaks down in dependence of dosage after loss of excretory function of the kidney (see curves a and b in Fig. 1). In contrast, in the remaining organs a short-termed enrichment of thallium takes place, followed by a washing-out process. High concentrations are again observed in the kidney[4] only after *ca.* 12 h. After 24 h an increased concentration of about the same order of magnitude is found in all organs.

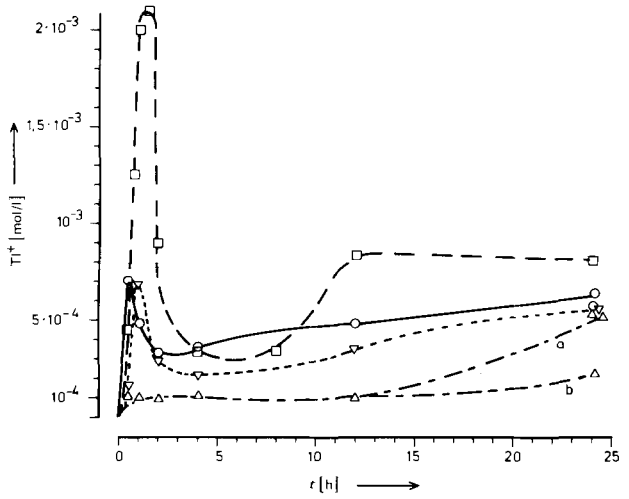


Fig. 1. Distribution of thallium with time in the heart ○, liver ▽, kidney □ and brain △ of mice after administration of 160 mg Tl per kg body weight. The enrichment and excretion processes are followed by a second, variable increase in thallium concentration. The brain takes up only small amounts of thallium; however, no excretion takes place. The curves a and b for the brain show the variable high increase in thallium concentration for thallium doses of 130 and 80 mg/kg, respectively.

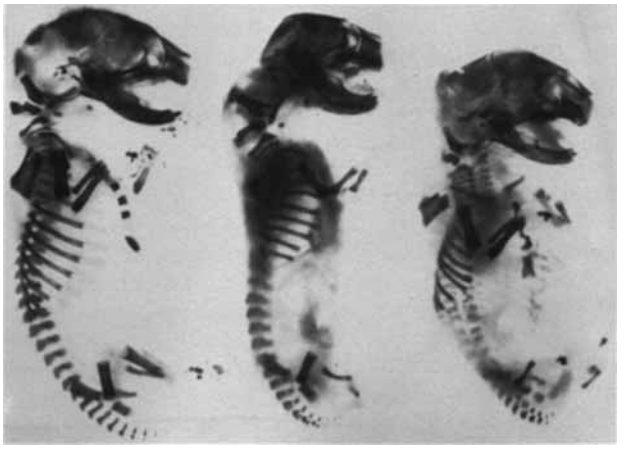


Fig. 2. Skeletons of mice embryos. Left: a normal embryo; center and right: damage after a single dose of 8 mg Tl/kg body weight to the mother animal.

For the teratological investigations pregnant mice were given doses of 8 mg Tl per kg body weight. At this dosage 50% of the embryos were found to have serious malformation of the skeleton (see Fig. 2). The teratogenic dose 50% was lower than the corresponding lethal dose 50% by a factor of approximately 40. As example, one mother proved to have 5.1×10^{-5} mol/l of thallium in the kidney, 1.5×10^{-6} mol/l in the brain, and 2.6×10^{-5} mol/l in the uterus together with the embryos. These values were found one hour after administration of the thallium. Furthermore, experiments with this line of test animals showed that even one thousandth part of the lethal dose 50% still gave 12.5% of fetal malformations. If this were transformed to humans it would mean that an oral dosage of *ca.* 10 microgram of thallium per kg body weight at the time of formation of the extremities and organs in the embryo would result in a significant enhancement of malformations.

Received: September 7, 1979 [Z 332 IE]
German version: Angew. Chem. *91*, 994 (1979)

CAS Registry numbers:
Tl, 7440-28-0

[1] *C. Achenbach, O. Hauswirth, C. Heindrichs, R. Ziskoven, F. Koehler, U. Bahr, A. Heindrichs, H.-R. Schulten*, J. Toxicol. Environ. Health, submitted for publication.

[2] *H. D. Beckey, H.-R. Schulten*, Angew. Chem. *87*, 425 (1975); Angew. Chem. Int. Ed. Engl. *14*, 403 (1975).

[3] *W. D. Lehmann, H.-R. Schulten*, Angew. Chem. *89*, 180 (1977); Angew. Chem. Int. Ed. Engl. *16*, 184 (1977); *W. D. Lehmann, U. Bahr, H.-R. Schulten*, Biomed. Mass Spectrom. *5*, 536 (1978); *W. D. Lehmann, H.-R. Schulten*, Anal. Chem. *49*, 1744 (1977); *H.-R. Schulten, R. Ziskoven, W. D. Lehmann*, Z. Naturforsch. *C 33*, 178 (1978); *H.-R. Schulten, W. D. Lehmann, R. Ziskoven, ibid. C 33*, 484 (1978); *H.-R. Schulten, U. Bahr, W. D. Lehmann*, Mikrochim. Acta *1979*, I, 191.

[4] *A. Lund*, Acta Pharmacol. Toxicol. *12*, 260 (1956).

Specialist Periodical Reports: General and Synthetic Methods, Vols. 1 and 2. Senior Reporter: *G. Pattenden.* The Chemical Society, London. Vol. 1: 1978, 445 pages, bound, £ 30.00, Vol. 2: 1979, 263 pages, bound, £ 26.00.

The first two volumes of a new series of "Specialist Periodical Reports" are now available. They are literature surveys for the years 1976 (Vol. 1) and 1977 (Vol. 2). The preparation and reactions of the main types of organic compounds are discussed, together with the use of novel reagents. The discussion is not limited to methods of wide and proven applicability, but also covers many reactions that are new and appear to have potential value in synthesis.

The present series differs from other similar series in that the methods are arranged by type of compound rather than by type of reaction. This makes the individual chapters more absorbing reading than works of more encyclopedic nature.

The first five chapters are concerned with hydrocarbons, aldehydes and ketones, carboxylic acids and their derivatives, alcohols, ethers, and halogen and nitrogen compounds. Although in the case of the hydrocarbons it is mainly novel reactions that are described, with the carbonyl compounds the emphasis is on their synthesis, plenty of space being devoted to butenolides, α-methylenebutyrolactones, and macrolides, where there has recently been much activity. A further chapter is concerned with the synthesis of oxygen, sulfur, and nitrogen heterocycles, beginning with oxiranes and going on to penicillins and cephalosporins. Similarly, new ring closure and annelation reactions for the preparation of carbocyclic compounds are presented, particularly with regard to their use in the synthesis of natural terpenoids.

Account is taken of the ever-increasing importance of organometallic compounds in synthesis, and there is a detailed description of transition-metal reagents which may be used catalytically or stoichiometrically; many examples are given to clarify the tremendous versatility obtainable by using main group elements in synthetic operations.

Unfortunately, the expositions on such important topics as synthesis planning and strategy are insufficient. Although the examples of the synthesis of naturally occurring materials are to some extent illustrative, the treatment of synthetic strategems is quite arbitrary. Retrosynthetic and synthon considerations are hardly mentioned, the concept of Umpolung has been misunderstood, and the treatment of methods for the production of optically active centers is too bald.

A suitable amplification of the topics handled is provided by the special chapter on phase transfer catalysis and complexing reagents. In addition, the reader interested in further study will find at the end of each volume a collection of review articles published in that year which deal with synthetic methods.

All in all, the first two volumes of the new series provide a thorough survey of the development of synthetic organic chemistry. They may be recommended to anyone interested in new synthetic reagents who wants to keep up to date with the range of synthetic methods available. However, the high price makes them appear more suitable for libraries than for a personal collection.

Herbert Siegel [NB 482 IE]

Highly Conducting One-Dimensional Solids. Edited by *J. T. Devreese, R. P. Evrard,* and *V. E. van Doren.* Plenum Press, New York 1979. xiii, 422 pages, bound, $ 51.00.

The second volume of the series "Physics of Solids and Liquids" contains seven papers by a total of ten internationally famous experts. The book is intended primarily for physicists who want to become acquainted with the physical peculiarities of one-dimensional metallic systems. The specific problems involved are presented in a short but very informative introduction *(A. J. Berlinsky)* that can also be understood by chemists. The following chapters on X-ray and neutron diffraction experiments *(R. Comès* and *G. Shirane),* "Charge Density Wave (CDW) phenomena" *(A. J. Heeger),* and the properties of "alloys" of various "organic" metals *(T. D. Schultz* and *R. A. Craven)* contain the fundamental experimental results obtained up to about 1977 on three selected one-dimensional metals (for the expert, these are TTF-TCNQ, TSeF-TCNQ, and KCP). Next come three theoretical sections *(L. J. Sham, V. J. Emery, H. Gutfreund,* and *W. A. Little).* The last two authors analyze the possible existence of exciton high-temperature superconductors. The final chapter *(J. Bardeen)* gives a critical comparison of the data in the previous sections and their interpretation. A brief survey of the possible future development of the field is appended.

The book gives a detailed and comprehensive presentation of the essential theoretical models and the special experimental methods used for the study of one-dimensional metals, on the basis of a few well-chosen examples. Nevertheless, the chemist will regret the absence of a brief summary of the materials that have been synthesized and clearly characterized up to the present.

To judge by the literature references, the printing of this book seems to have taken a very long time.

Heimo J. Keller [NB 483 IE]

Solid Electrolytes. General Principles, Characterization, Materials, Applications. Edited by *P. Hagenmuller* and *W. van Gool.* Academic Press, New York 1978. xvii, 549 pages, bound, $ 52.00.

The field of solid ionic conductors or solid electrolytes has rapidly developed and extended over recent years and the process is still continuing. The attempt of the present book to give a survey of the entire field is therefore welcome. The book contains 32 contributions from a large number of authors and is divided into three parts.

The first part deals with the theory of ionic conduction in solids, especially solids with very high conductivities, which are sometimes called "super ionic conductors" or "optimized ionic conductors". Both transport mechanisms and the experimental methods used to characterize solid ionic conductors are discussed. These include AC measurements and scattering experiments, but unfortunately the standard methods such as DC measurements, polarization measurements, and measurements with electrochemical potential probes have been omitted.

The second part contains most of the known solid ionic conductors, arranged by substance classes. These include sodium-ion-conducting β-aluminas, oxygen-ion conductors based on zirconium dioxide, fluorine-, copper- and silver-ion conductors, *etc.*

Finally, in the third part, the most important practical applications of solid electrolytes are discussed. These include high-temperature fuel cells, the sodium-sulfur cell as a high-energy accumulator, electrochemical measurement probes, and other systems. Reference is also made to solids with mixed ionic and electronic conduction, which are of importance as electrodes in galvanic cells.

This book will certainly be very useful for scientists working in the field of solid electrolytes, since not only does it per-

mit a rapid overview of the various parts of the subject but it also simplifies a more detailed study of specific problems by means of its extensive literature references.

Hans Rickert [NB 484 IE]

Chemical Kinetics and Transport. By *P. C. Jordan.* Plenum Press, New York 1979. xvi, 368 pages. Bound, $ 25.80.

In many open systems the interaction of chemical reaction and transport processes determines both the kinetics at steady state and the transient behavior. This applies not only to continuously operated reactors, all heterogeneous catalytic reactions, flames, and combustion systems but also to living cells and structures containing living cells. Yet, anyone buying this book in the expectation of learning something about the coupling of a chemical reaction and transport processes in such systems will be disappointed, since this subject is not discussed at all.

It is rather a theoretically oriented textbook of chemical kinetics in the usual sense, preceded by a 70-page introduction to the kinetic theory of gases and the theory of transport processes in electrolyte solutions. On further reading it is found, surprisingly enough, that there is no discussion of the coupling of a chemical reaction and macroscopic transport processes, even where it would be necessary, as in the section on heterogeneous catalysis. (The general statement that diffusion of the reactants to the catalyst is rate-determining only at very low pressures is certainly wrong.) The definition of the reaction rate used in the book applies only to closed, homogeneous systems at constant volume, and the treatment in general is limited to such systems.

The at first sight somewhat misleading title is justified by the last three chapters, which are essentially devoted to the theory of reaction rate constants, the emphasis being on aspects based on the kinetic theory of matter, *i. e.* on collisions. Gas reactions and the results of experiments with crossed molecular beams are in the foreground, but brief reference is also made to the relation between self-diffusion and the upper limits of the rates of bimolecular reactions in solutions. The comparison with transition state theory and the critical discussion of different theoretical concepts may be interesting and valuable to readers who are familiar with the subject.

It appears doubtful, however, whether this book is also suitable for students with only basic knowledge of chemical thermodynamics and statistical mechanics, as indicated in the preface. The present reviewer would not recommend it without reservations to this class of potential readers. Inaccurate statements and a somewhat carefree usage of definitions can be tolerated by the well-initiated reader but inaccurancy may be rather cumbersome if the subject matter is unfamiliar.

Lothar Riekert [NB 486 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. All the publications listed are available through Buchhandlung Chemie, Boschstrasse 12, D-6940 Weinheim (Germany).

Physical Chemistry. By *M. K. Kemp.* Marcel Dekker, New York 1979. xxii, 1034 pp., bound, SFrs. 52.00.—ISBN 0-8247-6640-7

Kirk-Othmer: Encyclopedia of Chemical Technology, Vol. 5. Castor Oil to Chlorosulfuric Acid. John Wiley & Sons, London 1979. 3rd edit. xxv, 880 pp., £ 60.00.—ISBN 0-471-02041-9; Index Volume 1 to 4 (A to Cardiovascular Agents) (gratis for subscribers)

Praxis der Hochleistungs-Flüssigchromatographie. By *V. Meyer.* Diesterweg/Salle/Sauerländer, Frankfurt 1979. viii, 198 pp., ring book, DM 39.00.—ISBN 3-425-05452-X (Diesterweg); 3-7941-1816-2 (Sauerländer); a volume of the series "Laborbücher Chemie"

Topics in Enzyme and Fermentation Biotechnology. Edited by *A. Wiseman.* John Wiley & Sons, London 1979. 3rd edit. 294 pp., bound, £ 19.50.—ISBN 0-470-26635-X

Wasser und Wasseruntersuchung. By *L. A. Hütter.* Diesterweg/Salle/Sauerländer, Frankfurt 1979. 223 pp., ring book, DM 34.00.—ISBN 3-425-05074-5 (Diesterweg); 3-7941-1718-2 (Sauerländer); a volume of the series "Laborbücher Chemie"

Physicochemical Measurement by Gas Chromatography. By *J. R. Conder* and *C. L. Young.* John Wiley & Sons, London 1979. xix, 632 pp., bound, £ 30.00.—ISBN 0-471-99674-2

Developments in Polymerisation—1. Edited by *R. N. Haward.* Applied Science Publishers, London 1979. ix, 202 pp., bound, $ 50.00.—ISBN 0-85334-822-7

The Plastically Crystalline State. Edited by *J. N. Sherwood.* John Wiley & Sons, London 1979. xxvi, 383 pp., bound, £ 19.50.—ISBN 0-471-99715-3

Metabolic Activation of Polynuclear Aromatic Hydrocarbons. By *W.-S. Tsang* and *G. W. Griffin.* Pergamon Press, New York 1979. vii, 125 pp., bound, $ 25.00.—ISBN 0-08-023835-1

Styrene Polymers: Technology and Environmental Aspects. By *C. A. Brighton, G. Pritchard,* and *G. A. Skinner.* Applied Science Publishers, London 1979. vii, 284 pp., bound, $ 45.00.—ISBN 0-85334-810-3

Foundations of Molecular Pharmacology, Vol. 1. Medicinal and Pharmaceutical Chemistry. By *J. B. Stenlake.* The Athlone Press, London 1979. xi, 936 pp., bound, £ 36.00.—ISBN 0-485-11171-3; **Vol. 2: The Chemical Basis of Drug Action.** 318 pp., bound, £ 18.50.—ISBN 0-485-11172-1

Techniques of Chemistry, Vol. XIII. Laboratory Engineering and Manipulations. Edited by *E. S. Perry* and *A. Weissberger.* John Wiley & Sons, New York 1979. 3rd edit. xi, 531 pp., bound, $ 53.00.—ISBN 0-471-03275-1

Fluid Flow and Heat Transfer. By *A. L. Lydersen.* John Wiley & Sons, London 1979. x, 357 pp., bound, £ 16.95.—ISBN 0-471-99697-1

Liquid Chromatographic Analysis of Food and Beverages, Vol. 1. Edited by *G. Charalambous.* Academic Press, New York 1979. xiii, 236 pp., bound, $ 16.00.—ISBN 0-12-169001-6

ANGEWANDTE CHEMIE
International Edition in English
Volume 18 · Number 12
December 1979
Pages 887–966

Nodal Nomenclature—General Principles

By Noël Lozac'h, Alan L. Goodson, and Warren H. Powell[*]

A new, comprehensive graph-based nomenclature system for chemical substances is proposed. Substances are named by using nodal nomenclature to name graphs derived from their structures by ignoring chemical details such as atom identities, bonding, charges, *etc.* After the fundamental graph is named, these chemical details are introduced by modifications and additions to the name of the graph to yield the name of the actual substance. Although development of nodal nomenclature originated with problems in naming some organic systems, it is not limited to organic substances. In this paper, only general principles for naming the graph are described; applications to specific substances will be discussed in future papers.

1. Preface

The work reported here originated as a suggestion by one of us (N. L.) during the 1973 meeting of the Commission on the Nomenclature of Organic Chemistry (CNOC) of the International Union of Pure and Applied Chemistry (IUPAC). It soon became apparent that this concept, conceived as a basis for naming a class of compounds known as "cyclophanes", had a very much wider applicability. In fact, its potential surpasses the confines of organic chemistry.

Independently, as part of a continuous review of nomenclature procedures, a study of ring nomenclature was started at Chemical Abstracts Service (CAS) in 1972 which developed into an effort to produce a general, graph-based nomenclature system.

When, at the 1975 meeting of CNOC, it became apparent that the CAS work and nodal nomenclature were developing along very similar lines, the evaluation and further development of nodal nomenclature became a joint effort.

Chemical nomenclature has developed in a rather random manner, paralleling the development of chemistry. Its principles were therefore not conceived from the beginning with a clear, overall plan, resulting in a mixture of nomenclature systems with overlapping rules, inconsistencies, and inadequate treatment for some types of compounds. An extensive set of organic nomenclature rules has been published[1–4], which is primarily a codification of the practices used by the chemical community insofar as these practices were determined to be sound.

The main objective of CNOC now is to improve this existing system of organic nomenclature. Accordingly, CNOC is engaged in revising its rules mainly through simplification, systematization, and extension, as necessary, and plans to publish these revised rules[5].

Nodal nomenclature will not be included in the proposed revised rules because to do so would not conform to the established CNOC policy of recommending the codified use of existing nomenclature practices. However, the potential of the nodal nomenclature system has been recognized and CNOC has therefore encouraged the publication of its basic principles and some guidelines for its use. This will enable nodal nomenclature to be used and evaluated by the chemi-

[*] Prof. N. Lozac'h [+]
Institut des Sciences de la Matière et du Rayonnement
Université de Caen
14032 Caen Cedex (France)
Dr. A. L. Goodson and Dr. W. H. Powell
Chemical Abstracts Service
P.O. Box 3012
Columbus, Ohio 43210 (USA)
[+] To whom correspondence should be addressed.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0887 $ 02.50/0*

cal community where current nomenclature systems prove difficult, cumbersome, or inadequate. The experience gained will provide constructive criticism and guidance for further development. We do not regard nodal nomenclature as fully developed at this time and anticipate that some minor modifications may be necessary or desirable before it is considered by CNOC for assimilation into the IUPAC system of organic nomenclature.

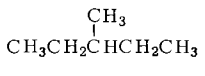
We have taken considerable care to ensure that nodal nomenclature is compatible with existing nomenclature systems as well as with the proposed revised rules in order that nodal nomenclature will be as widely applicable as possible. Thus, some of the traditional practices of present nomenclature systems need not be abandoned.

One of the most important features of nodal nomenclature is that this is the first time a comprehensive, computer-compatible system has been introduced to name structure graphs systematically, although numerous papers have been published dealing with structure graphs as an aid to describing ring systems. Furthermore, the resulting names are easily modified to describe actual chemical substances.

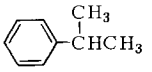
Complex examples with long systematic names are used at times in this paper to demonstrate the wide scope and facile application of nodal nomenclature, but it must be emphasized that nodal nomenclature has not been developed solely for naming unusual or complex structures; it is a system with completely general applicability. Structures which can be named easily by traditional nomenclature systems can be named just as easily by nodal nomenclature with attendant supplementary advantages.

2. Introduction

Development of nodal nomenclature was prompted by the recognition of various shortcomings in existing organic nomenclature systems. Most of these deficiencies are related in one way or another to the fact that even relatively simple structures, such as hydrocarbons, must be often described by substitutive principles, for example:



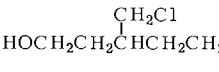
3-Methylpentane



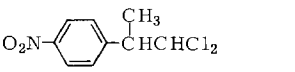
2-Phenylpropane
or
Isopropylbenzene

Consequences of using the substitutive principles of existing organic nomenclature systems include: (a) the names of simple structures, such as those illustrated above, are obscured and often completely lost when the structures are substituted by characteristic groups; (b) multiple occurrences of characteristic groups are often scattered throughout the name; and (c) unique locants are not available to denote each skeletal atom in the structure. These problems are illustrated in the following derivatives of the hydrocarbons shown above.

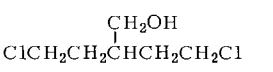
These problems are sometimes avoided in traditional organic nomenclature by use of a number of trivial names, *i.e.* simple names implying relatively large structural units, usually with complete unique numberings and often with implied stereochemistry. Such trivial names coexist with systematic names which are usually longer because they are derived from smaller structural units. The examples below illustrate this situation.



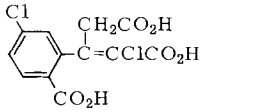
3-(Chloromethyl)-1,5-pentanediol



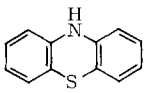
1,1-Dichloro-2-(4-nitrophenyl)propane
or
1-(2,2-Dichloro-1-methylethyl)-4-nitrobenzene



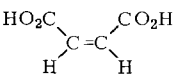
4-Chloro-2-(2-chloroethyl)-1-butanol



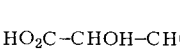
3-(2-Carboxy-5-chlorophenyl)-2-chloro-2-pentenedioic acid



Phenothiazine
or
10*H*-Dibenzo[*b*,*e*][1,4]thiazine



Maleic acid
or
cis-Butenedioic acid



Tartaric acid
or
2,3-Dihydroxybutanedioic acid

Nodal nomenclature describes the graph of a compound and avoids the deficiencies noted above by providing a unique locant for each position in the structure (see Section 3). However, even though substitutive principles need not be used to describe the graph of a substance, as is the case in traditional systems, they may be used to indicate characteristic groups in names for specific compounds. This will be discussed in later papers.

3. General Concepts of Nodal Nomenclature

The basic logic of nodal nomenclature resides in the description of a structure in terms of its graph. The term "node"[6] is derived from the Latin "nodus" and has the meaning of a knot, bulge, or intersection of branches. It is applied to single skeletal units, *i.e.*, atoms, of a structure. It may also be applied to groups of atoms forming important structural units, such as a benzene ring in a cyclophane, an amino acid fragment in a polypeptide, or a mononuclear component of a polynuclear acid. Nodes representing such groups of atoms can be called "contraction nodes".

General nodal nomenclature, the subject of this paper, describes the numbering and arrangements of nodes of a graph. It does not specify the nature of the nodes. *Specific nodal nomenclature,* on the other hand, describes the nature or structure of the nodes, specifies the bonding between the nodes, *etc.* It will be discussed in subsequent publications.

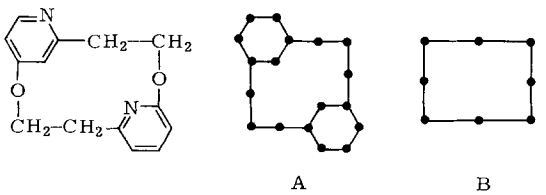
Since the graph concept for naming and numbering[*] structures is most easily illustrated by use of graphs derived

[*] Here "numbering" means the assignment of locants to nodes or skeletal atoms (and of module seniority numbers to module seniority descriptors).

from organic structures, the rules of general nodal nomenclature are often illustrated in this paper by graphs derived from hydrocarbons and heterocycles. In addition, we use the suffix "-ane" (as "nodane") which denotes saturated structures in traditional organic nomenclature. However, this should not be taken to imply in any way that nodal nomenclature is not equally applicable to other types of compounds, such as coordination compounds. Furthermore, the examples and terminology of this paper should not conceal a fundamental difference between the concepts of classical organic nomenclature and those of nodal nomenclature. In classical organic nomenclature, the skeletal atoms are usually atoms of the common nonmetallic elements (such as carbon, nitrogen, and oxygen) and have defined ligancies based on classical valence considerations. On the other hand, in general nodal nomenclature, the ligancy of a node is not limited in any way and therefore a node can have a ligancy of any value, which becomes apparent only when the nature of the node is defined.

In contrast to classical organic nomenclature, nodal nomenclature provides a unique numerical locant for every node of a graph. This may also be useful in some specialized areas of traditional organic nomenclature, such as steroids and alkaloids, where trivial names may be preferred to systematic ones. Although proliferation of trivial names is not desirable, they are simpler than systematic organic names and often imply considerable stereochemical information. One rather serious problem with many trivial names is that the associated numbering is sometimes incomplete, often arbitrary, and may vary from structure to structure within the same class. Nodal nomenclature, on the other hand, provides a general numbering system that can be used with any trivial name or nomenclature system.

Before any specific compound can be named by nodal nomenclature, two decisions dealing with its structure need to be made. First, the parts of the structure that are to be excluded from the portion of the structure to which general nodal nomenclature is to be applied—and are therefore to be treated as substituents—must be determined. This choice is not necessary in the most general application of nodal nomenclature, but is peculiar to classical organic nomenclature. It is included here because, as noted above, we want to make general nodal nomenclature as compatible as possible with existing nomenclature systems (see Section 1). Secondly, the nature of the nodes that will be named by nodal nomenclature must be determined. General nodal nomenclature does not define the nature of the nodes; this is dependent on the type of compound and the circumstances in which it is reported. However, in order to name the graph by the principles of general nodal nomenclature, it is necessary to define the nature of the individual nodes. For example, the structure shown below can be named on the basis of graph A (in which each node is an atom) or of graph B (in which each pyridine ring has been "contracted" to a single node (contraction node) to simplify the graph, as has been proposed for naming cyclophanes)[7].



A B

Once the graph has been defined, general nodal nomenclature is used to describe the arrangement and numbering of the nodes, as detailed in this paper. Then, as will be discussed in subsequent papers, specific nodal nomenclature is used to describe the nodes, bonding, and substituents expressed as prefixes and/or suffixes.

Only after the nodes and bonds of the graph have been specified are the ligancies of the nodes satisfied by attaching hydrogen as needed if *substitutive nomenclature* is to be used. Thus, in general nodal nomenclature the graph of 3-methylpentane (see Section 2) would be named [5.1^3]hexanodane. In specific (substitutive) nodal nomenclature this parent hydrocarbon could be named, according to the rules of Section G[5], as [5.1^3]hexacarbane, or, more traditionally, as [5.1^3]hexane. The silicon analog could be named [5.1^3]hexasilane. Such parent hydrides can be substituted by characteristic groups as in classical organic nomenclature to yield names such as 5,6-dichloro[5.1^3]hexacarban-1-ol; according to current rules the compound has the name 5-chloro-3-(chloromethyl)-1-pentanol.

It is evident from the preceding discussion that, in comparison with classical organic nomenclature, nodal nomenclature has many advantages, including:

1. consistent treatment of chains and rings, and of assemblies of chains and rings;
2. systematic numbering of the atoms in complex structures, as commonly occur in natural products, such numberings being equally applicable to structures described by trivial or semisystematic names;
3. applicability to structures with nodes of high ligancy as, for example, occur in coordination compounds;
4. logical description of an assembly of subunits or modules of any type or degree of complexity, such as: (a) cyclic systems in ring assemblies, protophanes and cyclophanes; (b) amino acid fragments in polypeptides and proteins; (c) mononuclear components in polynuclear acids;
5. the nomenclature is suitable for computerization.

4. Glossary

For the usual terms of classical organic nomenclature, the definitions given in References [1–4] are followed. In addition, there are certain terms used in this and subsequent papers in this series which have a new or special meaning. These terms are defined as follows:

General Nodal Nomenclature: The description and numbering of the arrangement of nodes in a graph.

Assembly (of modules): A structure graph composed of more than one cyclic module or of at least one acyclic module and at least one cyclic module.

Contraction (of a module): The operation by which a module is reduced to a contraction node to simplify the descriptor and name a structure or to facilitate the numbering.

Contraction node: A group of nodes, that can be named as a unit in specific nodal nomenclature, which is contracted to a single node to facilitate the description of a complex system in general nodal nomenclature.

Descriptor: The numeric portion of a nodal name[8], enclosed in brackets, providing an unambiguous description of a graph.

Graph (Structure Graph): An arrangement of nodes and lines representing, respectively, the atoms or groups of atoms and bonds (or connectivities) forming a molecule.

Module: A single node or an entirely cyclic or acyclic subset of nodes that is treated as a separate entity during the numbering and naming of a graph assembly.

Module Seniority Descriptor A capital letter assigned to each module to designate its relative seniority in an assembly of modules.

Module Seniority Graph An arrangement of module seniority descriptors used for determining the order in which the various modules of an assembly are to be numbered.

Module Seniority Number Arabic numeral assigned to a module seniority descriptor in a module seniority graph.

Node[6]: The simplest unit of a graph, representing either a single atom or a group of atoms.

Principal Module: The senior module where numbering of the module seniority graph and unique numbering of the corresponding assembly begins.

Senior Module: The module, or one of the modules, of highest seniority in an assembly.

Specific Nodal Nomenclature: The description and numbering of a chemical structure, the specific nodal name being obtained by adding to the general nodal name a description of such details as the nature of the nodes, bonding, charges, *etc.*

Structure Graph (see *Graph*): Used principally to ensure that graphs related to chemical structures are not confused with other types of graph, *e.g.*, graphs related to reaction sequences.

5. Proposed Rules for General Nodal Nomenclature

Rule N-1—*Acyclic Graphs*

N-1.1. *An acyclic graph* is an unbranched chain of nodes or two or more unbranched chains of nodes connected to each other without formation of a cyclic structure. No matter how complex, it is never considered as a combination of separate structural parts[9].

N-1.2. The *main chain* in an acyclic graph is the longest unbranched chain of nodes and is numbered first, from one end to the other. When an acyclic graph has two or more equal unbranched chains of greatest length, the main chain is the one having the longest branches (see **Rule N-1.3**) attached to it. The main chain is numbered so that the lowest possible locants are given to these longest branches. If a choice remains, see **Rule N-1.6.**

N-1.3. *Branches* in an acyclic graph are unbranched chains of nodes attached to the main chain or to other, longer branches. Each is numbered from one end to the other, beginning always with the node attached to the part of the graph already numbered.

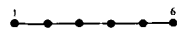
N-1.4. *Branches* in an acyclic graph are numbered successively in order of decreasing length. When two or more branches are of equal length, they are numbered in increasing order of the locants already assigned for the nodes of the chain(s) to which they are attached.

N-1.5. The *descriptor* of an acyclic graph consists of square brackets enclosing: (a) an Arabic numeral indicating the number of nodes in the main chain; (b) a period, followed by Arabic numerals denoting the number of nodes in each branch, cited in the order of their numbering (see **Rule N-1.4**); and (c) a superscript locant for each branch numeral denoting the node of the part of the graph already numbered to which the branch is attached[10].

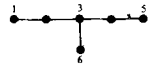
N-1.6. When two or more *alternative descriptors* for an acyclic graph can be derived, the correct descriptor is the one having the lowest superscript number at the first point of difference when these locants are compared term by term from the beginning of the descriptor[11].

N-1.7. The *name* of an acyclic graph consists of: (a) the descriptor derived as in **Rule N-1.5**; (b) a multiplying prefix, such as "di-", "tri-", "tetra-", *etc.*[12], denoting the total number of nodes; and (c) the ending "-nodane"[13].

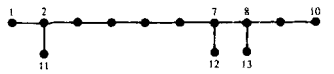
Examples[14]:

1. 

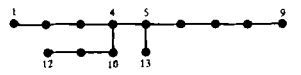
[6]Hexanodane

2. 

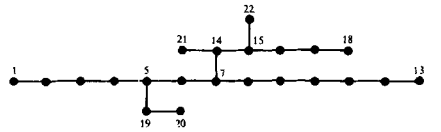
[5.1^3]Hexanodane

3. 

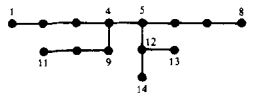
[10.1^{2}1^{7}1^8]Tridecanodane

4. 

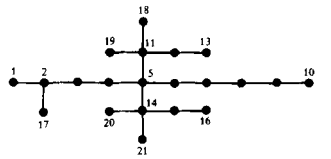
[9.3^{4}1^5]Tridecanodane

5. 

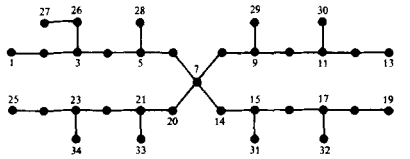
[13.5^{7}2^{5}1^{14}1^{15}]Docosanodane

6. 

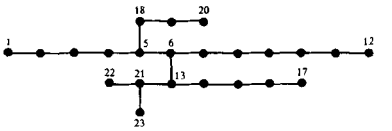
[8.3^{4}2^{5}1^{12}]Tetradecanodane

7. 

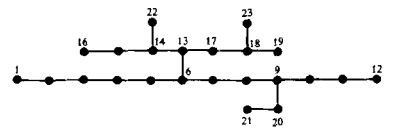
[10.3^{5}3^{5}1^{2}1^{11}1^{11}1^{14}1^{14}]Henicosanodane

8. 

[13.6^{7}6^{7}2^{3}1^{5}1^{9}1^{11}1^{15}1^{17}1^{21}1^{23}]Tetratriacontanodane

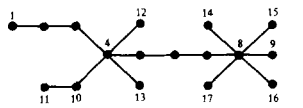
9. 

[12.5^{6}3^{5}2^{13}1^{21}]Tricosanodane

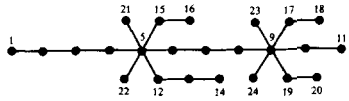
10. 

[12.4^{6}3^{13}2^{9}1^{14}1^{18}]Tricosanodane

Note: The descriptor [12.4^{6}3^{13}2^{9}1^{15}1^{17}] is not correct because the locant series 6,13,9,*15*,17 is higher than 6,13,9,*14*,18 **(Rule N-1.6).**

11. 

[9.2^{4}1^{4}1^{4}1^{8}1^{8}1^{8}1^8]Heptadecanodane

12. 

[11.3^{5}2^{5}2^{9}2^{9}1^{5}1^{5}1^{9}1^9]Tetracosanodane

Rule N-2.—*Monocyclic Graphs*

N-2.1. Monocyclic graphs are *numbered* sequentially from any node in either direction until all nodes are numbered.

N-2.2. The *descriptor* of a monocyclic graph consists of square brackets enclosing a zero (indicating the presence of a ring) and an Arabic numeral denoting the number of nodes forming the ring.

N-2.3. The *name* of a monocyclic graph consists of: (a) the descriptive prefix "cyclo"; (b) a descriptor derived according to **Rule N-2.2**; (c) a multiplying prefix indicating the number of nodes in the ring[12,15]; and (d) the ending "-nodane"[13].

Example:



Cyclo[08]octanodane

Rule N-3.—*Polycyclic Graphs*[*]

N-3.1. A *polycyclic graph* consists of a monocyclic ring of nodes and one or more bridges, which are valence bonds or chains of nodes connecting nodes of the main ring and/or other bridges in the polycyclic system.

N-3.2. The *main ring* in a polycyclic graph is the monocyclic ring containing the greatest number of nodes. When two or more monocyclic rings have the same number of nodes, the main ring is chosen according to **Rule N-3.6.**

N-3.3. The *main bridge* in a polycyclic graph is the longest unbranched chain of nodes both ends of which are attached to the main ring[16]. When two or more chains are of equal length, the main bridge is chosen according to **Rule N-3.6.** Other bridges are called *secondary* bridges.

N-3.4. The *numbering* of a polycyclic graph begins at one of the nodes of the main ring to which the main bridge is attached (bridgehead) and proceeds in the direction that gives the lower locant to the other bridgehead. The main bridge is numbered sequentially after the main ring, beginning with the node of the main bridge connected to the node in the main ring having the locant 1. The secondary bridges are numbered successively in the same manner, beginning always with the longest bridge (or one of the longest bridges) connected to nodes of the graph previously numbered[17]. When there is a choice between two or more bridges of the same length, the first to be numbered is the one attached to

[*] In nodal nomenclature phanes can be treated as mono- or polycycles.

the node having the lowest locant in the part of the graph previously numbered. Each bridge is numbered beginning with the node of the bridge connected to the node of the part of the graph previously numbered having the lower locant.

N-3.5. The *descriptor* of a polycyclic graph consists of square brackets enclosing: (a) a zero indicating the presence of a ring followed by an Arabic numeral indicating the number of nodes in the main ring (see **Rule N-2.2**); (b) a period followed by Arabic numerals denoting the number of nodes in each bridge, cited in the order of their numbering (see **Rule N-3.4**); and (c) a pair of superscript locants for each bridge numeral, separated by a comma and cited in increasing numerical order, denoting the nodes in the part of the polycyclic graph already numbered to which each bridge is attached[18].

N-3.6. When two or more *alternative descriptors* for a polycyclic graph can be derived because there is a choice for the main ring, main bridge, starting point and/or direction of numbering, Arabic numerals, in each descriptor, denoting the lengths of the bridges *and* the positions of the bridges in the graph are compared term by term in the order they appear (see **Rule N-3.5**). The correct descriptor is the one with the preferred Arabic numeral at the first difference: if the first difference corresponds to a bridge length, the preferred numeral is higher; if the first difference appears in a superscript numeral (locant), the preferred numeral is lower[19].

N-3.7. The *name* of a polycyclic graph consists of: (a) a descriptive prefix, such as "bicyclo-", "tricyclo-", *etc.*, indicating the number of rings in the ring system[20]; (b) the descriptor derived according to **Rules N-3.5** and **N-3.6**; (c) a multiplying prefix[12] indicating the total number of nodes; and (d) the ending "-nodane"[13].

Examples[21]:

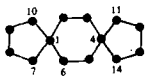
1.  Bicyclo[06.$2^{1,4}$]octanodane

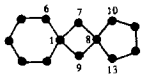
2.  Bicyclo[05.$4^{1,1}$]nonanodane

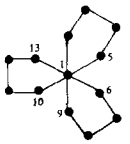
3.  Bicyclo[07.$1^{1,4}$]octanodane

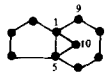
Note: The descriptor [07.$1^{1,5}$] is not correct because, for the main bridge, the locant series 1,*5* is higher then 1,*4* **(Rule N-3.4).**

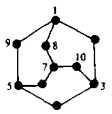
4.  Tricyclo[08.$1^{1,4}1^{5,8}$]decanodane

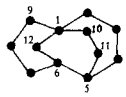
5.  Tricyclo[06.$4^{1,1}4^{4,4}$]tetradecanodane

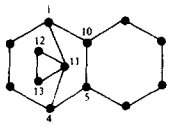
6.  Tricyclo[06.$3^{1,1}4^{8,8}$]tridecanodane

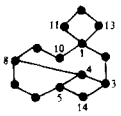
7.  Tricyclo[05.$4^{1,1}4^{1,1}$]tridecanodane

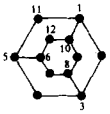
8.  Tricyclo[09.$1^{1,5}0^{1,5}$]decanodane
*[4.3.1]Propellane

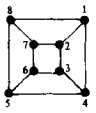
9.  Tricyclo[08.$1^{1,5}1^{3,7}$]decanodane
*Adamantane

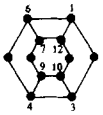
10.  Tricyclo[09.$2^{1,5}1^{1,6}$]dodecanodane

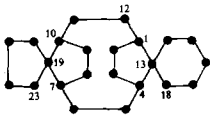
11.  Tetracyclo[010.$1^{1,4}2^{11,11}0^{5,10}$]-tridecanodane

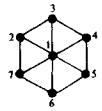
12.  Tetracyclo[010.$3^{1,1}1^{3,5}0^{4,8}$]-tetradecanodane

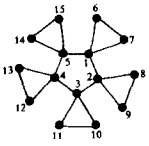
13.  Tetracyclo[010.$1^{1,5}1^{6,10}0^{3,8}$]-dodecanodane
*Iceane

14.  Pentacyclo[08.$0^{1,4}0^{2,7}0^{3,6}0^{5,8}$]-octanodane
*Cubane

15.  Pentacyclo[012.$0^{1,6}0^{3,10}0^{4,9}0^{7,12}$]-dodecanodane
*Tetraasterane

16.  Pentacyclo[012.$1^{1,4}5^{13,13}1^{7,10}4^{19,19}$]-tricosanodane

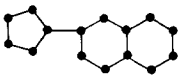
17.  Hexacyclo[07.$0^{1,3}0^{1,4}0^{1,5}0^{1,6}0^{2,7}$]-heptanodane

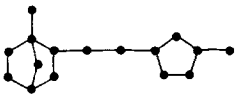
18.  Hexacyclo[05.$2^{1,1}2^{2,2}2^{3,3}2^{4,4}2^{5,5}$]-pentadecanodane
*[5]Rotane

Rule N-4.—*Assemblies of Cyclic and Acyclic Graphs*

N-4.1. A structure graph is called an *assembly* if it is composed of more than one cyclic module or of at least one acyclic module and at least one cyclic module[9].

Examples:

1. 

2. 

N-4.11. An *acyclic module* is a single node or a branched or unbranched chain of nodes in an assembly.

N-4.12. A *cyclic module* is the graph of a ring or ring system in the conventional meaning of these terms[1]. Assemblies of directly-connected, identical cyclic modules, such as the structure graph of terphenyl, are not considered as one module; each component is considered as a separate cyclic module.

N-4.2. An *assembly descriptor* consists of square brackets enclosing: (a) in parentheses, the nodal descriptor of the principal module (which is the senior module (determined by **Rule N-4.3**), or one of the senior modules, chosen according to **Rules N-5.34** and **N-5.4**); (b) in parentheses, the nodal descriptors of the remaining modules, cited in order of numbering according to **Rules N-5.3** and **N-5.4**[22]; and (c) numerical locants, separated by colons, indicating the nodes through which each pair of modules is linked, each locant set linking the appropriate pair of module descriptors.

Example: [(06)1:7(4)10:11(05)]

N-4.21. The *descriptor* of each module in an assembly is identical with the descriptor of the corresponding isolated graph except that the enclosing square brackets are replaced by parentheses. Accordingly, this descriptor retains its original numbering, *i.e.*, the numbering that would be used to describe it if it were an isolated graph.

Example: [(06.$1^{1,4}$)2:10(4.1^{2})]

N-4.22. The *locant set* separating each pair of module descriptors in an assembly descriptor is derived from the definitive sequential numbering for the whole assembly as given in **Rule N-5.** Each locant set is written as follows: (a) the locant of the node, in the part of the graph previously numbered, through which the following module is attached; (b) a colon; and (c) the locant of the node, in the following module, through which that module is attached to the part of the graph previously numbered.

Example: [(06.$1^{1,4}$)2:10(4.1^{2})]

N-4.23. In an *unbranched assembly* with a *terminal* principal module, the first locant of any locant set refers to the immediately preceding module. Each locant is higher than the immediately preceding locant in the descriptor.

Example: [(06)1:7(06)10:13(06)16:19(06)]

Note: The locant series 1,7,10,13,16,19 increases steadily.

N-4.24. In an *unbranched assembly* with a *nonterminal* principal module and in a *branched assembly,* the first locant of at least one locant set refers to a module cited in the descriptor earlier than the immediately preceding module. This locant is lower than the immediately preceding locant in the descriptor.

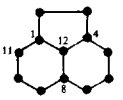
Examples:

1. [(06)1:7(05)4:12(05)]
   Note: In this descriptor of an assembly with a nonterminal principal module, the locant series 1,7,4,12 does not increase steadily and the locant 4, being lower than 7, refers to the first module cited in the descriptor, and not to the second module.
2. [(06)1:7(06)9:13(06)11:19(06)]
   Note: In this descriptor of a branched assembly, the locant series 1,7,9,13,11,19 does not increase steadily and the locant 11, being lower than 13, refers to the second module in the descriptor, and not to the third module.

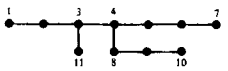
N-4.3. *Seniority of modules* in an assembly is determined by the following criteria, which are applied successively until a decision is reached[19]:

a) Largest number of nodes.
b) Cyclic module preferred to acyclic module.
c) Largest number of rings or branches (side chains).
d) Largest main ring or longest chain.
e) Longest bridge or branch (side chain).
f) Lowest locants for attachment of bridges or branches (side chains).

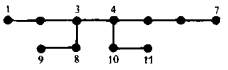
Examples (in order of decreasing seniority: the criterion deciding the seniority of an example over the one following is noted in each case):

1.  Tricyclo[011.$1^{1,4}0^{8,12}$]dodecanodane

(senior to the following module, according to criterion a)

2.  [7.$3^{4}1^{3}$]Undecanodane

(senior to the following module, according to criterion e)

3.  [7.$2^{3}2^{4}$]Undecanodane

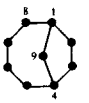
(senior to the following module, according to criterion a)

4.  Tricyclo[07.$2^{1,4}0^{5,7}$]nonanodane

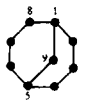
(senior to the following module, according to criterion e)

5.  Tricyclo[07.$1^{1,3}1^{4,7}$]nonanodane

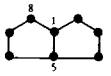
(senior to the following module, according to criterion c)

6.  Bicyclo[08.$1^{1,4}$]nonanodane

(senior to the following module, according to criterion f)

7.  Bicyclo[08.1^{1,5}]nonanodane

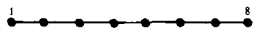
(senior to the following module, according to criterion a)

8.  Bicyclo[08.0^{1,5}]octanodane

(senior to the following module, according to criterion d)

9.  Bicyclo[07.1^{1,3}]octanodane

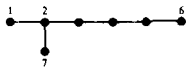
(senior to the following module, according to criterion b)

10.  [8]Octanodane

(senior to the following module, according to criterion a)

11.  [5.1^{2}1^3]Heptanodane

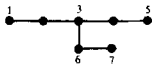
(senior to the following module, according to criterion c)

12.  [6.1^2]Heptanodane

(senior to the following module, according to criterion f)

13.  [6.1^3]Heptanodane

(senior to the following module, according to criterion d)

14.  [5.2^3]Heptanodane

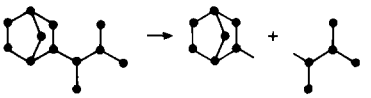
N-4.4. The *name* of an assembly consists of: (a) a descriptive prefix (such as "cyclo", "bicyclo", *etc.*) indicating the total number of rings in the assembly; (b) the assembly descriptor (see **Rule N-4.2**); (c) a multiplying prefix[12] indicating the total number of nodes in the assembly; and (d) the ending "-nodane"[13].

Example: Bicyclo[(06)1:7(05)4:13(3)]tetradecanodane

Rule N-5.—*Definitive Numbering of Assemblies*

N-5.1. The *definitive numbering* of an assembly defines the correct assembly descriptor. This numbering begins with the principal module (see **Rule N-4.2**) for which the original numbering is retained. The other modules are renumbered sequentially, beginning with a module adjoining the principal module and proceeding, where necessary, as described in **Rules N-5.3** and **N-5.4**. Each module is renumbered by adding to each of its original locants a number equal to the total number of nodes in the assembly that have already been assigned definitive locants. When there is a choice for the origin and/or the direction of numbering in a module, the correct numbering is the one giving the lowest locants to the nodes of attachment of the module to other modules in the assembly.

Example:



A B

This assembly consists of two modules, A and B. The procedure for numbering this assembly is:

a) Module A, the senior module of the assembly (see **Rule N-4.3a)**, is numbered and the descriptor generated according to **Rule N-3**.

 [06.1^{1,4}]

Since this module is the principal module of the assembly (see **Rule N-4.2**), it retains this numbering in the final numbering of the assembly. However, in this module there are two possible origins for numbering, each with two possible directions. Hence, in the assembly, the module is numbered so that the locant for the node of the attachment to the next module is as low as possible, *i.e.*, 2 (not 3, 5 or 6).

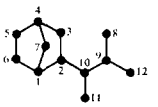
b) Module B is numbered and the descriptor generated according to **Rule N-1**.

 [4.1^2]

c) Module B is renumbered by adding 7 (the total number of nodes in module A) to each original locant.



d) The modules are recombined with their new numberings, where needed, and named according to **Rule N-4.4.**



Bicyclo[(06.1^{1,4})2 : 10(4.1^2)]dodecanodane

N-5.11. All assemblies in which the principal module terminates a *single linear chain of modules* are numbered and named by extension of the procedure described in **Rule N-5.1.**

Example:

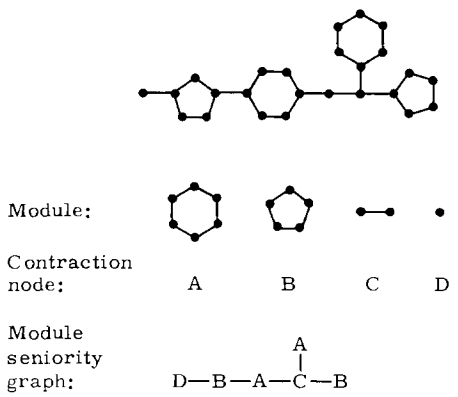


Bicyclo[(06)1 : 7(4)10 : 11(05)]pentadecanodane

N-5.12. In assemblies in which the principal module is attached to *a single, branched chain of modules or to two or more linear or branched chains of modules* and in which two or more definitive numberings are possible, the correct numbering is chosen on the basis of the order of *module seniority numbers* assigned to the *module seniority descriptors* of the *module seniority graph* (see **Rules N-5.2** and **N-5.3**). When this is not definitive, the correct numbering is chosen by comparing the descriptors derived from the various possible numberings (see **Rule N-5.4**).

N-5.2. The *module seniority graph* of an assembly is a representation of the component modules of the assembly in terms of their relative seniorities. Each component module is represented in the module seniority graph by a capital letter, *i.e.* a module seniority descriptor, signifying its relative seniority and its position in the assembly. The most senior module(s) is (are) denoted by A, the next most senior by B *etc.*

Example:

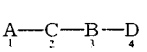


N-5.3. *Numbering of the module seniority graph, i.e.* assignment of the module seniority numbers, which determines the order of assignment of the definitive sequential numbering of the assembly (see **Rule N-5.1**), begins with the principal module (see **Rule N-4.2**) and proceeds, in order of decreasing seniority as defined in **Rule N-5.33**, through each chain of contraction nodes attached to the principal module[23].

N-5.31. *Module seniority numbers* are assigned to each chain of contraction nodes attached to the principal module of the seniority graph.

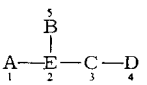
N-5.311. An *unbranched chain* of contraction nodes is numbered sequentially after the principal module whose seniority number is 1, according to **Rule N-5.1.**

Example:



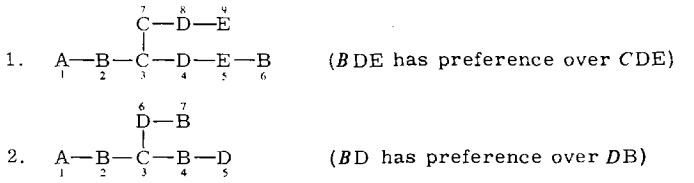
N-5.312. In a branched module seniority graph, the *longest unbranched chain* of module seniority descriptors (the main chain) is numbered first according to **Rule N-5.311**, followed by the branches attached to the main chain, in order of decreasing seniority as given in **Rule N-5.313**, where necessary.

Example:



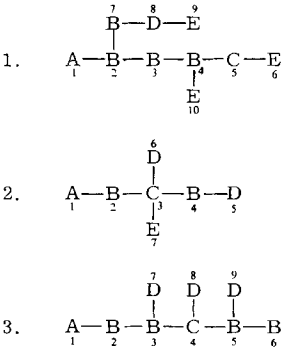
N-5.313. When, in a branched module seniority graph, two or more chains are of equal length, seniority numbers are first assigned to the unbranched chain in which the most senior contraction node is encountered at the first difference, the module seniority descriptors being compared term by term in order of seniority as defined in **Rule N-4.3**, regardless of their positions in the chain, and then in order of their position in the chain.

Examples:



N-5.314. *Branches* to the main chain of contraction nodes are numbered according to the following criteria which are applied successively as far as necessary in order to achieve a definitive numbering: (a) in order of decreasing length; (b) in order of seniority of the module seniority descriptors as defined in **Rule N-5.313**; (c) in order of the increasing numerical value of the seniority number for the contraction node to which the branch is attached in the part of the chain already numbered.

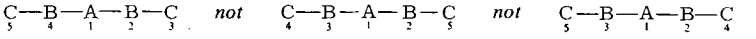
Examples:



N-5.315. *Branched branches* of contraction nodes are numbered by following the procedures given in **Rules N-5.312** and **N-5.313.**

N-5.32. When two or more chains of contraction nodes are attached to the principal module, *module seniority numbers* are assigned to each chain in its entirety, as described in **Rule N-5.31**, before proceeding to the next.

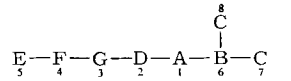
Example:



N-5.33. *Module seniority numbers* are assigned to two or more chains of contraction nodes attached to the principal module in order of seniority according to the following criteria, considered successively until a definitive numbering is obtained:

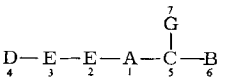
a) Largest number of contraction nodes in the entire chain.

Example:



b) Longest unbranched chain of contraction nodes.

Example:



c) The most senior contraction node encountered at the first difference, the module seniority descriptors being compared term by term in order of seniority as defined in **Rule N-4.3**, regardless of their positions in each chain.
Example:

D—B—A—C—B (BC *not* BD)
5 4 1 2 3

d) The most senior contraction node having the lowest seniority number
Example:

B—C—A—B—C *not* B—C—A—B—C
5 4 1 2 3 3 2 1 4 5

(*BC not CB*, because 2 is lower than 3)

N-5.34. When a module seniority graph contains two or more modules of highest seniority, *i. e.* with module seniority descriptor = A, the *principal module* is that senior module to which is attached the most senior chain of contraction nodes, as determined by the criteria described in **Rule N-5.33.**
Examples:

a) A—A—B *not* A—A—B
1 2 3 2 1 3
(see Rule N-5.33a)

b) A—A—A (A at 4) *not* A—A—A (A at 4)
1 2 3 3 1 2
(see Rule N-533a)

c) C—B—A—A—B—C—D (D at 8) *not* C—B—A—A—B—C—D (D at 5)
7 6 1 2 3 4 5 4 3 2 1 6 7 8
(see Rule N-5.33b)

d) D—A—B—A—C *not* D—A—B—A—C
5 1 2 3 4 4 3 2 1 5
(ABA*C*, *not* ABA*D*, see Rule N-5.33c)

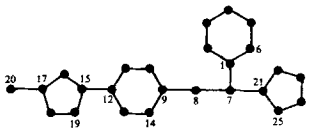
e) C—A—D—B—B—A—C *not* C—A—D—B—B—A—C
6 5 4 3 2 1 7 7 1 2 3 4 5 6
(*B*B, *not* *D*B, see Rule N-5.33d)

N-5.35. When the *numbering of the module seniority graph* is defined unambiguously by **Rules N-5.31** through **N-5.34,** an assembly is numbered by the procedure of **Rule N-5.1** applied to the modules in order of increasing numerical value of their seniority numbers.

Example (see the assembly illustrating **Rule N-5.2** above):

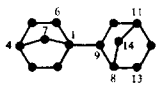
Module seniority graph: D—B—A—C—B (A at 1)
5 4 3 2 6

Module Seniority Number	Contraction Node Seniority	Number of Nodes	Module Locants	Assembly Locants
1	A	6	1—6	1—6
2	C	2	1—2	7—8
3	A	6	1—6	9—14
4	B	5	1—5	15—19
5	D	1	1	20
6	B	5	1—5	21—25



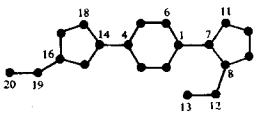
Tetracyclo[(06)1 : 7(2)8 : 9(06)12 : 15(05)17 : 20(1)-7 : 21(05)]pentacosanodane

N-5.4. When a *definitive order for numbering* the modules of an assembly cannot be determined by sole application of the principles of the module seniority graph **(Rules N-5.2** and **N-5.3)**[22], the correct order corresponds to the assembly descriptor that has the lowest locants defining the attachments of the modules. The set of lowest locants is the locant series having the lowest locant at the first point of difference when two or more series are compared term by term in order of appearance in each assembly descriptor.
Examples:

1. 

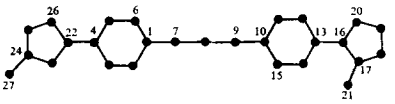
Tetracyclo[(06.1^{1,4})1 : 9(06.1^{1,4})]-tetradecanodane

Note: The descriptor [(06.1^{1,4})2:8(06.1^{1,4})] is not correct because the locant series for the module attachments *2,8* is higher than *1,9*.

2. 

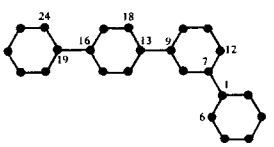
Tricyclo[(06)1 : 7(05)8 : 12(2)4 : 14(05)16 : 19(2)]icosanodane

Note: The descriptor [(06)1:7(05)9:12(2)4:14(05)15:19(2)] for this assembly, whose seniority graph is C-B-*A*-B-C, is not correct because the locant series 1,7,*9*,12,4,14,15,19 is higher than 1,7,*8*,12,4,14,16,19.

3. 

Tetracyclo[(06)1 : 7(3)9 : 10(06)13 : 16-(05)17 : 21(1)4 : 22(05)24 : 27(1)]heptacosanodane

Note: The descriptor [(06)1:7(3)9:10(06)13:16(05)18:21(1)4:22(05)23:27(1)] for this assembly, whose seniority graph is D-B-*A*-C-*A*-B-D, is not correct because the locant series 1,7,9,10,13,16,*18*,21,4,22,23,27 is higher than 1,7,9,10,13,16,*17*,21,4,22,24,27.

4. 

Tetracyclo[(06)1 : 7(06)9 : 13(06)16 : 19(06)]tetracosanodane

Note: The descriptor [(06)1:7(06)10:13(06)15:19(06)] is not correct because the locant series 1,7,*10*,13,15,19 is higher than 1,7,*9*,13,16,19.

6. A Procedure for Deriving the Correct Numbering and Name of an Assembly

The concept of the module seniority graph (see **Rules N-5.2** and **N-5.3**) enables even very complex assemblies to be numbered and named with ease. We now illustrate a procedure that has worked well for us in numbering and naming assemblies. We have deliberately chosen a very complex assembly because it illustrates well the use of the module seniority graph, even though most assemblies normally encountered in chemical substances are much simpler.

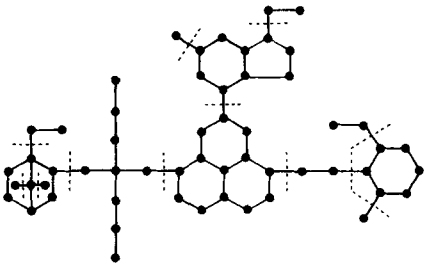
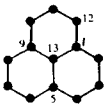
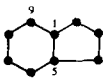
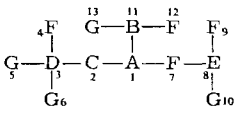
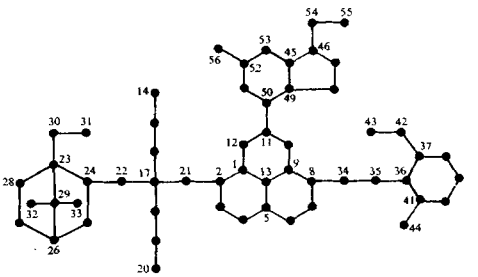


Fig. 1. Separation of an assembly into its modules.

Module Structure	Number of Nodes	Module Descriptor	Module Seniority	Module Seniority Number	Assembly Locants
	13	[012.1^{1,5}0^{9,13}]	A	1	1—13
	9	[7.1^{4}1^{4}]	C	2	14—22
	9	[09.0^{1,5}]	B	11	45—53
	7	[06.1^{1,4}]	D	3	23—29
	6	[06]	E	8	36—41
	2	[2]	F	4	30—31
	2	[2]	F	7	34—35
	2	[2]	F	9	42—43
	2	[2]	F	12	54—55
	1	[1]	G	5	32
	1	[1]	G	6	33
	1	[1]	G	10	44
	1	[1]	G	13	56

Module seniority graph:





Octacyclo[(012.1^{1,5}0^{9,13})2 : 21(7.1^{4}1^{4})22 : 24(06.1^{1,4})23 : 30-(2)29 : 32(1)29 : 33(1)8 : 34(2)35 : 36(06)37 : 42(2)41 : 44-(1)11 : 50(09.0^{1,5})46 : 54(2)52 : 56(1)]hexapentacontanodane

Fig. 2. Illustrative procedure for derivation of correct numbering and name of an assembly.

An assembly, such as the one shown on p. 897, is numbered and named in the following stepwise manner: (1) the assembly is separated into its modules as indicated in Figure 1; (2) the modules are sorted in order of decreasing number of nodes; (3) each module is numbered according to **Rule N-1, N-2,** or **N-3**; (4) the descriptor is derived for each module; (5) seniority is assigned to each module according to **Rule N-4.3;** (6) the seniority graph is drawn and the module seniority numbers assigned according to **Rules N-5.2** and **N-5.3**; (7) assembly locants are assigned by renumbering each module according to **Rules N-5.1** and **N-5.3**, or **N-5.4;** (8) the assembly locants are added to the structure of the assembly; (9) the assembly name is generated (see **Rule N-4.4**); and (10) the name is checked against the structure. This procedure is illustrated in Figure 2.

Nodal names are easily checked against the structure for accuracy. In the absence of the structure, nodal names provide a wealth of information about the structure. As in von Baeyer nomenclature, the descriptor portion of a nodal name contains all the information necessary to derive the structure; all the rest of the name, while essentially superfluous, provides a check on the descriptor and is also of value for listing in an alphabetical index.

Preliminary inspection of a nodal name provides much useful information that aids checking the name and in visualizing the structure. For example, inspection of the name [7.1^{4}1^4]nonanodane indicates: (1) the structure is acyclic since there is no "cyclo" term at the beginning of the name and no zero immediately precedes the first numeral of the descriptor; (2) the main chain consists of seven nodes and there are two one-atom branches attached to the fourth node; and (3) the total number of nodes is nine, obtained by summing the nonsuperscript numerals, which is confirmed by the term "nona" following the descriptor.

Similarly, inspection of the name bicyclo[06.1^{1,4}]heptanodane indicates: (1) the structure is cyclic because of the term "cyclo" before the descriptor and the zero immediately preceding the first numeral of the descriptor; (2) the structure consists of two rings, since there are two terms in the descriptor and the term "bi" precedes cyclo; and (3) the total number of nodes in the structure is seven, obtained by summing the nonsuperscript numerals of the descriptor, which is confirmed by the term "hepta" following the descriptor.

Such inspection is especially useful when checking the name of a complex assembly such as the one generated above (Fig. 2). From the assembly descriptor, we can see that there are eight rings in all, obtained by adding the number of nonsuperscript numerals in the module descriptors that begin with a zero (*i.e.*, 3+2+1+2); thus the numerical prefix "octa" to the term cyclo should be found in front of the assembly descriptor. By adding the values of all the nonsuperscript numbers, the total number of nodes in the structure is found to be 56 (*i.e.*, 12+1+7+1+1+6+1+2+1+1+2+6+2+1+9+2+1); this should correspond to the numerical prefix "hexapentaconta" which is found following the descriptor.

7. Deriving the Structure of an Assembly from its Name

Inspection of the assembly descriptor is also extremely valuable when deriving the structure of a complex assembly from its name. By using the following name,

Octacyclo[(012.1^{1,5}0^{9,13})2:21(7.1^{4}1^4)22:24(06.1^{1,4})23:30(2)29:32(1)29:33(1)8:34(2)35:36(06)37:42(2)41:44(1)11:50(09.0^{1,5})46:54(2)52:56(1)]hexapentacontanodane,

derived for the complex assembly given in Section 6, we can learn the following information by inspection of the descriptor: (1) the structure is an assembly of thirteen modules since

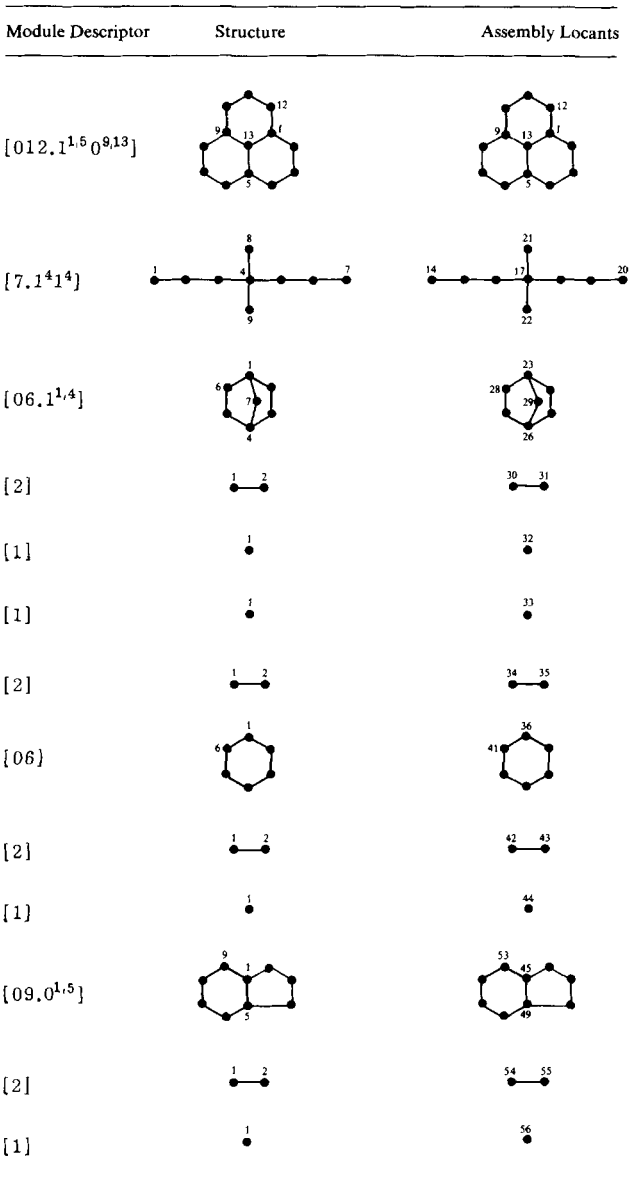


Fig. 3. Illustrative procedure for derivation of the structure of an assembly from its name.

there are thirteen descriptors, each enclosed in parentheses, in the total assembly descriptor defined by the square brackets; (2) four of the modules are cyclic since four module descriptors have a "zero" preceding the first numeral in the descriptor; (3) the assembly has a total of eight rings since the four modules defining cyclic structures have a total of eight terms and the prefix "octa" precedes cyclo in the name; (4) the assembly has nine acyclic modules, one of which is branched; and (5) the total assembly has 56 nodes, deter-

mined by summing all nonsuperscript numbers within the parentheses and confirmed by the numerical prefix "hexapentaconta" following the assembly descriptor.

The structure of this assembly may be derived from the name as follows: (1) each of the thirteen modules is drawn and numbered, according to its descriptor, in order of appearance in the name; (2) the assembly numbering is assigned to each module by adding to each locant the total number of preceding locants; (3) the modules are assembled in accordance with the locant sets for each pair of modules in the assembly descriptor; (4) the structure (see Fig. 2) is checked against the name as outlined above.

This procedure is summarized in Figure 3.

8. Conclusion

We have presented a comprehensive system for numbering and naming graphs of chemical compounds. The system can easily be adapted to naming chemical compounds and it avoids a number of shortcomings apparent in existing nomenclature systems. Not only does this system result in uniformity and a new approach for organic nomenclature, but it also provides new approaches for the nomenclature of complex coordination, inorganic, and biochemical systems. Future publications will delineate the application of this general system to specific types of compounds.

Received: November 28, 1978 [A 296 IE]
German version: Angew. Chem. *91*, 951 (1979)

---

[1] IUPAC: Nomenclature of Organic Chemistry (1969), Sections A and B, 3rd Edit., and Section C, 2nd Edit. (combined), Butterworths, London (1971).

[2] IUPAC: Nomenclature of Organic Chemistry, Section D (Tentative), IUPAC Information Bulletin Appendices on Tentative Nomenclature, Symbols, Units, and Standards, No. 31, August, 1973.

[3] IUPAC: Nomenclature of Organic Chemistry, Section E, Stereochemistry (Recommendations, 1974), Pure App. Chem. *45*, 11 (1976).

[4] IUPAC: Nomenclature of Organic Chemistry, Section F, Natural Products and Related Compounds, IUPAC Information Bulletin Appendices on Provisional Nomenclature, Symbols, Terminology, and Conventions, No. 53, December, 1976.

[5] IUPAC: Nomenclature of Organic Chemistry, Section G, in preparation.

[6] The term "node" has been used for multivalent centers by *M. Gordon* and *W. B. Temple* in *A. T. Balaban:* Chemical Applications of Graph Theory, Academic Press, London, 1976, p. 312. This term was introduced by *J. J. Sylvester*, Am. J. Math. *1*, 64 (1878) as follows: "The conception of hydrocarbon graphs as 'trees with nodes, branches and terminals' ... [is] exclusively my own and [was] used by me in my communications with Professor Crum Brown on the subject and stated by me in a letter to Professor Cayley who has adopted [it] as the basis of his own isomerical researches". It should be noted that it is convenient in nodal nomenclature for the term "node" to include terminals, (*i.e.*, "univalent" centers) and for the term "graph" to be conceptually distinct from chemical structures with specified nodes and bonds.

[7] *K. Hirayama*, Tetrahedron Lett. *1972*, 2109—2112; *Th. Kauffmann*, Tetrahedron *28*, 5183 (1972).

[8] As in the extended von Baeyer nomenclature system, the descriptor is sufficient, by itself, for the derivation of the structure in the nodal system.

[9] In contrast to classical organic nomenclature, all acyclic nodes not interrupted by cyclic nodes are treated together as one unit.

[10] The sum of the numbers denoting the lengths of the chains is equal to the total number of nodes and, since the locants for the attachment of chains are indicated by the superscript numbers, the descriptor itself is sufficient for deriving the structure. The same is true in the extended von Baeyer system currently in use.

[11] Since the lengths of the branches are cited in the order of their numbering, *i.e.*, in order of decreasing length, the only difference occurs in the superscript locants (cf. **Rule N-3.4**).

[12] The multiplying prefixes are the same as given by **Rule A-2.5** in [1] and Table III, p. 142, in [2], except that the prefix "mono" is not used and—in accordance with the most recent recommendation of CNOC (see [24])—the prefix for twenty is spelled "icosa" rather than "eicosa".

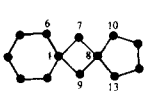
[13] As indicated in Section 3, for convenience only, we are illustrating the principles of nodal nomenclature mainly with graphs derived from organic structures, and we are using the general ending "-ane" of classical hydrocarbon nomenclature. However, this is not meant to imply that nodal nomenclature is designed only for use in substitutive nomenclature. Because the ending "-nodane" could convey the concept of a fully hydrogenated parent system in substitutive nomenclature, the selection of another ending derived from the same root "nod" is under consideration for use in the most general applications of nodal nomenclature.

[14] To facilitate the comparison between nodal nomenclature and traditional organic nomenclature, most of these examples correspond to the acyclic hydrocarbons given in Section A in [1].

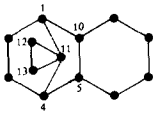
[15] In nodal names for monocyclic graphs, the prefix "cyclo" and the "zero" are mutually redundant, as are the Arabic numbers and the multiplying prefix. They are retained, however, in order to distinguish monocyclic modules from unbranched acyclic modules in assembly descriptors. Without the zero denoting the presence of a ring, a name such as "cyclo[(5)1:6(4)]nonanodane" is ambiguous: it could represent either "cyclo[(05)1:6(4)]nonanodane" or "cyclo[(5)1:6(04)]nonanodane".

[16] Thus, two rings joined only by a single common (spiro) atom do not, together, constitute a main ring, but form a main ring and a bridge.

[17] Occasionally, as shown in the examples below, a longer bridge is present, but cannot be numbered until after a shorter bridge has been numbered.



Tricyclo[06.$3^{1,1}4^{8,8}$]-tridecanodane



Tetracyclo[010.$1^{1,4}2^{11,11}0^{5,10}$]-tridecanodane

[18] The total number of terms in the descriptor of a polycyclic graph is the same as the number of rings and the sum of the nonsuperscript numerals is equal to the number of nodes in the total graph.

[19] Seniority order for polycyclic modules (**Rule N-4.3**) does not follow the method of selection for polycyclic descriptors (**Rule N-3.6**). Selection of the descriptor for polycyclic graphs follows the method used for numbering the structure. At each step, the numbering continues by the longest possible bridge attached to nodes with the lowest locants in the part of the graph previously numbered. As a consequence, all numerals representing either bridge lengths or locants are successively compared in their order of appearance in the descriptor, preference being given to the descriptor where, at the first difference, either the longest bridge or the lowest locant occurs. On the other hand, for selecting the senior module of an assembly, it seems to be more consistent with usual practice to compare first the bridge lengths and then, only if a choice remains, superscript locants. It should be noted that, in many cases, either method of selection will lead to the same result. Comments on this decision will be welcome.

[20] The number of rings in a polycyclic system is equal to the minimum number of scissions needed to convert the system into an acyclic structure (see **Rule A-32.12** in [1]).

[21] For some of these examples, the trivial or semisystematic name of the corresponding hydrocarbon is given and marked by an asterisk.

[22] Symmetry of the module seniority graph often precludes the determination of the correct order for numbering of the modules attached to the principal module, or the choice of the principal module from two or more modules of the same highest seniority.

[23] Selection rules for numbering the module seniority graph (**Rule N-5.3**) differ from those applied to acyclic graphs (**Rule N-1**) because module seniority graphs deal with constituent units (modules) which may greatly differ in structural complexity. Accordingly, rules for the module seniority graph take into consideration the nature of the contraction nodes, while, according to **Rule N-1**, the nature of the nodes does not affect the numbering of the graph.

[24] *Note added in proof:* [1–4] have been revised and published as IUPAC: Nomenclature of Organic Chemistry, Sections A, B, C, D, E, F, and H. Pergamom Press, Oxford 1979.

Developments in Arylnitrene Chemistry: Syntheses and Mechanisms

New synthetic methods (31)

By B. Iddon, O. Meth-Cohn, E. F. V. Scriven, H. Suschitzky, and P. T. Gallagher[*]

Aryl- and heteroaryl-nitrenes can take part in intra- and intermolecular reactions in both of their possible electronic states (triplet and singlet). In this review we have endeavored to highlight recent synthetic uses of these reactive intermediates as well as draw attention to avenues open to further exploration in this field. Singlet arylnitrenes will interact with suitable *ortho*-positioned substituents to give a variety of fused azoles, some in excellent yield. In suitable solvents and in presence of amines and alcohols, phenylnitrenes undergo ring expansion to azepines which can also occur in nitrenes of certain fused bicyclic aromatics (naphthalene, quinoline, isoquinoline, benzo[*b*]thiophene). The latter nitrenes may also give rise to *o*-diamines which are useful starters for further heterocyclic synthesis. Triplet arylnitrenes (usually regarded as having only a nuisance effect in synthetic work) may also be utilized in practicable heterocyclic syntheses within a suitable molecular framework. Decomposition of aryl azides in a mixture of an organic and polyphosphoric acid leads to fused oxazoles. The mechanism is discussed for all the reactions considered.

1. Introduction

The study of nitrenes and nitrenoid intermediates has if anything been intensified over the last 10—15 years as is evident from the stream of publications, a recent monograph[1], and reviews[2] on the subject. It is not intended to duplicate any of the existing surveys or to present a comprehensive article on the whole field. Our aim is to deal concisely with the recent observations in the field of aryl- and hetarylnitrenes, to a large extent made in our own laboratories, and draw especial attention to the less recognized synthetic possibilities of these reactive intermediates in solution. Their chemistry in the gas phase is outside our domain and this fruitful field has been recently reviewed[2h].

Arylnitrenes are uncharged, electron-deficient, reactive intermediates possessing a sextet of electrons in their outer shell. Two of these electrons are located in a formal carbon-nitrogen single bond, two in a lone pair orbital, and the remainder may be arranged in either a spin paired configuration in a non-bonded orbital giving rise to an electrophilic

(1) Aryl–N̈ Aryl–N̈: *(2)*

singlet nitrene *(1)* or alternatively orthogonally and unpaired giving the biradical triplet nitrene *(2)*.

Arylnitrenes have been shown to have a triplet ground state by *Smolinsky et al.*[3] who recorded the low temperature ESR spectra of several triplet nitrenes.

[*] Prof. Dr. H. Suschitzky [+], Dr. B. Iddon, Dr. O. Meth-Cohn, Dr. E. F. V. Scriven, Dr. P. T. Gallagher
The Ramage Laboratories
Department of Pure and Applied Chemistry
University of Salford, Salford M5 4WT (England)
[+] To whom correspondence should be addressed.

2. Generation of Arylnitrenes

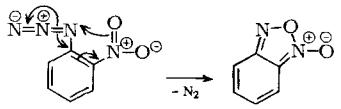
Many methods have been described that give rise either to distinct arylnitrenes or to nitrene-like intermediates (nitrenoid used here in its generic sense). The latter type is equally useful for synthetic purposes and its participation is usually diagnosed from indirect evidence, such as the formation of typical nitrene products. We shall, however, only list those preparations that have at least some synthetic merit. The best approach is usually the thermal or photodecomposition of aryl azides in solution.

2.1. Thermolysis of Aryl Azides

Thermal decomposition of an aromatic azide *(3)* produces initially a singlet nitrene *(1)* because of spin conservation. Pyrolysis temperatures are usually in the range of 100—180 °C. With *ortho*-substituents, *e.g.* nitro-, phenylazo-, and carbonyl groups, the rate of decomposition is usually accelerated and the temperature of pyrolysis often lowered. *Dyall*[4] has proposed that the neighboring group participates in a pericyclic process [*(4)*→*(5)*] with little nitrene character developing, which in some cases leads to a heterocyclic ring such as furoxan.

Aryl–N_3 $\xrightarrow{\Delta}$ Aryl–N̈ + N_2

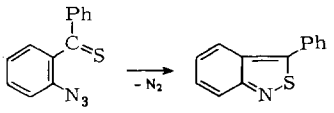
(3) *(1)*



(4) *(5)*

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0900 $02.50/0

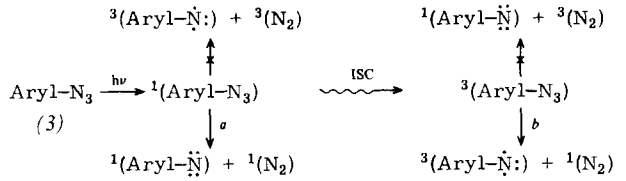
An extreme example of anchimeric assistance is the explosive formation of 3-phenyl-2,1-benzisothiazole *(7)* at room temperature from *o*-azidothiobenzophenone *(6)*[5] as shown.



(6) *(7)*

2.2. Photolysis of Aryl Azides

Reiser and *Marley*[6] have shown that the primary step in the photolytic decomposition of aryl azides is light absorption by the aromatic nucleus. This is followed by vibrational transmission of the absorbed energy to the azido moiety which decomposes to give a nitrene. Once excitation of the azido-group has occurred, four pathways[2g] are available for its decomposition either to singlet or to the less favorable triplet nitrene (Scheme 1).



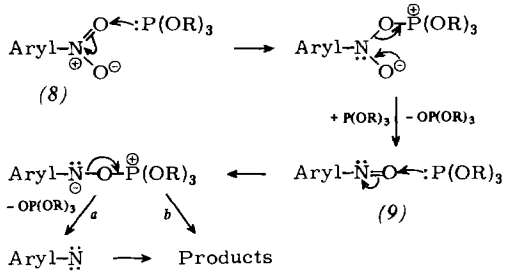
Scheme 1. Photolysis of arylnitrenes. ISC = intersystem crossing.

That the pathways *a* and *b* are followed was demonstrated by *Reiser* and *Leyshon*[7] who detected 12—13% of triplet nitrene when photolyzing phenyl azide. Sensitization can vary the ratio of products obtained from photolyses[8]. Singlet sensitized photolyses are believed to involve an electron transfer process, whereas triplet sensitization involves initial light absorption by the sensitizing agent which then sensitizes the azide directly to the triplet spin state. A marked effect on changing the sensitizing agent was observed by *Swenton*[9] who found that photolysis of 2-azidobiphenyl gave carbazole *(17) via* the nitrene *(31)* (71%) (see Section 3.1.1) whilst in the presence of acetophenone (a triplet sensitizer) the azobiphenyl (43%) was formed at the expense of the carbazole (8%). Conversely, photolysis in the presence of the triplet quencher piperylene reduced the formation of azo compound (4%) and stepped up the yield of carbazole (89%).

By the judicious use of sensitizers and solvents it is possible to form nitrenes in either the triplet or singlet states by photolysis[10–13], which is a useful way of controlling the nature of the product by way of the spin state.

2.3. Deoxygenation of Arylnitro- and Arylnitroso Compounds

Arylnitrenes are possible intermediates in the deoxygenation of arylnitro- *(8)* and arylnitroso compound *(9)* using tervalent phosphorus reagents *e.g.* R_3P or $(RO)_3P$. The evidence is based largely on the similarity of the nature and ratio of products in deoxygenation reactions to those found in the photolysis of aryl azides[14–18]. The position is, however, by no means resolved and a nitrene as well as a non-nitrene pathway can be envisaged (Scheme 2).



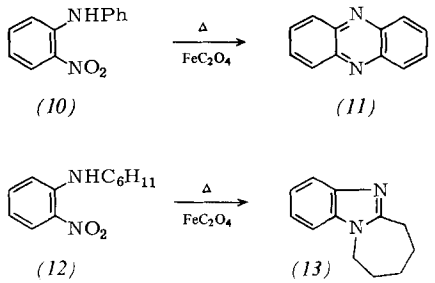
(8) *(9)*

Scheme 2. Deoxygenation *via* nitrenes (pathway *a*) and *via* the non-nitrene route (pathway *b*).

Thus, in the deoxygenation of 2-nitrosobiphenyl a charged intermediate involving both reactants was postulated to explain the kinetic data obtained[19] and further support for a non-nitrene pathway has been adduced from labeling experiments by *Brooke et al.*[20].

Arylnitroso compounds *(9)* deoxygenate rapidly at room temperature with tervalent phosphorus reagents but arylnitro compounds require usually prolonged reflux in solvents such as chlorobenzene or cumene.

Deoxygenation of nitro compounds has also been effected with ferrous oxalate. Thus, *o*-nitrodiphenylamine *(10)* was made to cyclize to give phenazine *(11)*[21], and *N*-cyclohexyl-*o*-nitroaniline *(12)* yielded a benzimidazole *(13)* by a non-nitrene route[22].

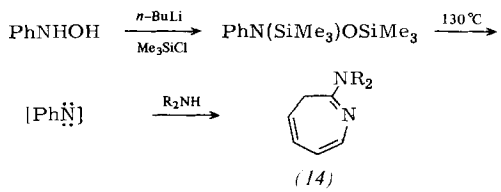


(10) *(11)*

(12) *(13)*

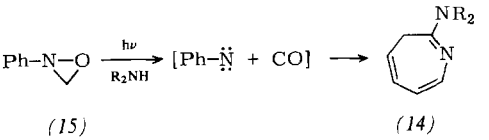
2.4. Miscellaneous Methods

A recently reported synthesis of 2-dialkylamino-3*H*-azepine *(14)* by thermal elimination of hexamethyldisiloxane from *N,O*-disilylated *N*-phenylhydroxylamine[23] gives the highest yield (95%) so far reported for an arylnitrene ring expansion to an azepine in presence of an amine. The scope of this method is undoubtedly restricted in view of the unavailability of arylhydroxylamines.



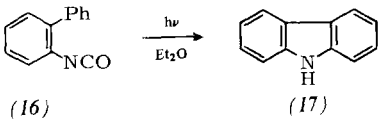
(14)

An arylnitrene intermediate is postulated in the photolysis of oxaziridines *(15)*[24] because azepines of type *(14)* are formed in the presence of amines. Also, irradiation of isocyanates such as *(16)* is reported[25] to yield occasionally carba-



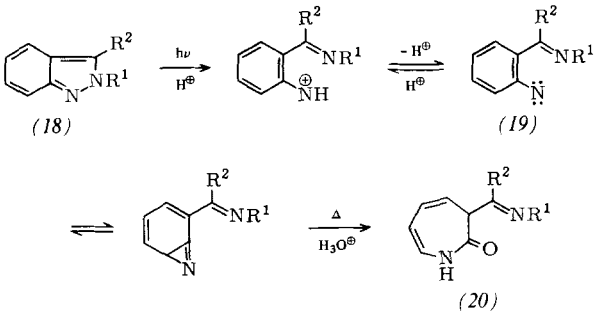
(15) (14)

zoles such as *(17)* which could be derived from an intermediate arylnitrene.



(16) (17)

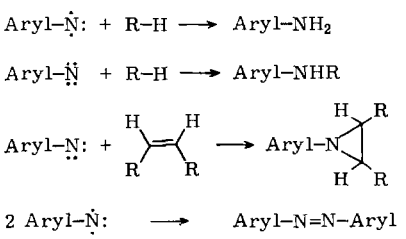
Finally, a recent synthesis of azepinones *(20)* from 2-substituted indazoles *(18)* was postulated[26] to proceed *via* an *ortho*-substituted arylnitrene *(19)* as shown.



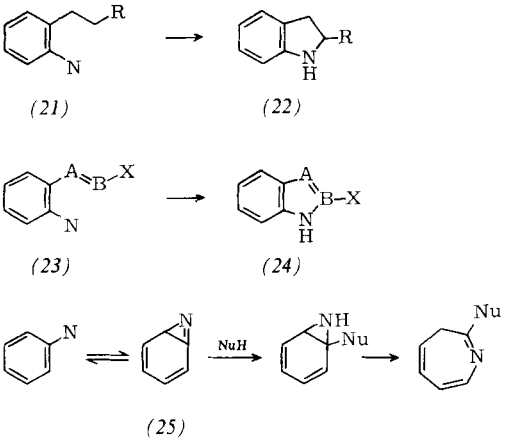
(18) (19) (20)

3. Reactions of Arylnitrenes

Reactions of nitrenes can be discussed under various headings, for instance (a) "intermolecular" and (b) "intramolecular". The former is exemplified by abstraction of hydrogen from the solvent to give an amine, insertion into a single bond (usually C—H), or addition to a multiple bond (rare for arylnitrenes) or a formal dimerization to an azo compound.

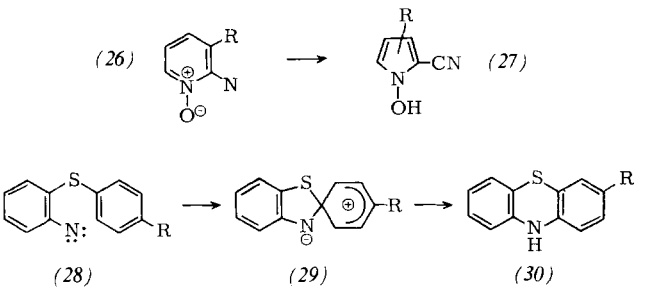


"Intramolecular" reactions [type (b)] involve cyclization onto an *ortho*-substituent or a saturated [*(21)*→*(22)*] or unsaturated side-chain [*(23)*→*(24)*] giving rise preferentially to five-membered nitrogen heterocycles. This behavior constitutes one of the most important synthetic applications of arylnitrenes because of its scope. Alternatively, an arylnitrene can interact with its own ring to give an azirine such as *(25)* which in the presence of a suitable nucleophile (NuH) ring-expands to an azepine or sometimes ring-opens in polycyclic nitrenes to an *ortho*-substituted amine. We shall show that these reactions are also of considerable synthetic utility.



(21) (22) (23) (24) (25)

Other less common observations are that certain nitrenes, *e.g.* those derived from 2-azidopyridine 1-oxides[27] ring-contract leading to 1-hydroxy-2-pyrrolecarbonitriles [*(26)*→*(27)*] or that aryl 2-(arylthio)arylnitrenes *(28)* undergo rearrangement to phenothiazines *(30)*[2f,28] (nitrenes with other bridges often reacting in an analogous way, cf. *(46)*).



(26) (27) (28) (29) (30)

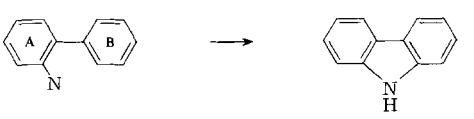
An alternative to the above classification of nitrene reactions is to consider the chemistry of the singlet and the triplet species separately, both of which can partake in inter- and intra-molecular reactions. We shall present our discussion substantially on this basis, which we feel will best illustrate the synthetic versatility of arylnitrenes.

3.1. Singlet Nitrene Reactions

Singlet arylnitrenes are sluggish electrophiles on the nitrene scale of reactivity and only with strongly electron-withdrawing groups present does the full spectrum of reactions observed with the aliphatic ethoxycarbonylnitrene show up. However, some general reactions are now of wide application and importance.

3.1.1. Intramolecular Cyclization Yielding Five-Membered Rings

The archetype of this reaction is the well-known synthesis of carbazole *(17)*[1]. This reaction is unique in the arylnitrene field, in that high yields of products are obtained irrespective of the nature or position of substituents (except that nitro- or cyano groups *ortho* to the nitrene-precursor group divert the

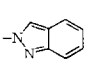
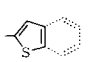


(31) (17)

reaction to give products of non-nitrene pathways). Furthermore, ring B of the biphenyl may be replaced successfully by electron-rich (*e.g.* thienyl, furyl, or mesoionic) or electron-poor (*e.g.* pyridyl, benzothiazolyl, or benzimidazolyl) rings or even by alkene (—CH=CHR) or Schiff base (—CH=NR) moieties to give the corresponding heterocycles. A wide range of ring-systems (*e.g.* thienyl, benzo[*b*]thienyl, or pyridyl) have replaced ring A with equal facility. Some typical examples are shown in Table 1, the majority of the reactions proceeding in high yield. Other examples will be found in the literature[40–44].

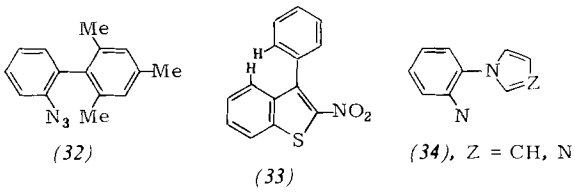
Table 1. Some recent analogues of the carbazole reaction. The site of nitrene attack is shown in bold print.



A (+N)	B	Nitrene source [a]	Ref.	Heterocyclic product
		X, Y, Z	[1]	Carbazole
		X, Y, Z	[33]	Indole
		Z	[33d]	Indazole
			[34]	Indole
		Z	[35]	Furano-indole
		Z	[36]	Thiazolo-indole
	 N = S, NR	X, Y, Z	[37]	Indazolo-benzothiazole Benzimidazo-loindazole
		X, Y, Z	[38]	Pyrazolo-benzo-triazole
		X, Y	[32]	Pyrido-indazole
		X, Y, Z	[39]	Indazolo-benzo-triazole
		X, Z	[1, 30]	(Benzo)-thienoindole
		X, Z	[40]	Benzo-thienopyrrole
		X, Z	[30]	Benzo-thienoindole

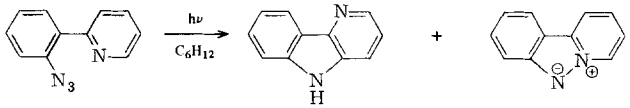
[a] X: thermolysis of azide, Y: photolysis of azide, Z: deoxygenation of nitro compound.

Very few limitations have been observed for this reaction. These include (i) steric limitations such as in the biphenyl *(32)*[29] and the *peri*-interaction effect in *(33)*[30]; (ii) the presence of a "bridgehead" nitrogen in ring B [*e.g. (34)*][29b]; and (iii) the action of added nucleophiles (*e.g.* diethylamine) which may divert some of the nitrene to yield an azepine.



(32) *(33)* *(34)*, Z = CH, N

As well as the above factors, the course of the reaction is dependent upon (i) the reaction temperature (for both thermal *and* photolytic methods)[31,29b]; (ii) the solvent (particularly in the case of photolyses); and (iii) the wavelength of the light used[32]. Thus, the highest temperature commensurate with product stability has been recommended for thermal decomposition of azides[31] (2-azidobiphenyl gave 100% yield of carbazole *(17)* at 360 °C in liquid paraffin solution[29b]). On the other hand, it is often advantageous to photolyze azides at ≈ 107 °C (below their thermal decomposition temperature) to optimize yields[31]. Two types of solvent effects have been noted; the "heavy atom" effect during both thermal and photochemical routes causes a small increase in triplet-derived products (*e.g.* the amine or azo compound corresponding to the azide) at the expense of carbazole[29b]; more dramatically, triplet photosensitization using ketones such as acetophenone totally alters the reaction pathway (see Section 3.2.1). Little has been reported on the influence of the wavelength of the light used during photolyses but a good example of this unexplained phenomenon is shown in Scheme 3, where the usually noted preference for attack at a ring nitrogen is diminished at shorter wavelength[32].

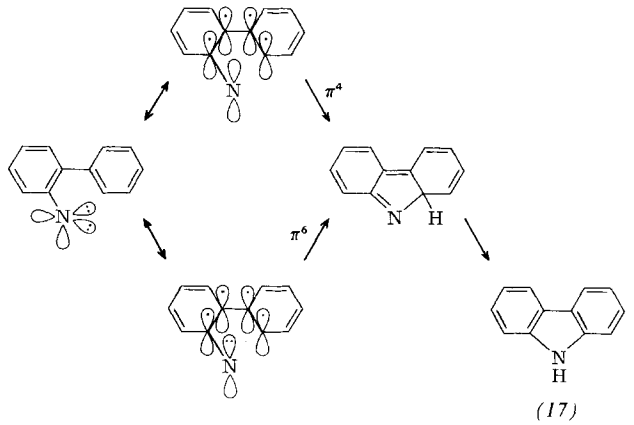


λ = 254nm	36%	61%
λ = 350nm	15%	80%

Scheme 3. Influence of wavelength in photolysis.

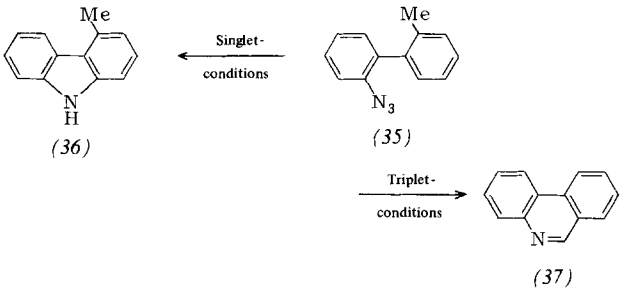
Despite much early evidence in support of a triplet-nitrene pathway to carbazoles (including matrix isolation[45] and flash photolysis studies[46]), it is now clear that this reaction is characteristic of a singlet nitrene[47,29b]. The above data speak strongly for a concerted (π^4 or π^6 depending upon whether an empty or full orbital of the singlet nitrene is utilized[*]) low-energy route, capable of accommodating substituent effects by choice of the appropriate nitrene orbital, but being very sensitive to steric effects (which limit ring coplanarity) and to "bridgehead" heteroatoms (which interfere with the concertedness of the process by requiring higher-energy dipolar transition states and intermediates). *Sundberg*[47c] has elegantly demonstrated that the lifetime of the

[*] *Wentrup* [48] has recently also drawn attention to the importance of this dual role of singlet carbenes and nitrenes in his vapor-phase work, and he underlines the consequent electrophilic or nucleophilic property of the nitrene that this duality implies.



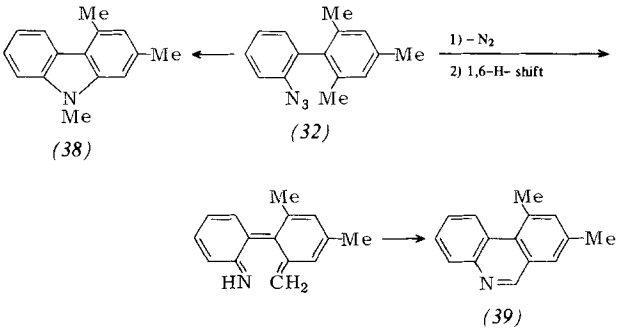
(17)

species supposed to be the triplet nitrene noted above, does not conform to the time-scale of the carbazole-forming reaction, and that the competitive conversion into an azepine in the presence of added amines[47] speaks for the singlet nitrene. We have also noted a choice of pathways for 2-azido-2'-methylbiphenyl *(35)* when singlet and triplet nitrene-forming conditions are chosen leading to carbazole *(36)* or phenanthridine *(37)* respectively (Table 2), again supporting



(36) (35) (37)

Table 2. Reaction of 2-azido-2'-methylbiphenyl *(35)* under singlet and triplet conditions to give *(36)* and *(37)*, respectively.



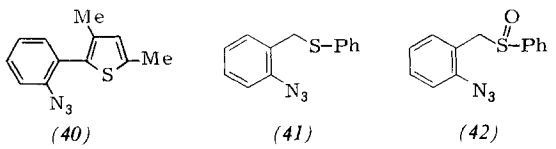
(38) (32) (39)

(36) Yield [%]	Conditions (1% solution)	*(37)* Yield [%]
100	Paraffin, 360 °C	0
98	PhBr [a], 156 °C	1.5
95.5	Tribromothiophene [a], 156 °C	4.5
90	PhCl, 107 °C, *hν*	4.5
18	PhAc [b], 107 °C, *hν*	36

[a] "Heavy atom effect". [b] Triplet photosensitizer.

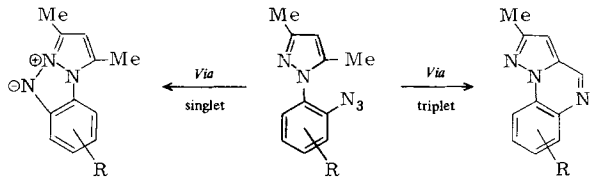
the contention that the triplet nitrene does not lead efficiently to carbazole[29b,31]. A similar competitive study of the products derived from thermal decomposition of the azide *(32)* at various temperatures was also revealing. At temperatures high enough to facilitate coplanarity of the two phenyl rings, formation of the carbazole *(38)* did not increase beyond 8% but an alternative singlet-nitrene mediated, concerted pathway to the phenanthridine *(39)* was observed instead, as indicated by the diminution of the typical triplet products (the 2-aminobiphenyl *(32)*, NH_2 in place of N_3) with increase in yield of the phenanthridine as the temperature of reaction was raised[31].

Examination of Table 2 demonstrates that the site of ring-closure may be carbon or nitrogen, and that the latter site, being nucleophilic, is preferred where a choice exists. Despite much effort, almost no successful attack at sulfur (either intra- or inter-molecular) by an arylnitrene has been noted. The more electrophilic sulfonylnitrenes have been long known to yield sulfoximides, for example in dimethyl sulfoxide[49a], as does pentafluorophenylnitrene[49b]. However, as well as those cases recorded in Table 2 no trace of attack at sulfur was noted in the three azides *(40)*, *(41)*, and *(42)* under a wide variety of conditions[29b,31,50].



(40) (41) (42)

Apart from the carbazole-type reaction, which clearly involves a very low activation energy for ring-closure, nitrene cyclizations are often sensitive to substituent effects. Thus, the pyrazole *(43)* which has a choice of both singlet or triplet cyclization routes, yields solely the singlet product *(44)* when electron-withdrawing substituents (Cl, CF_3, NO_2) are *meta* to the azide group. When similar *para* substituents (Cl, Br, CF_3) are present the ylide *(44)* (57—70%)[38] is the main product.



(44) (43) (45)

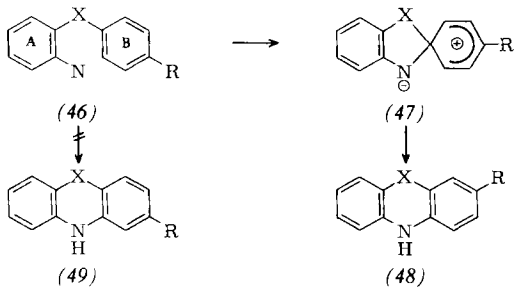
However, when electron-releasing groups conjugate with the nitrene (OMe, NMe_2), and thus reduce its electrophilicity, no singlet product is isolated, the pyrazoloquinoxaline *(45)* being formed by radical coupling[38].

3.1.2. Intramolecular Cyclization Yielding Six-Membered Rings

One of the peculiarities of nitrene cyclizations is their propensity to prefer five-membered rather than six-membered ring formation. Indeed, many reactions included in this chapter occur initially by formation of a five-membered ring followed by rearrangement.

A typical reaction of this type is depicted *(46)*→*(48)*. Reaction involving initial formation of a dipolar spirodiene *(47)* from a nitrene *(46)* results in a phenothiazine *(48)* by a Smiles-type rearrangement which has been studied extensively by *Cadogan et al.*[28,51,21]. The substituent acts as a la-

bel for indicating the nature of the rearrangement since the expected product would be *(49)*. The variations of the bridge X are also indicated.

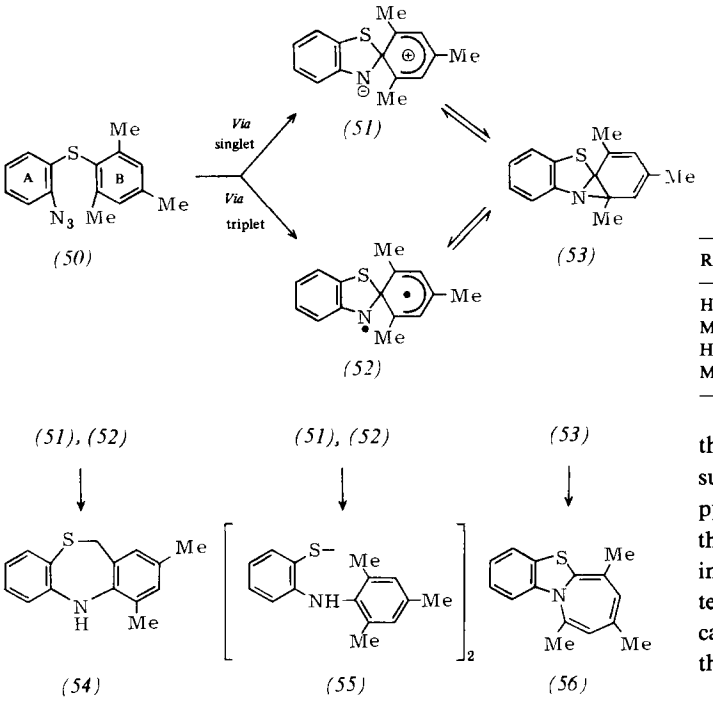


X = S, O, NAc, CH_2, CO, SO_2

(46)-(48), X = S ≡ *(28)-(30)*

This reaction is unique for nitrenes because conditions that favor formation of singlet or triplet nitrenes can give rise to the same products, the variation in the ratio of the products being delicately dependent on the reaction temperature and solvent as demonstrated for the azide *(50)* (Table 3).

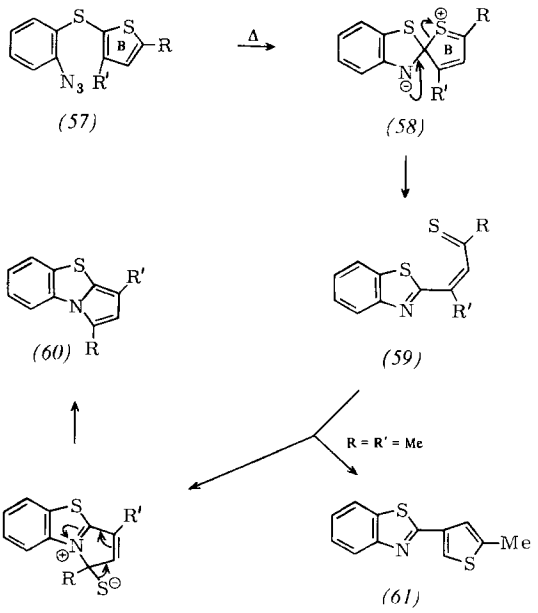
Table 3. Dependence of product ratio upon conditions of reaction of the azide *(50)*.



Conditions	*(54)* [%]	*(55)* [%]	*(56)* [%]	Ref.
Δ/Decalin/180 °C	45	33	0	[51c]
Δ/PhBr/154 °C	50	17	6	[52]
hν/PhAc/20 °C	Trace	28	20	[52]
hν/PhAc/107 °C	14	45	20	[53]

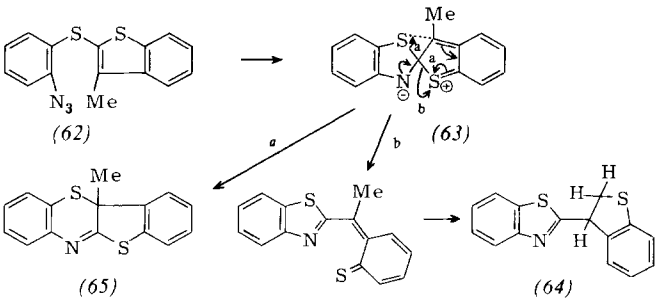
We rationalize these results by the equilibria shown and further underline this delicate balance by noting that introduction of a chloro substituent *para* to the azido group (which we find increases efficiency of both singlet and triplet reactions) gives the corresponding disulfide of type *(55)* (51%) and azepinobenzothiazole of type *(56)* (48%) on photolysis in acetophenone at 20 °C. The phenothiazine reaction itself *[(46)→(48)]* is also more efficiently brought about by photolysis in a hot (107 °C) acetophenone solution. Thus, 2-azido-4'-methyldiphenyl sulfide gives double the yield of the phenothiazine (69%)[53] compared to the thermal[51c] route[*].

An interesting variant of the phenothiazine reaction derives from replacing the B ring in *(46)* by a heterocycle. When this ring has a heteroatom α to the site of nitrene attack [*e.g.* as in *(57)*] the *spiro* intermediate *(58)* becomes an ortho-ester analogue and is thus prone to fission of ring B [*e.g.* to *(59)*] rather than rearrangement. In the case of the



R	R'	*(60)*, [%]
H	H	23
Me	H	19
H	Me	65
Me	Me	74

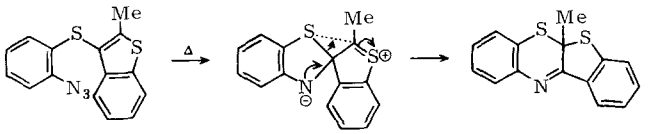
thiophenes *(57)* a highly reactive intermediate *(59)*[**] is presumably formed which cyclizes to the hitherto unreported pyrrolobenzothiazole *(60)*, but which may also give a little 2-thienylbenzothiazole *(61)* when R' = Me[54]. The corresponding benzothiophene *(62)* yields a spirodiene *(63)* in which the tendency for rearomatization of the ring B is a major factor, causing formation of both a benzothiazole *(64)* and a benzothiazine *(65)* derivative in about equal amounts[55].



[*] It is, however, possible that a different mechanism may operate in hot acetophenone solution.

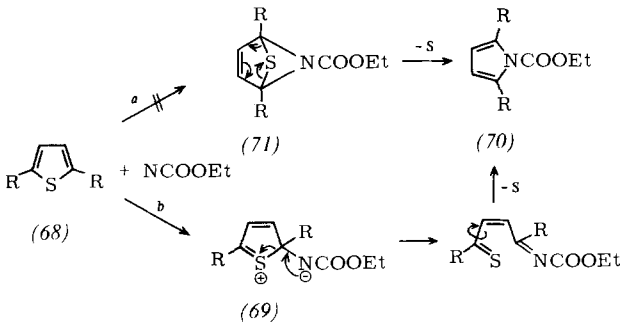
[**] Despite much effort, we have not yet been able to trap these intermediates.

The 2-azidophenyl benzothienyl sulfide *(66)* isomeric to *(62)*, not surprisingly, gives an almost quantitative yield of the benzothiazine *(67)* with no ring-fission products since the ortho-ester-like spiro intermediate of type *(63)* cannot form in this case[55].

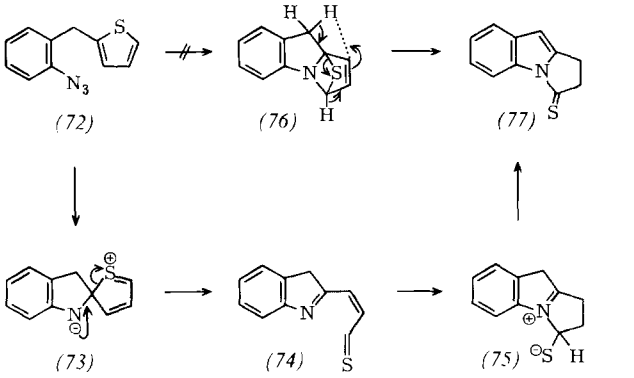


(66) *(67)*

The tendency of nitrenes to react as an electrophile as evidenced by the intermediate spiro system (see above) encourages us to reinterpret certain reported reactions such as the action of ethoxycarbonylnitrene on thiophenes *(68)* as an electrophilic attack at position 2 of the thiophene ring in *(69)* followed by a ring-opening/ring-closure process (path *b*) leading to the pyrrole *(70)* rather than the unprecedented 1,4-addition *via (71)* previously suggested[56].



(68) *(69)* *(71)* *(70)*

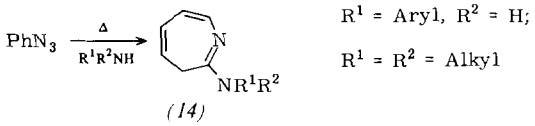


(72) *(76)* *(77)* *(73)* *(74)* *(75)*

An analogous interpretation which involves the intermediates *(73)*, *(74)*, and *(75)* rather than *(76)* as suggested[57] appears to us also more plausible for explaining the product *(77)* derived from 2-azidobenzylthiophene *(72)*.

3.1.3. The Singlet-Nitrene⇌Benzazirine Pathway

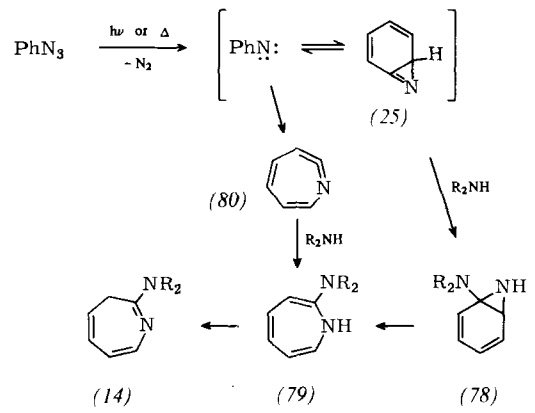
In 1912 *Wolff* thermolyzed phenyl azide in aniline and isolated from the reaction product a crystalline base in small yield which he called "dibenzamil"[58]. The structure of dibenzamil remained uncertain for nearly fifty years (although an incorrect structure found its way into a textbook[59]) until *Huisgen* assigned to it an azepine structure and rationalized the mechanism of its formation[60]. The 3*H*-azepine was confirmed by NMR[61] and photolysis of phenyl azide in aliphatic amines was also shown to lead to ring expansion[3] (Scheme 4).



(14)

Scheme 4. Ring expansion of phenyl azide to azepines.

The accepted mechanism of this ring expansion is considered to involve unimolecular loss of nitrogen[60,61] leading to the formation of the equilibrium mixture singlet nitrene ⇌ benzazirine *(25)*. The benzazirine undergoes nucleophilic attack in the presence of an amine to give an aziridine *(78)* which yields ultimately a 3*H*-azepine *(14)* *via* a 1*H*-azepine intermediate *(79)*[62a].



(25) *(80)* *(14)* *(79)* *(78)*

An alternative mechanism to the benzazirine pathway was put forward recently[62b]. It was observed that irradiation of phenyl azide in an argon matrix at 8 K gave a new photoproduct to which the structure of 1-aza-1,2,4,6-cycloheptatetraene *(80)* was assigned on the basis of infrared data. It was suggested that *(80)* could feasibly react with nucleophiles such as R_2NH to give a 3*H*-azepine *(14)*. It remains, however, to be seen whether this alternative singlet nitrene route is relevant for reactions at room temperature and applies to the interpretation of other photoproducts such as *o*-diamines and azepines derived from fused bicyclic arylnitrenes (see below).

The success of the azepine reaction was found to be dependent upon the substituents in the benzene ring. For instance, thermolysis of *p*-anisyl azide[63] and *p*-nitrophenyl azide[60] in aniline gives no detectable azepines. Recently it has been found that irradiation of phenyl azide in triethylamine also yields the azepine *(14)*, R = Et[65].

The use of oxygen and sulfur nucleophiles has not proved as rewarding as that of amines in promoting ring expansion to azepines. Photolysis of phenyl azide in methanol[64] or in hydrogen sulfide/diethyl ether[61] has been reported to give a very modest yield of the azepines *(81)* and *(82)*, respectively.

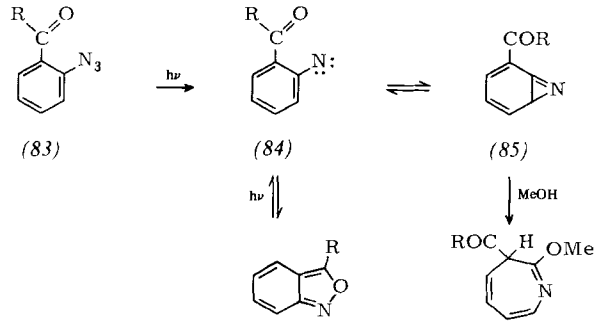
Very much better yields of azepines are obtained when aryl azides of type *(83)* bearing an *o*-carbonyl substituent are photolyzed in methanol (or other alcohols)[66]. This effect

may be attributable to coordination of the singlet nitrene by the carbonyl group, suppressing intersystem crossing to trip-



(81) (82)

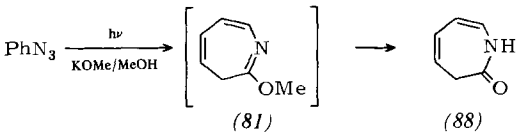
let nitrene and consequently promoting attack by the weak nucleophile methanol [(85)→(86)]. It is noteworthy that anthranils (87) also yield azepines on photolysis in methanol[67].



(83) (84) (85) (87) (86)

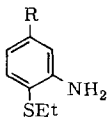
R = OMe, OPh, NHPh, NH_2 40-80%

Increase in the strength of the nucleophile provides another method of raising the yield of azepine. For instance, *Rigaudy et al.*[68a] reported that photolysis of 2-naphthyl azide and 2-anthryl azide in the presence of concentrated potassium methoxide in methanol gives the corresponding azepines. We found that photolysis of phenyl azide under these conditions affords 1*H*-azepin-2(3*H*)-one (88) (32%), presumably *via* 2-methoxy-3*H*-azepine (82), which undergoes hydrolysis during work-up[68b]. Carrying out the above procedure in the presence of a small amount of [18]crown-6 ether raises the yield of (88) to 48%[68b].



(81) (88)

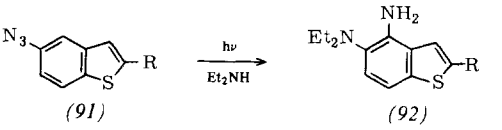
Photolysis of phenyl and *p*-tolyl azide in ethanethiol does not give azepines; instead the anilines (89) and (90) are the major products[69]. Thermolysis of phenyl azide in benzenethiol was found to give *o*-aminodiphenyl sulfide. The formation of this product was attributed to aromatic substitution of phenylthio radicals[70]. *Sundberg* and co-workers have deox-



(89), R = H
(90), R = Me

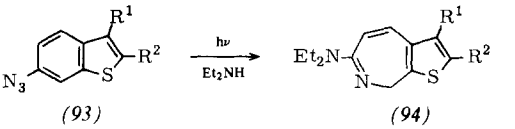
ygenated nitrosobenzene in methanol and obtained substituted anilines rather than azepines, by a route which was considered to involve nucleophilic attack on a phosphorus intermediate[64,71].

The potential synthetic application of the above ring expansion reactions (Scheme 4) to the synthesis of benzazepines from aromatic bicycles was appreciated early by *Huisgen*. On thermolysis of naphthyl azides in aniline only naphthylamines and tars[60b] were produced, which is typical of involvement of a triplet nitrene. More recently a series of bicyclic aromatic azides has been decomposed successfully in our laboratories to give bicyclic azepines. While photolysis of 5-azidobenzo[*b*]thiophenes (91) in diethylamine using a high pressure mercury lamp with a pyrex filter, gave *o*-diamines



(91) (92)

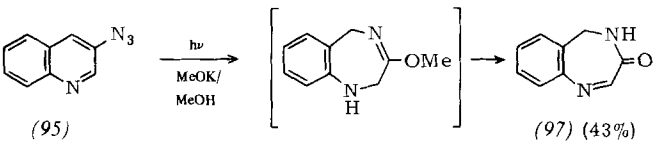
R = H (24%); R = CO_2Et (43%)



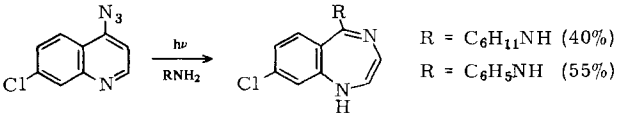
(93) (94)

$R^1 = R^2$ = Br (22%); R^1 = H, R^2 = CO_2Me (34%)

(92) in fair yield but no ring expansion[72] similar treatment of 6-azidobenzo[*b*]thiophene (93) led to the ring-expansion product thienoazepine (94). This represented the first example of a bicyclic aromatic azide undergoing ring enlargement to give a novel heterocyclic system; some derivatives of (94) showed biological activity[73]. Irradiation of the 4- and the 7-azidobenzo[*b*]thiophene under similar conditions merely gave the corresponding amines, presumably *via* the triplet nitrene[72,74]. We also obtained the 1,4-benzodiazepines (97) and (98), (99), and (100) by photolysis of 3-quinolyl azide (95) and 7-chloro-4-quinolyl azide (96) in the presence of methoxide ions or amines[75]. Recently[76] 1,3,5-triazepines were obtained by photolysis of various azidouracils which are, however, vinylic rather than heteroaromatic azides.

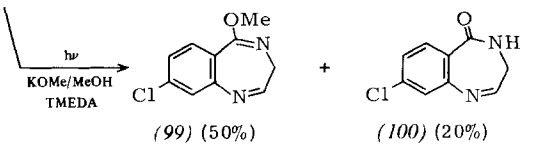


(95) (97) (43%)



(96) (98)

R = $C_6H_{11}NH$ (40%)
R = C_6H_5NH (55%)



(99) (50%) (100) (20%)

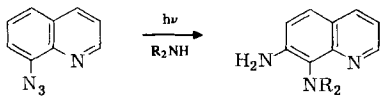
A variety of bicyclic aromatic azides has been photolyzed in diethylamine and other secondary amines to give the appropriate *o*-diamines in most cases and an azepine in a few: 1- and 2-naphthyl azide[77,78a], 3-, 4-, 5-, 6-, 7-, and 8-quino-

lyl azide[77,79] (2-quinolyl azide forms a stable tetrazole), 4-, 5-, 6-, and 7-indolyl azides[80], 4-, 5-, 6-, and 7-azidobenzo[*b*]thiophenes[72–74] and 6-azidobenzothiazole[74] (giving 7-amino-6-diethylaminobenzothiazole in 33% yield) are among them.

A few guidelines arising from the above results may be more helpful to gauge the synthetic scope and limitation of the reaction involving bicyclic arylnitrenes with secondary amines than giving a comprehensive list of the products and yields obtained so far.

"β-Azido compounds" ("β" referring to the benzene ring) generally yield *o*-diamines in fair to excellent yields. With "α-azido compounds" *o*-diamines are not usually formed, but instead low yields of the corresponding amines and tars are produced. An exception is 8-quinolyl azide *(101)* (an α-azide) which gives high yields of *o*-diamines with most common secondary aliphatic amines (Table 4). It appears to hold that the larger the attacking secondary amine the lower the yield of *o*-diamines, probably due to steric hindrance. Carrying out these photolyses with a small amount of TMEDA (tetramethylethylenediamine) results in an increased yield of *o*-diamines (Table 4)[79].

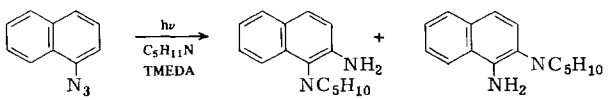
Table 4. Photolysis of 8-quinolyl azide *(101)* in secondary amines.



(101)

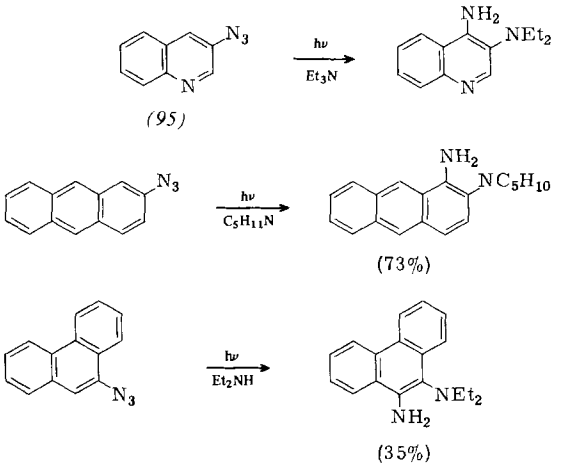
R_2NH	Yield [%]
Diethylamine	86
Pyrrolidine	36
Piperidine	47
Piperidine + Tetramethylethylenediamine (TMEDA)	60

Photolysis of 1-naphthyl azide *(102)* in secondary amines leads to a small yield of 1-naphthylamine, azonaphthalene, and tars; however, in piperidine with TMEDA as a co-solvent the nature of the products unexpectedly changes to a mixture of isomeric *o*-diamines *(103)* and *(104)*[77]. The size of the amine does not affect the yield of *o*-diamines from 2-naphthyl azide photolysis, probably because attack occurs at a β-position[81]. Triethylamine and dioxane have been found to be as efficient as TMEDA in promoting these reactions. Triethylamine can itself behave as the nucleophile in some cases, as with 3-quinolyl azide *(95)*[79]. Some tricyclic aromatic azides, such as 2-anthryl azide and 9-phenanthryl azide can also be converted into the respective *o*-diamines on irradiation in the presence of secondary amines[78b].



(102) *(103)* (50%) *(104)* (25%)

Unexpectedly, bicyclic α-aryl azides can be made to give azepines on decomposition in primary aliphatic amines. Thus, photolysis of 8-quinolyl azide *(101)* in cyclohexylamine was found to give mainly ring-expansion to an azepine *(108a)* rather than just the expected *o*-diamine *(109a)* (cf. Table 4)[82]. The yields of azepine and diamine can be optimized by varying the ratio of primary amine to TMEDA used as solvent. Several other α-azidobicyclic arenes also undergo this reaction, but β-azidobicyclics have so far only been found to give *o*-diamines (Table 5).

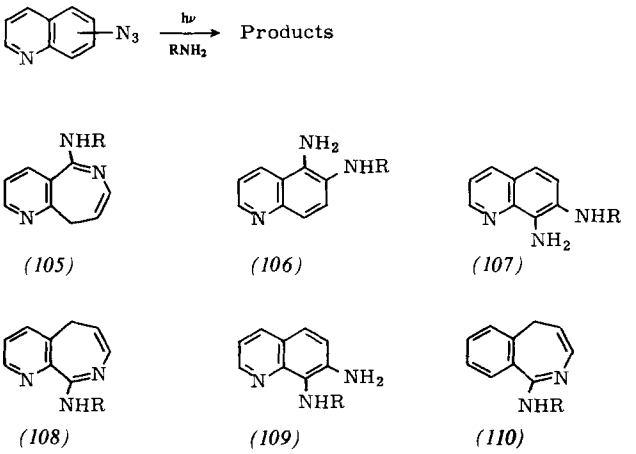


(95)

(73%)

(35%)

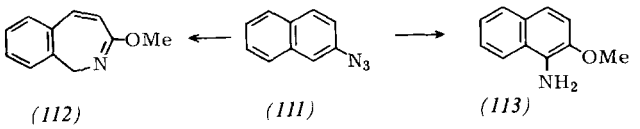
Table 5. Photolysis products of some bicyclic aryl azides in primary amines.



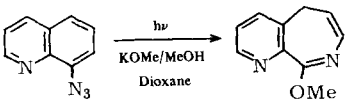
(a), R = C_6H_{11}; *(b)*, R = n-C_3H_7

Quinolyl azide N_3 on C-	Solvent	Product	Yield [%]	M.p. [°C]
5	$C_6H_{11}NH_2$	*(105a)*	42	125
	n-$C_3H_7NH_2$	*(105b)*	43	98
6	$C_6H_{11}NH_2$	*(106a)*	67	118
7	$C_6H_{11}NH_2$	*(107a)*	57	47
8	$C_6H_{11}NH_2$	*(108a)*	40	91
		(109a)	29	69
	$C_6H_{11}NH_2$ + TMEDA	*(108a)*	57	91
	15:1	*(109a)*	27	69
	$C_6H_{11}NH_2$ + TMEDA	*(108a)*	26	91
	1:15	*(109a)*	49	69
	n-$C_3H_7NH_2$	*(108b)*	42	58
1-Naphthyl azide	$C_6H_{11}NH_2$	*(110a)*	12	111

As previously mentioned, *Rigaudy* and co-workers[68a] have found that irradiation of 2-naphthyl azide *(111)* in 3 M KOMe/MeOH/dioxane gives either a high yield of methoxyazepine *(112)* or *o*-methoxyamine *(113)*, respectively. Recently, we found that various α-azidobicyclics also undergo this reaction in high yield; for instance, 8-quinolyl azide *(101)* yields the methoxypyridoazepine *(114)*[83].

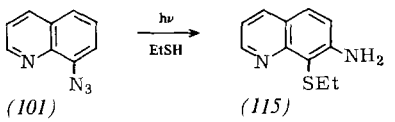


(112) (111) (113)

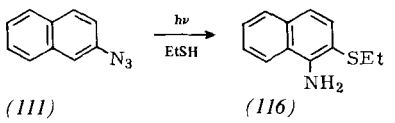


(101) (114)

Little work has been done on the decomposition of bicyclic aromatic azides in alkanethiols. In the few cases studied, ring expansion has not been observed but *o*-amino thioethers *(115)* and *(116)* were formed from *(101)* and *(111)* in the the presence of ethanethiol.



(101) (115)



(111) (116)

Certain principles summarized below are emerging from the above results which should be borne in mind in any synthesis utilizing arylnitrenes.

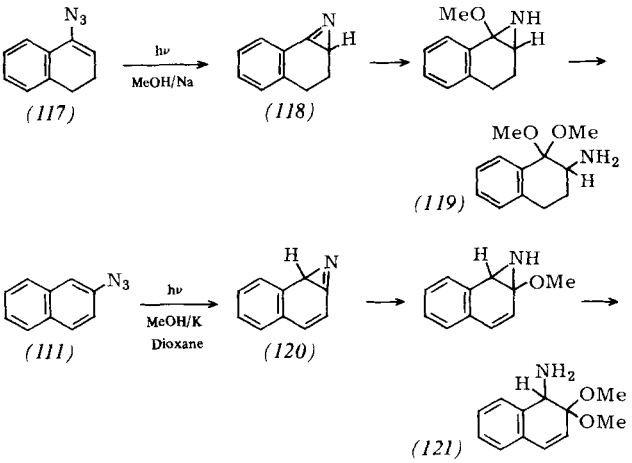
Factors that influence the overall yield of singlet nitrene derived products: These devolve mainly upon stabilizing the singlet nitrene which is believed to be in equilibrium with a benzazirine [such as *(25)*] to prevent intersystem crossing to triplet nitrene. This may be done in three ways: (a) carrying out nitrene reactions in co-solvents with lone pairs, *e.g.* TMEDA[77], dioxane[68], THF[84], triethylamine[79], and dichloromethane. (b) Intramolecular stabilization by an *ortho*-substituent, *e.g.* CO_2Et[66,67]. (c) Intrinsic stabilization by substituents *e.g.* electron-withdrawing groups in the second ring appear to lead to an increase in yields of products attributed to azirine intermediates[73,74].

Azepine versus o-diamine formation: Azepines are thought to be the products of kinetic control and so any stabilizing features they possess should promote their formation. In all the azepines prepared so far from bicyclic compounds by ring expansion of arylnitrenes the following points were observed: (a) the annelated aromatic ring always undergoes rearomatization; (b) the saturated C-atom (or N-atom) in the azepine always appears next to the ring junction; (c) considering azides of naphthalene and heteronaphthalenes: an amidine unit is incorporated into the azepine if possible. α-Azides with *primary* amines give azepines and *o*-diamines and yields may be optimized using a co-solvent (cf. Table 5)[82]. α-Azides with *secondary* amines give the corresponding parent amine. β-Azides give *o*-diamines with *primary* and *secondary* amines. α- and β-Azides give azepines or *o*-methoxyamines with methoxide/methanol/dioxane depending upon reaction conditions[68a]; considering azides of indene and heteroindenes: the products from these reactions cannot be as clearly delineated because of lack of examples. Generally, α-azides give the corresponding parent amine with secondary amines (*i.e.* the triplet product) while β-azides give mainly *o*-diamines with *secondary* amines and frequently a small yield of azepine. The behavior towards primary amines is being investigated.

Some mechanistic aspects relating to the photolysis of bicyclic aryl azides in nucleophilic solvents leading to the formation of bicyclic azepines and/or *o*-diamines are appropriately considered as an extension of the above guidelines.

Both products, azepines and *o*-diamines originate initially from addition of the nucleophile to the azirine intermediate which has so far defied isolation. However, indirect evidence goes some way to support its involvement.

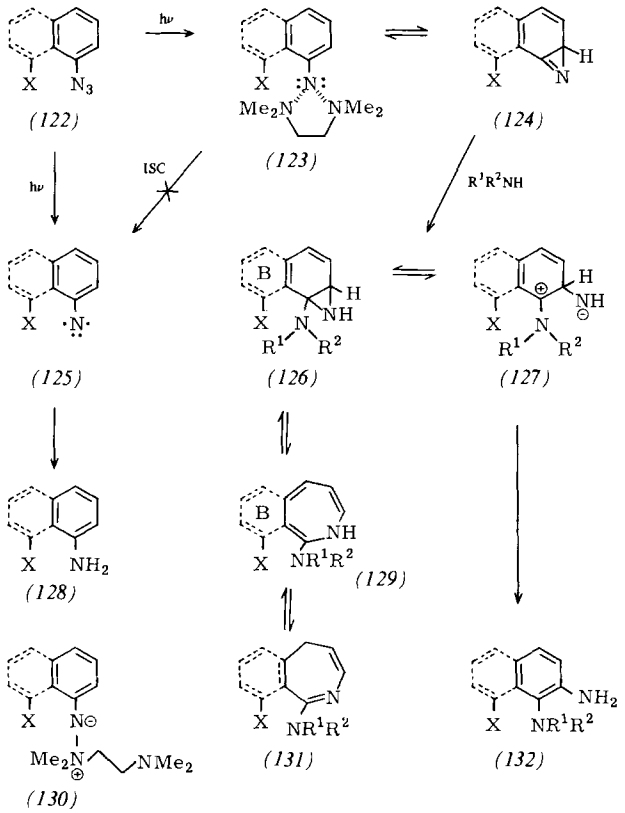
Abramovitch was the first to suggest a singlet nitrene ⇌ azirine equilibrium[2b]. *Hassner*[85] decomposed a vinyl azide *(117)* in methanol, a type of azide which is known to give azirine *(118)* and obtained an aminoketal *(119)*. Similarly, an aminoketal *(121)* was also obtained[68a] from the decomposition of the aromatic 2-naphthyl azide *(111)* in the presence of methoxide/methanol which not unreasonably points to a close analogy between the two pathways.



(117) (118) (119)

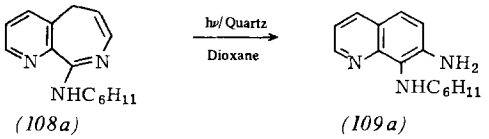
(111) (120) (121)

Moreover, on the basis of an azirine intermediate, formation of azepine and diamine may be rationalized by considering Scheme 5. Irradiation of the azide *(122)* in a primary or secondary amine with TMEDA as co-solvent gives the singlet nitrene which coordinates with co-solvent as shown *(123)*[12] or forms an ylide *(130)*[11]. This suppresses unwanted intersystem crossing to triplet nitrene, thus promoting benzazirine formation *(124)* which in turn is then available for nucleophilic attack. The formation of a small amount of triplet nitrene *(125)* presumably directly from the azide cannot easily be prevented. Nucleophilic attack on *(124)* by an amine leads to the equilibrium *(126)*⇌*(127)* the position of which depends on the nature of R^2 [R^2 = alkyl, favors *(127)* while R^2 = H favors *(126)*]. The zwitterion *(127)*, R^2 = alkyl, readily aromatizes to give the diamine *(132)*, the product of thermodynamic control. The aziridine *(126)*, R^2 = H, may slowly equilibrate to *(127)* with subsequent rearomatization or it can ring-expand to the 1*H*-azepine *(129)*. Several factors affect the position of the equilibrium *(127)*⇌*(126)*⇌*(129)*. In fused bicyclic aromatic systems loss of aromaticity in ring B during the rearrangement militates against ring expansion whilst relief of unfavorable *peri*-interaction between NR^1R^2



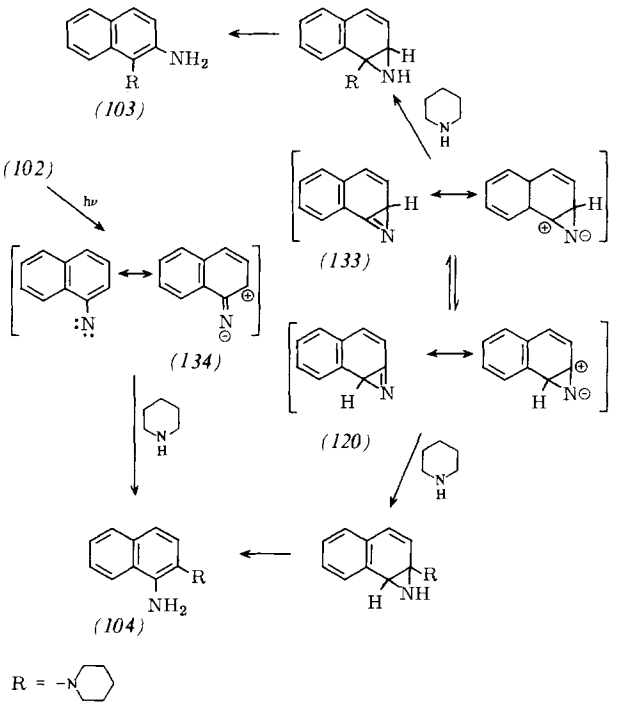
Scheme 5. Photochemical reactions of bicyclic α-azidoarenes. ISC = intersystem crossing. *(132)* is a product of thermodynamic control, and *(131)* of kinetic control. R^1 = alkyl, R^2 = H or alkyl, X = H or lone pair on a heteroatom.

and X should promote ring expansion of *(126)* to *(129)*. The matter is further complicated because 1*H*-azepines such as *(129)* rapidly interconvert to more stable 4*H*-azepines such as *(131)* usually by 1,5 hydrogen shifts. Therefore, any stabilizing features in a potential azepine product (*e.g.* aromatic ring B, incorporation of an amidine unit or an sp^3 C-atom adjacent to the ring junction) will favor its formation. That *(129)*⇌*(131)* is indeed an equilibrium was confirmed when the azepine *(108a)* was irradiated (using a medium pressure mercury lamp, quartz cell) in dioxane to give a quantitative yield of *o*-diamine *(109a)*[79].



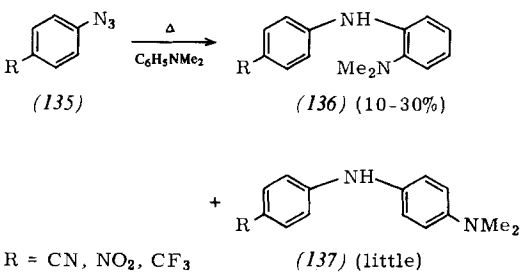
(108a) *(109a)*

Photolysis of 1-naphthyl azide *(102)* in piperidine/TMEDA gives a mixture of isomeric *o*-diamines as previously described[77] [*(103)* and *(104)*; 50 and 25%]. The mechanism is still under investigation but could be rationalized by an interconversion between two benzazirines *(133)* and *(120)*. Other explanations are, however, possible: the unprecedented interconversion of azirines can be avoided by postulating competitive attack by piperidine at the 2-position on a canonical form *(134)* of the nitrene to give *(104)*[86].



3.1.4. Intermolecular Reactions

Few *inter*molecular reactions of singlet phenylnitrene itself or its derivatives were known up to 1969, apart from the observation that arylnitrenes could be intercepted by carbon monoxide at high pressure to give isocyanates[87]. *Abramovitch*[88] reasoned that if the singlet arylnitrene could be made more electrophilic and longer lived (for example by an electron-withdrawing substituent) attack on a suitable solvent should occur. Indeed, thermolysis of such *para*-substituted aryl azides *(135)* in a solvent activated towards electrophilic attack gave diarylamines *(136)* and *(137)* as predicted[88]. The mechanism of this reaction was further probed by generating

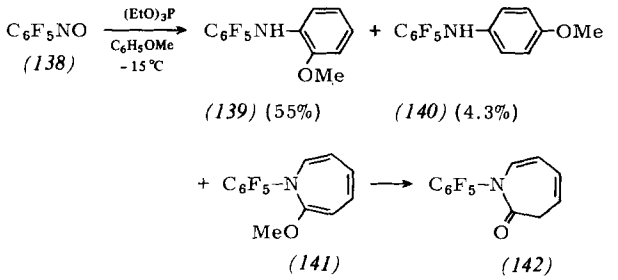


(135) *(136)* (10-30%)

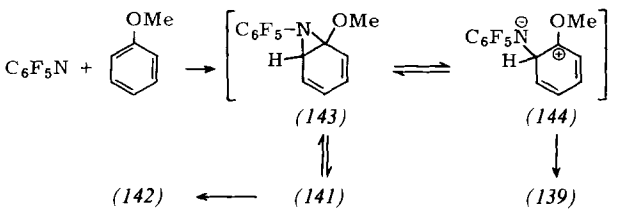
R = CN, NO_2, CF_3 *(137)* (little)

perfluorophenylnitrene in the presence of anisole by deoxygenation of nitrosoperfluorobenzene *(138)*[89]. A mixture of diarylamines *(139)* and *(140)* was found as expected and also the azepinone *(142)* resulting from a ring expansion to a methoxyazepine *(141)* and hydrolysis during work-up. The formation of the inter- and intra-molecular types of product may be rationalized by considering the factors influencing the equilibrium *(143)*⇌*(144)*. Substituents that can stabilize positive charges (*e.g.* methoxy) clearly shift this equilibrium in favor of *(144)* and thereby promote rearomatization to give *(139)*, the product of thermodynamic control. As the ring expansion step *(143)*⇌*(141)* is reversible, substituents that

stabilize *(141)* (*e.g.* strongly electron-withdrawing groups on N-1)[90] favor this ring enlargement. Reaction conditions (and work-up conditions) clearly should be kept as mild as possible to obtain the azepines *(141)* or *(142)* which are the products of kinetic control.



(138) *(139)* (55%) *(140)* (4.3%) *(141)* *(142)*



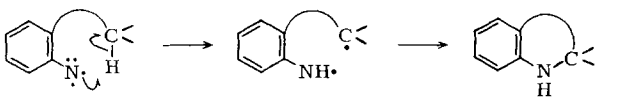
(143) *(144)* *(142)* *(141)* *(139)*

3.2. Triplet Nitrene Reactions

The synthetic utility of triplet arylnitrenes is generally underrated owing to their dominant tendency to yield either an amine (usually the parent of the nitrene precursor) by hydrogen abstraction or an azo compound by apparent dimerization. This latter reaction is in fact little understood and it often competes efficiently with easy intramolecular alternatives. The synthetic usefulness of the triplet species has recently been demonstrated in both intra- and inter-molecular pathways and its value can be heightened by the appropriate choice of substrates and methods of generating this intermediate.

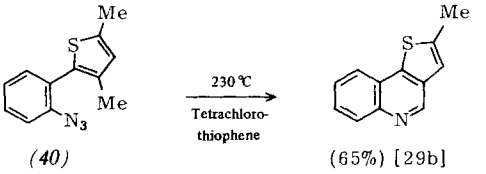
3.2.1. Intramolecular Triplet Arylnitrene Reactions

Probably the most versatile and useful cyclization involving a triplet arylnitrene is hydrogen abstraction from a nearby alkyl group followed by spin inversion and cyclization

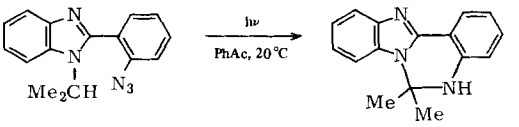


(145) *(146)* *(147)*

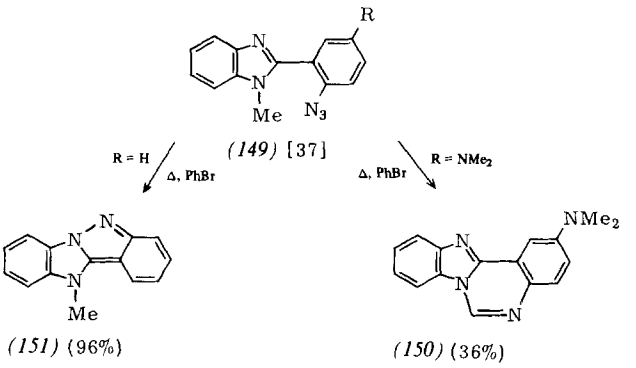
[*(145)*→*(146)*→*(147)*]. Since decomposition of an azide usually generates a singlet nitrene which decays to the triplet species relatively slowly compared with many competitive singlet reactions, special methods are needed to optimize the triplet reactivity. These include triplet photosensitization, use of "heavy atom" solvents to accelerate the intersystem crossing, and substituents which deactivate the singlet species by conjugation with the nitrene. Each of these methods has its limitations, but when no competitive singlet pathway exists, the thermal method is the best synthetic approach. Some recent examples are the reactions of the azides *(40)*, *(148)*,



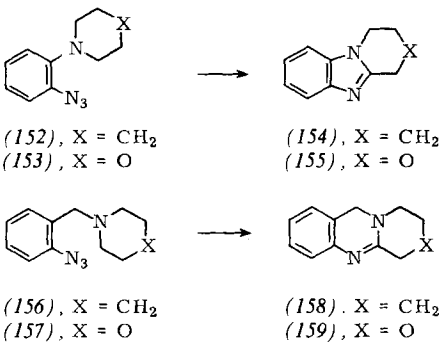
(40) (65%) [29b]



(148) (59%) [37]

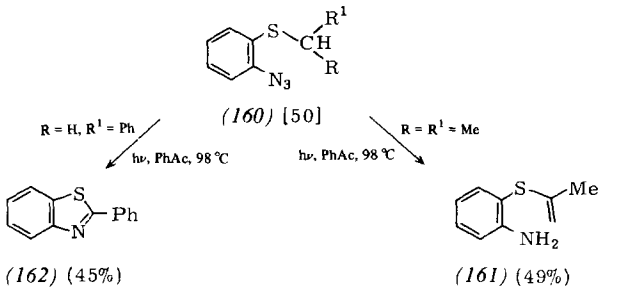


(149) [37] *(151)* (96%) *(150)* (36%)



(152), X = CH_2 *(154)*, X = CH_2
(153), X = O *(155)*, X = O

(156), X = CH_2 *(158)*, X = CH_2
(157), X = O *(159)*, X = O



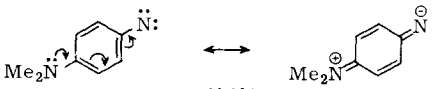
(160) [50] *(162)* (45%) *(161)* (49%)

Table 6. Examples of triplet arylnitrene reactions.

Azide	X	Conditions	Product	Yield [%]
(152)	CH_2	Δ, PhBr	*(154)*	45
		hν, PhAc, 98 °C		85
(153)	O	Δ, PhBr	*(155)*	48
		hν, PhAc, 98 °C		96
(156)	CH_2	Δ, Cumene	*(158)*	0
		hν, PhAc, 98 °C		56
(157)	O	Δ, Cumene	*(159)*	0
		hν, PhAc, 98 °C		42

(149), (152), (153), (156), (157), and *(160)* (see also Table 6)[29b, 37, 50].

The use of solvents without aliphatic protons is advantageous for triplet cyclizations and yields are often considerably improved by use of high temperatures and short reaction times. Thus boiling bromobenzene, trichlorobenzene, or tetrachlorothiophene are very suitable solvents. Lower temperatures favor azo-compound formation, apparently an energetically easier alternative to H-abstraction. The dimethylamino-group is especially effective in causing deactivation of a singlet nitrene by mesomerically satisfying its "electrophilic thirst" [*(163)*].

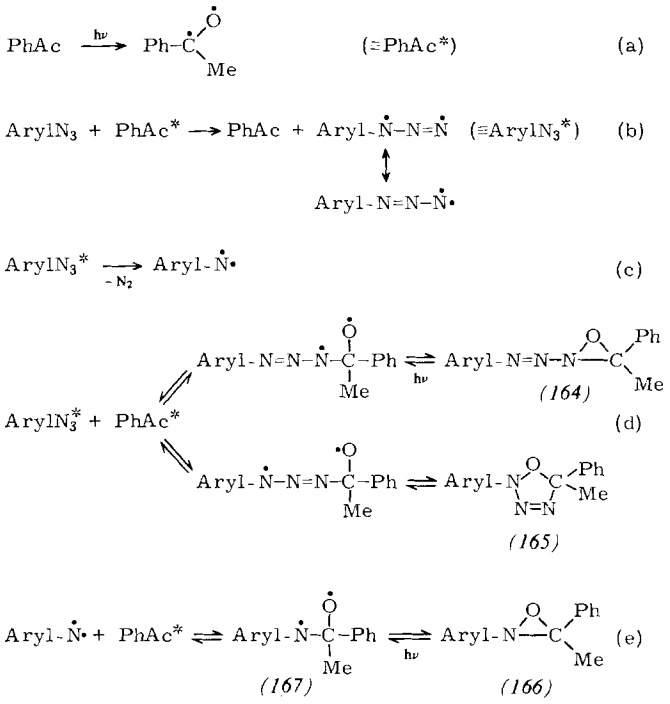


(163)

Thus 2-(2-azidophenyl)-1-methylbenzimidazole *(149)* R = H, gives no triplet cyclization product *(150)*, H in place of NMe_2, at all on thermolysis but 96% of the singlet-derived benzimidazoloindazole *(151)*[37]. However, introduction of dimethylamino group *para* to the azide group [*(149)*, R = NMe_2] results in a complete reversal, thermolysis giving only triplet nitrene-derived products, *e.g. (150)*. It also illustrates the efficiency of photosensitization (especially with acetophenone) for bringing about selective triplet cyclizations, further exemplified by reactions of *(148), (152), (153), (156), (157),* and *(160)*. As observed earlier, it is often advantageous to conduct such sensitized photolyses at elevated temperature but low enough as not to cause thermolysis of the azide, but only to energize the triplet nitrene and, thereby, avoid azo-compound formation. In our experience the photo-generated triplet nitrene is a relatively low energy species. A bonus of this thermal excitation is that the time for photolysis is substantially reduced. However, this method occasionally leads to interesting side reactions. Thus, the secondary role of triplet acetophenone as a dehydrogenating agent is highly effective for the synthesis of the annelated benzimidazoles *(154)* and *(155)*, perhaps because the preferred *cis* geometry of the dihydro intermediate allows two hydrogen atoms to be abstracted simultaneously.

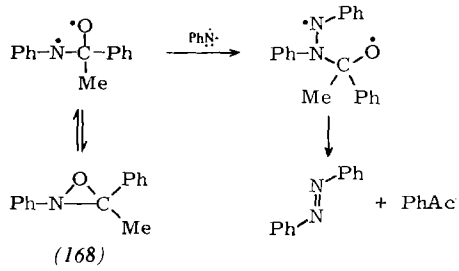
An unusual alternative to cyclization open to an appropriate *o*-azidophenyl derivative is the concerted abstraction of two vicinal hydrogen atoms from a paraffinic side-chain as in the reaction *(160)* → *(161)*.

Another more deep-seated change in reactivity is sometimes noted in sensitized photolyses which, we believe, are best explained as reactions of the triplet *azide* or of a triplet nitrene-triplet ketone derived molecule. We would include in this category: (a) the unexpected ease of azo-compound formation often at the expense of ready intramolecular alternatives[29b, 31, 91]; (b) the co-production of apparently singlet-derived products during triplet photosensitized reactions[29b]; and (c) the occasional formation of unexpected by-products, sometimes containing two or more[*] of the azide nitrogen atoms. These reactions may be seen to derive from a new family of longer-lived reactive intermediates visualized as the oxaziridines [see *(164)* and *(166)*] or oxatriazole *(165)* which may behave as masked singlet or triplet azides or nitrenes as shown in Scheme 6.



Scheme 6. Reactions of triplet nitrenes. * indicates a triplet state.

The oxaziridine *(168)* possibly derived as indicated in eq. (e) which is a known photo-source of triplet nitrene products[24], may behave as a "template" for azo-compound formation, the triplet nitrene having been scavenged by the steady state concentration of triplet acetophenone. Formation of azo compound could also be envisaged as occurring from the intermediates *(164)* and *(165)* in an analogous manner.



(168)

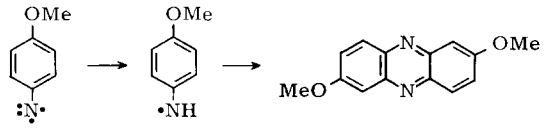
We believe that the unexplained origin of azo compounds from arylnitrenes (or their precursors) could be related to the above ideas. Thus formation of a "long-lived triplet nitrene complex" [cf. *(167)*] with reaction solvents or even vessel walls could form a template upon which further attack by a triplet nitrene would give the azo compound. Such complexes could involve a π-cloud of an aromatic solvent, for example. We hope that these tentative ideas may stimulate discussion of the little understood problem of azo-compound formation observed in nitrene decompositions.

3.2.2. Intermolecular Triplet Arylnitrene Reactions

Formation of phenazines: Walker and *Waters*[92] observed the formation of 2,7-dimethoxyphenazine *(171)* on thermoly-

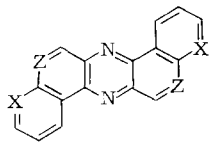
[*] A footnote in an early paper [92] on the photolysis of phenyl azide reported the slow formation of benzotriazole, though we have not been able to corroborate this.

sis of *p*-methoxyphenyl azide in cumene in trace yield. The result can be interpreted as a dimerization of the appropriate radicals *(170)* derived from a triplet nitrene *(169)* by hydrogen abstraction. While no other monocyclic arylnitrenes have been reported so far to give phenazines we have found certain fused bicyclic azides to give small yields of phenazines on thermolysis in bromobenzene, which is known to promote singlet → triplet intersystem crossing[93]. Thus, thermolysis of 1- and 2-naphthyl azide gives a dibenzophenazine *(172)* and other triplet products such as the corresponding



(169) *(170)* *(171)*

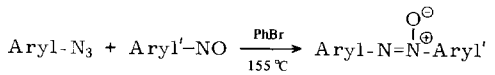
amines and azo compounds[78]. Similarly, thermolysis of the 3- or 5-quinolyl azide gives the corresponding phenazines[79] *(173)* and *(174)* apart from the expected azo- and amino compounds. As these yields were not optimized and polycyclic phenazines would only be available through multistep and cumbersome syntheses the scope of this method deserves further study.



(172), Z = X = CH
(173), Z = N, X = CH
(174), Z = CH, X = N

Formation of unsymmetrical diarylazoxy compounds: Practicable yields of azoxy compounds *(175)* can be realized when aryl azides with electron donating substituents especially in the *para*-position (Me, MeO) or naphthyl azides are thermolyzed in the presence of *p*-nitroso-*N,N*-dimethylaniline (Table 7)[94a]. Only one of the two possible azoxy compounds is formed and the method is thus unambiguous with regard to the position of the oxygen. The mechanism obviously involves a triplet nitrene which is intercepted by a nitrosoarene, a well-known spin-trap for radicals[95]. This promising approach to mixed azoxy compounds which resulted from a chance observation[96] is open to improvement and widening of the scope.

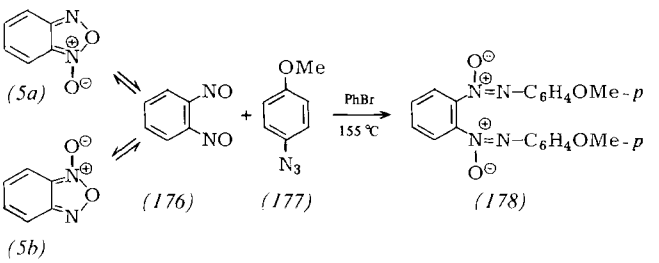
Table 7. Synthesis of unsymmetrical diarylazoxy compounds *(175)*.



(175)

Aryl	Aryl′	Yield [%]
p-$MeOC_6H_4$	*p*-$Me_2NC_6H_4$	69
p-MeC_6H_4	*p*-$Me_2NC_6H_4$	25
Ph	*p*-$Me_2NC_6H_4$	3
p-$Me_2NC_6H_4$	Ph	27
α-$C_{10}H_7$	*p*-$Me_2NC_6H_4$	92
β-$C_{10}H_7$	*p*-$Me_2NC_6H_4$	93

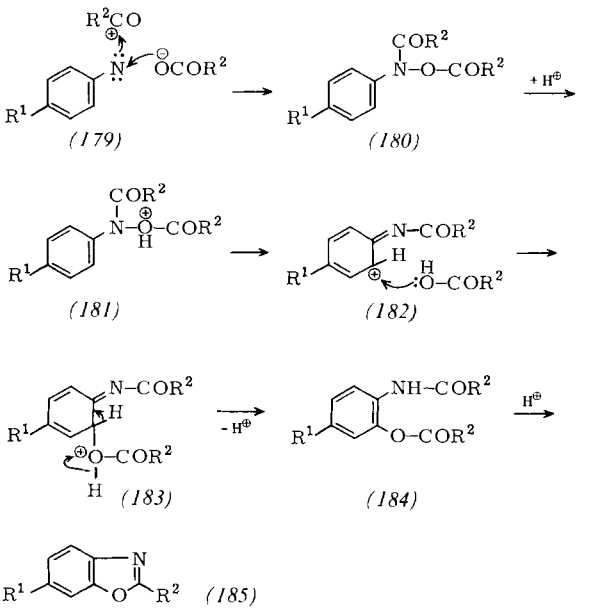
The trapping of nitroso compounds with arylnitrenes was used to demonstrate the tautomerism between benzofuroxan and *o*-dinitrosobenzene *(5)*⇌*(176)*[94b]. On heating *p*-anisyl azide *(177)* in bromobenzene (a triplet promoter) in the presence of benzofuroxan *(5)* the *o*-bis(azoxy) compound *(178)* was one of the products (40%). Its significance as a chemical proof for the existence of the equilibrium between *(5)* and *(176)* is plain.



(5a) *(5b)* *(176)* *(177)* *(178)*

4. Acid-Catalyzed Decompositions of Aryl Azides—Formation of Benzoxazoles

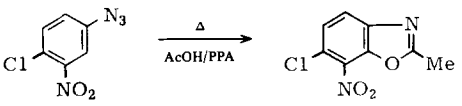
Derivatives of phenyl azide substituted by electron-withdrawing groups and with the *para*-position blocked yield 2,6-disubstituted benzoxazoles *(185)* when heated in a mixture of carboxylic acid and polyphosphoric acid (PPA). For example, in mixtures of polyphosphoric acid and acetic, propionic, or benzoic acid, *p*-nitrophenyl azides give 2-methyl- (83% yield), 2-ethyl- (75%), and 2-phenyl-6-nitrobenzoxazole (70%), respectively[97] [*(185)*, $R^1 = NO_2$, R^2 = Me, Et, Ph].



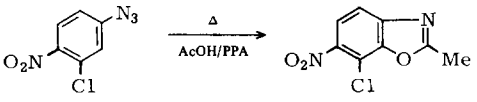
(179) *(180)* *(181)* *(182)* *(183)* *(184)* *(185)*

A rational mechanism for these reactions is shown. It is proposed that the initially generated singlet arylnitrene *(179)* inserts into the anhydride of the carboxylic acid (although a triplet insertion is also possible)[98] to give the corresponding *N,O*-diacylphenylhydroxylamine *(180)*. This is followed by transfer of the acyloxy moiety to the *ortho*-position. The nucleophilic nature of the attack [*(182)*→*(183)*] is supported by the necessary presence of an electron-withdrawing group in the *para*-position of phenyl azides, but also by the fact that 4-chloro-3-nitro *(186)* and 3-chloro-4-nitro-phenyl azide *(188)*

gave mainly the oxazoles *(187)* and *(189)* respectively, *i.e.* the acyloxy group moved to the most electron depleted point of the ring[97]. The function of the polyphosphoric acid is probably threefold: (i) to promote formation of the carboxylic acid anhydride; (ii) to promote a Bamberger-type rearrangement of the *N,O*-diacylphenylhydroxylamine *(180)*; and (iii) to cyclize the key *N,O*-diacylated *o*-aminophenol intermediates *(184)*. In some cases these species can be isolated and cyclized under more vigorous conditions.



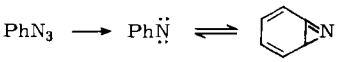
(186) *(187)*



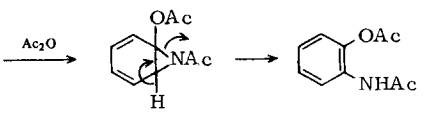
(188) *(189)*

In a mixture of acetic and polyphosphoric acids, phenyl azide itself gives *p*-acetamidophenyl acetate (75% yield) by a Bamberger-type rearrangement of the intermediate *N,O*-diacylphenylhydroxylamine *(180)*, $R^1 = H$, $R^2 = Me$, whilst compounds substituted by electron-donating groups (Me, MeO) in the *para*-position yield the corresponding amine and tars[97].

Thermal decomposition of phenyl azide and several of its simple derivatives (*o*-Me, *p*-Me, *o*-Cl, *p*-Br) in acetic anhydride alone yields the corresponding *N,O*-diacetylated *o*-aminophenol *(184)*[98] while photolysis in acetic acid affords *o*-acetamidophenol[49a]. Under these conditions *ortho*-disubstituted products are formed even when the *para*-position is free. At first these reactions were thought to involve a Claisen-type rearrangement[98] but we now favor addition of acetic anhydride to an intermediate azirine [*(25)*→*(190)*] followed by ring-opening and rearrangement to give *(191)*[99] which is more in keeping with the accepted mechanism of azide decompositions in the presence of nucleophiles.

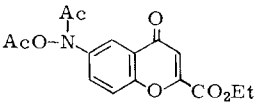


(25)

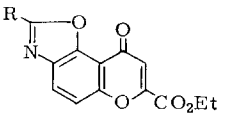


(190) *(191)*

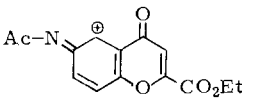
The possibility that aryl azides react in mixtures of polyphosphoric acid and a carboxylic acid by an *intra*molecular process of the Claisen type appears unlikely since the chromone derivative *(192)* analogous to *(180)* synthesized independently gave a mixture of two oxazoles *(193)* and *(194)* when heated in a mixture of polyphosphoric and propionic acids[100]. This result can be rationalized by competitive attack of the added propionic acid and migration of the acyl group in the cation *(195)*.



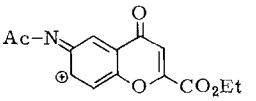
(192)



(193), R = Me
(194), R = Et

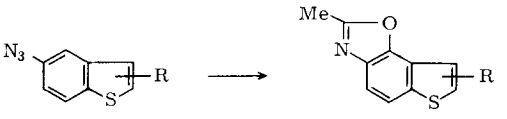


(195)

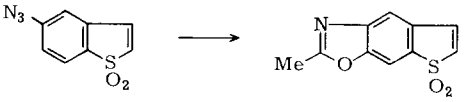


(196)

The formation of the angular [*(193)* and *(194)*] rather than linear products can be attributed to the greater stability of intermediate *(195)* as against *(196)*[100]. Only in *(195)* is the aromaticity of the γ-pyrone system preserved. Likewise, 5-azidobenzo[*b*]thiophenes *(197)* gives the angular products *(198)*[101]. By contrast, however, the sulfone *(199)* yields the linear product *(200)*[101]. In this case the thiophene ring is no longer aromatic and steric hindrance proves decisive.



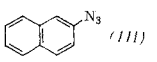
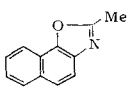
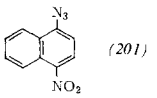
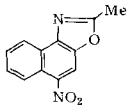
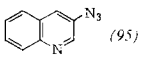
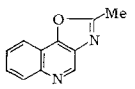
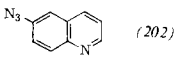
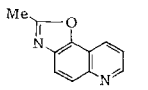
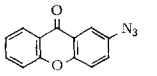
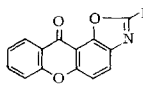
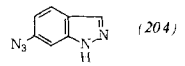
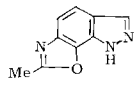
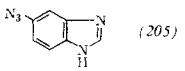
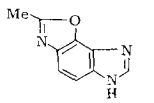
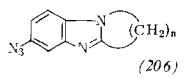
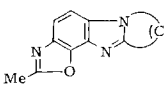
(197) *(198)*



(199) *(200)* (38%)

In view of the synthetic utility of this reaction its scope is illustrated in Table 8 (for other examples see references[73,74,101]). The advantage of the method lies clearly in the fact that it obviates the necessity for an *o*-aminophenol as starting material, as in the conventional synthesis of benzoxazoles. This is particularly valuable in the case of polynuclear aromatics [cf. Table 8, *e.g.* quinolines *(90)*, xanthones *(203)*] where the preparation of the required *o*-aminophenol would be cumbersome in the extreme. The scope of this reaction should be further investigated in other polycyclic aromatic systems when novel fused oxazoles could be produced. Moreover, as described above [*(179)*→*(185)*] *o*-aminophenols of fused polycyclics could also be prepared by this method as starting materials for novel azoles, azines, azepines, and possibly large rings by suitable cyclization procedures. These aminophenols are, of course, also obtainable by alkaline hydrolysis of the corresponding oxazoles.

Table 8. Synthesis of oxazoles by thermolysis of aryl azides in acetic acid/polyphosphoric acid.

Azide	Product	Yield [%]	Ref.
 *(111)*		5 [a]	[102]
 *(201)*		25	[97]
 *(95)*		50 [b]	[97]
 *(202)*		70 [b]	[102]
 *(203)*		92 [b]	[102]
 *(204)*		60	[102]
 *(205)*		60	[97]
 *(206)*		30–81 [c]	[103]

[a] A 35% yield of the intermediate *N,O*-diacetylated 2-amino-1-naphthol was isolated also which could be cyclized by heating in a solvent or by sublimation. [b] An *o*-acetamidohydroxy compound was first isolated which cyclized on further heating. [c] Yield depending on the nature of the alicyclic ring.

5. Conclusion

A strong inducement for continuing research into arylnitrenes lies in their application as photoresists in the solid state industry and in their versatility for photoaffinity labeling by irradiation of aryl azides in the presence of appropriate acceptors.

There exists, moreover, a wide scope for further exploration on the basis of the known synthetic uses of arylnitrenes. For instance, the successful diamine formation, ring expansion, and oxazole conversion elaborated by us in bicyclic systems could obviously be extended into the field of tricycles which play a prominent role in neuropharmacology as antipsychotics and antidepressants[104]. This work may lead to novel azepino and oxazolo tricycles of potential biological activity. Germane to this topic is the further exploration of the phenothiazine reaction [*(46)*→*(48)*] which by replacing ring B in *(46)* may feasibly produce novel tricyclic systems.

While the ring expansion and diamine formation of bicyclic, fused arylnitrenes are well established, prediction as to which product will be formed or as to the ratio of the two products in advance of experimental trial is far from certain. Much basic work remains to be done and preliminary results[105] indicate that the nature of the products can be influenced by introducing appropriate substituents into the nitrene ring[27c].

The synthetic value of diamine formation would be considerably enhanced if instead of the type of diamine represented by *(92)* one could produce the corresponding free *o*-diamines (NH_2 in place of Et_2N). Attempts at using ammonia as a nucleophile for this purpose have failed. Such diamines would serve as versatile starting materials for a wide range of rather inaccessible heterocyclic systems. Obvious innovations by analogy with sulfur nucleophiles [such as *(89)* and *(115)*] would be the study of carbon and phosphorus nucleophiles as well as the use of bidentate reagents. The potential of the latter has already been demonstrated for the vinylic azidouracil in presence of certain amino esters[84].

An imaginative and novel synthetic use of arylnitrenes has recently been described for the preparation of pentacoordinate spirophosphoranes[106]; this method is wide open to further elaboration.

Biochemical interest in arylnitrenes has so far not been prominent. Yet in view of a striking analogy between the chemical behavior of arene oxides[107] and aromatic azirines, *e.g. (124)*, there may also be a parallel in their respective metabolism. That arylnitrenes and their numerous precursors could well be involved in carcinogenesis was in fact suggested some time ago[108].

There are a number of purely mechanistic problems in the arylnitrene field which need further clarification. Paramount amongst them is the role of the recently observed photointermediate 1-aza-1,2,4,6-cycloheptatetraene *(80)* which challenges the accepted mechanism *via* benzoazirine *(25)*. Similar matrix studies are being carried out on bi- and polycyclic arylnitrenes to establish "whether the tetraene intermediate is generally observable".

The novice to arylnitrene chemistry should be encouraged to know that aryl azides may be safely decomposed and handled in solvents and sufficiently purified for all purposes by chromatography or recrystallization. Unless heated dry to their decomposition point they are not explosive. It is hoped that the practical aspects described in this review will stimulate new ideas leading to fruitful experimentation.

We are indebted to our co-workers cited in the references for their enthusiasm and untiring collaboration. Our own laboratory work was generously sponsored by the Science Research Council, Glaxo-Allenburys Limited, I.C.I. Pharmaceuticals Limited, Smith Kline and French Laboratories (Philadelphia), Nicholas Laboratories Limited, and Pfizer Central Research (Kent).

Received: April 17, 1979 [A 297 IE]
German version: Angew. Chem. *91*, 965 (1979)

[1] *W. Lwowski:* Nitrenes. Wiley, New York 1970.
[2] a) *L. Horner, A. Christmann,* Angew. Chem. *75*, 707 (1963); Angew. Chem. Int. Ed. Engl. *2*, 599 (1963); b) *R. A. Abramovitch, B. A. Davis,* Chem. Rev. *64*, 149 (1964); c) *W. Lwowski,* Angew. Chem. *79*, 922 (1967); Angew. Chem. Int. Ed. Engl. *6*, 897 (1967); d) *G. L'abbé,* Chem. Rev. *69*, 345 (1969); e) *R. K. Smalley, H. Suschitzky,* Chem. Ind. (London) *1970*, 1338; f) *J. I. G. Cadogan,* Acc. Chem. Res. *5*, 303 (1972); g) *S. P. McManus:* Organic Reactive Intermediates. Academic Press, New York 1973; h) *C. Wentrup,* Top. Curr. Chem. *62*, 173 (1976).

[3] *G. Smolinsky, E. Wasserman, W. A. Yagar,* J. Am. Chem. Soc. *84,* 3220 (1962).
[4] *L. K. Dyall,* Aust. J. Chem. *28,* 2147 (1975); *30,* 2669 (1977); *L. K. Dyall, J. E. Kemp,* J. Chem. Soc. *B 1968,* 976.
[5] *J. Ashby, H. Suschitzky,* Tetrahedron Lett. *1971,* 1315.
[6] *A. Reiser, R. Marley,* Trans. Faraday Soc. *64,* 1806 (1968).
[7] *A. Reiser, L. J. Leyshon,* J. Am. Chem. Soc. *93,* 4051 (1971).
[8] *L. J. Leyshon, A. Reiser,* J. Chem. Soc. Faraday Trans. II *68,* 1918 (1972).
[9] *J. S. Swenton,* Tetrahedron Lett. *1968,* 3421.
[10] *G. R. Felt, S. Linke, W. Lwowski,* Tetrahedron Lett. *1972,* 2037.
[11] *M. Komatsu, S. Ichijima, Y. Oshiro, T. Agawa,* J. Org. Chem. *38,* 4341 (1973).
[12] *H. Takeuchi, K. Kinoshita, S. M. Abdul-Hai, M. Mitani, T. Tsuchida, K. Koyama,* J. Chem. Soc. Perkin Trans. II *1976,* 1201.
[13] *H. Takeuchi, N. Murata, Y. Nakagawa, T. Tsuchida, K. Koyama,* J. Chem. Soc. Perkin Trans. II *1977,* 80.
[14] *J. I. G. Cadogan,* Q. Rev. Chem. Soc. *22,* 222 (1968).
[15] *J. I. G. Cadogan, S. Kulik, C. Thomson, M. J. Todd,* J. Chem. Soc. *C 1970,* 2437.
[16] *J. I. G. Cadogan, S. Kulik,* J. Chem. Soc. *C 1971,* 2621.
[17] *J. Sauer, J. Engels,* Tetrahedron Lett. *1969,* 5175.
[18] *R. A. Abramovitch, J. Court, E. P. Kyba,* Tetrahedron Lett. *1972,* 4059.
[19] *J. I. G. Cadogan, A. Cooper,* J. Chem. Soc. *B 1969,* 883.
[20] *P. K. Brooke, R. B. Herbert, F. G. Holliman,* Tetrahedron Lett. *1973,* 761.
[21] *H. C. Waterman, D. L. Vivian,* J. Org. Chem. *14,* 289 (1949).
[22] *R. H. Smith, H. Suschitzky,* Tetrahedron *16,* 80 (1961).
[23] *F. P. Tsui, Y. H. Chang, T. M. Vogel, G. Zon,* J. Org. Chem. *41,* 3381 (1976).
[24] *E. Meyer, G. W. Griffin,* Angew. Chem. *79,* 648 (1967); Angew. Chem. Int. Ed. Engl. *6,* 634 (1967); *J. S. Splitter, M. Calvin,* Tetrahedron Lett. *1968,* 1445.
[25] *J. S. Swenton,* Tetrahedron Lett. *1967,* 2855.
[26] *W. Heinzelmann, M. Märky, P. Gilgen,* Helv. Chim. Acta *59,* 2362 (1976).
[27] *R. A. Abramovitch, B. W. Cue, Jr.,* J. Org. Chem. *38,* 173 (1973); Heterocycles *1,* 227 (1973).
[28] *J. I. G. Cadogan, J. N. Done, G. Lunn, P. K. K. Lim,* J. Chem. Soc. Perkin Trans. I *1976,* 1749.
[29] a) *G. Smolinsky,* J. Am. Chem. Soc. *82,* 4717 (1960); b) *J. M. Lindley, I. M. McRobbie, O. Meth-Cohn, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I *1977,* 2194.
[30] *K. E. Chippendale, B. Iddon, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I *1972,* 2023; Chem. Commun. *1971,* 203.
[31] *J. M. Lindley, I. M. McRobbie, O. Meth-Cohn, H. Suschitzky,* Tetrahedron Lett. *1976,* 4513.
[32] *J. H. Boyer, C.-C. Lai,* J. Chem. Soc. Perkin Trans. I *1977,* 74.
[33] a) *R. J. Sundberg,* J. Org. Chem. *30,* 3604 (1965); *33,* 487 (1968); b) *R. J. Sundberg, T. Yamazaki, ibid. 32,* 290 (1967); c) *R. J. Sundberg, H. F. Russell, W. V. Ligon, L.-S. Lin, ibid. 37,* 719 (1972); d) *J. I. G. Cadogan, M. Cameron-Wood, R. K. Mackie, R. J. G. Searle,* J. Chem. Soc. *1965,* 4831.
[34] *P. N. Preston, K. Turnbull,* J. Chem. Soc. Perkin Trans. I *1977,* 1229.
[35] *A. Tanaka, K. Yakushijin, S. Yoshina,* J. Heterocycl. Chem. *14,* 975 (1977).
[36] *K. T. Potts, J. L. Marshall,* J. Org. Chem. *41,* 129 (1976).
[37] *I. M. McRobbie, O. Meth-Cohn, H. Suschitzky,* Tetrahedron Lett. *1976,* 929.
[38] *I. M. McRobbie, O. Meth-Cohn, H. Suschitzky,* Tetrahedron Lett. *1976,* 925.
[39] *O. Tsuge, H. Samura,* Org. Prep. Proced. Int. *6,* 161 (1974); *A. J. Nunn, F. J. Rowell,* J. Chem. Soc. Perkin Trans. I *1975,* 629.
[40] *K. E. Chippendale, B. Iddon, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I *1973,* 129.
[41] a) *V. M. Colburn, B. Iddon, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I *1977,* 2436; b) *K. Srinivasan, K. G. Srinivasan, K. K. Balasubramanian, S. Swaminanthan,* Synthesis *1973,* 313; c) *S. Gronowitz, I. Ander,* Acta Chem. Scand. *29B,* 513 (1975); d) *S. Gronowitz, C. Westerlund, A.-B. Hornfeldt, ibid. 30B,* 391 (1976); e) *K. E. Chippendale, B. Iddon, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I *1973,* 125.
[42] *V. M. Colburn, B. Iddon, H. Suschitzky, P. T. Gallagher,* J. Chem. Soc. Perkin Trans. I *1979,* 1337.
[43] *P. Germeraad, H. W. Moore,* J. Org. Chem. *39,* 774 (1974).
[44] *P. K. Adhikary, S. K. Das, B. A. Hess,* J. Med. Chem. *19,* 1352 (1976).
[45] *A. Reiser, H. H. Wagner, G. Bowes,* Tetrahedron Lett. *1966,* 2635; *A. Reiser, G. Bowes, R. J. Horne,* Trans. Faraday Soc. *62,* 3162 (1966); *A. Reiser, F. W. Willets, G. C. Terry, V. Williams, R. Marley, ibid. 64,* 3265 (1968).
[46] *P. A. Lehmann, R. S. Berry,* J. Am. Chem. Soc. *95,* 8614 (1973).
[47] a) *R. J. Sundberg, M. Brenner, S. R. Suter, B. P. Das,* Tetrahedron Lett. *1970,* 2715; b) *R. J. Sundberg, R. W. Heintzelman,* J. Org. Chem. *39,* 2546 (1974); c) *R. J. Sundberg, D. W. Gillespie, B. A. DeGraff,* J. Am. Chem. Soc. *97,* 6193 (1975).
[48] *C. Mayor, C. Wentrup,* J. Am. Chem. Soc. *97,* 7467 (1975); *N. M. Lan, C. Wentrup,* Helv. Chim. Acta *59,* 2068 (1976).
[49] a) *L. Horner, A. Christmann, A. Gross,* Chem. Ber. *96,* 399 (1963); b) *R. E. Banks, A. Prakash,* J. Chem. Soc. Perkin Trans. I *1974,* 1365.
[50] *O. Meth-Cohn, D. N. Rogers, H. Suschitzky,* unpublished results.
[51] a) *J. I. G. Cadogan, B. S. Tait,* J. Chem. Soc. Perkin Trans. I *1975,* 2396; b) *J. I. G. Cadogan, D. S. B. Grace, P. K. K. Lim, B. S. Tait, ibid. 1975,* 2376. c) *M. Messer, D. Farge,* Bull. Soc. Chim. Fr. *1968,* 2832.
[52] *I. M. McRobbie, O. Meth-Cohn, H. Suschitzky,* J. Chem. Res. (S) *1977,* 17; (M) *1977,* 434.
[53] *J. M. Lindley, O. Meth-Cohn, H. Suschitzky,* unpublished results.
[54] *J. M. Lindley, O. Meth-Cohn, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I, in press.
[55] *D. G. Hawkins, O. Meth-Cohn, H. Suschitzky,* unpublished results.
[56] *K. Hafner, W. Kaiser,* Tetrahedron Lett. *1964,* 2185. (Professor *Hafner* has expressed guarded agreement with this view.)
[57] *G. R. Cliff, G. Jones, J. McK. Woollard,* J. Chem. Soc. Perkin Trans. I *1974,* 2072; Tetrahedron Lett. *1973,* 2401.
[58] *L. Wolff,* Justus Liebigs Ann. Chem. *394,* 59 (1912).
[59] *W. Schlenk:* Ausführliches Lehrbuch der Organischen Chemie. Bd. II. Deuticke, Vienna 1939, p. 151.
[60] a) *R. Huisgen,* Angew. Chem. *67,* 756 (1955); b) *R. Huisgen, D. Vossius, M. Appl,* Chem. Ber. *91,* 1 (1958); c) *R. Huisgen, M. Appl, ibid. 91,* 12 (1958).
[61] *W. v. E. Doering, R. A. Odum,* Tetrahedron *22,* 81 (1966).
[62] a) *R. J. Sundberg, S. R. Suter, M. Brenner,* J. Am. Chem. Soc. *94,* 513 (1972); b) *O. L. Chapman, J.-P. LeRoux, ibid. 100,* 282 (1978).
[63] *L. Horner, A. Christmann, A. Gross,* Chem. Ber. *96,* 399 (1963).
[64] *R. J. Sundberg, R. H. Smith,* J. Org. Chem. *36,* 295 (1971).
[65] *B. Nay, E. F. V. Scriven, H. Suschitzky, D. R. Thomas, S. E. Carroll,* Tetrahedron Lett. *1977,* 1811.
[66] *A. C. Mair, M. F. G. Stevens,* J. Chem. Soc. *C 1971,* 2317.
[67] *R. Purvis, R. K. Smalley, W. A. Strachan, H. Suschitzky,* J. Chem. Soc. Perkin Trans. I *1978,* 191; *M. Ogata, H. Matsumoto, H. Kano,* Tetrahedron *25,* 5205 (1969).
[68] a) *J. Rigaudy, C. Igier, J. Barcelo,* Tetrahedron Lett. *1975,* 3845; b) *E. F. V. Scriven, D. R. Thomas,* Chem. Ind. (London) *1978,* 385.
[69] *S. E. Carroll, B. Nay, E. F. V. Scriven, H. Suschitzky, D. R. Thomas,* Tetrahedron Lett. *1977,* 3175.
[70] *T. Shingaki,* Sci. Rep. Coll. Gen. Educ. Osaka Univ. *11,* 93 (1963); Chem. Abstr. *60,* 6734 d (1964).
[71] *R. J. Sundberg, C.-C. Lang,* J. Org. Chem. *36,* 300 (1971).
[72] *B. Iddon, H. Suschitzky, D. S. Taylor,* J. Chem. Soc. Perkin Trans. I *1974,* 579.
[73] *B. Iddon, M. W. Pickering, H. Suschitzky, D. S. Taylor,* J. Chem. Soc. Perkin Trans. I *1975,* 1686; J. Chem. Soc. Chem. Commun. *1974,* 759.
[74] *P. T. Gallagher, B. Iddon, H. Suschitzky,* unpublished results.
[75] *F. Hollywood, E. F. V. Scriven, H. Suschitzky, D. R. Thomas, R. Hull,* J. Chem. Soc. Chem. Commun. *1978,* 806.
[76] *S. Senda, K. Hirota, T. Asao, K. Maruhashi, N. Kitamura,* Tetrahedron Lett. *1978,* 1531.
[77] *S. E. Carroll, B. Nay, E. F. V. Scriven, H. Suschitzky,* Tetrahedron Lett. *1977,* 943.
[78] a) *S. E. Hilton, E. F. V. Scriven, H. Suschitzky,* J. Chem. Soc. Chem. Commun. *1974,* 853; b) *S. E. Hilton, E. F. V. Scriven, H. Suschitzky,* unpublished results.
[79] *B. Nay,* PhD Thesis, University of Salford 1977.
[80] *E. F. V. Scriven, H. Suschitzky, D. R. Thomas, R. F. Newton,* J. Chem. Soc. Perkin Trans. *1979,* 53.
[81] *S. E. Carroll, B. Nay, E. F. V. Scriven, H. Suschitzky,* Synthesis *1975,* 710.
[82] *B. Nay, E. F. V. Scriven, H. Suschitzky, Z. U. Khan,* Synthesis *1977,* 757.
[83] *E. F. V. Scriven, D. R. Thomas,* unpublished results (1977).
[84] *S. Senda, K. Hirota, M. Suzuki, T. Asao, K. Maruhashi,* J. Chem. Soc. Chem. Commun. *1976,* 731; *S. Senda, K. Hirota, T. Asao, K. Maruhashi,* J. Am. Chem. Soc. *99,* 7358 (1977).
[85] *A. Hassner, F. W. Fowler,* J. Am. Chem. Soc. *90,* 2869 (1968).
[86] *R. S. Atkinson* in *H. Suschitzky, O. Meth-Cohn:* Aromatic and Heteroaromatic Chemistry. Vol. 6. Chemical Society, London 1978, p. 237.
[87] *R. P. Bennett, W. B. Hardy,* J. Am. Chem. Soc. *90,* 3295 (1969).
[88] *R. A. Abramovitch, E. F. V. Scriven,* Chem. Commun. *1970,* 787.
[89] *R. A. Abramovitch, S. R. Challand, E. F. V. Scriven,* J. Am. Chem. Soc. *95,* 1374 (1972); J. Org. Chem. *37,* 2705 (1972).
[90] *R. A. Abramovitch, T. D. Bailey, T. Takaya, V. Uma,* J. Org. Chem. *39,* 340 (1974).
[91] *J. S. Swenton, T. J. Ikeler, B. H. Williams,* J. Am. Chem. Soc. *92,* 3103 (1970).
[92] *P. Walker, W. A. Waters,* J. Chem. Soc. *1962,* 1632.
[93] *A. G. Anastassiou,* J. Am. Chem. Soc. *89,* 3184 (1967).
[94] a) *A. B. Bulacinski, B. Nay, E. F. V. Scriven, H. Suschitzky,* Chem. Ind. (London) *1975,* 746; b) *A. B. Bulacinski, E. F. V. Scriven, H. Suschitzky,* Tetrahedron Lett. *1975,* 3577.
[95] *E. G. Janzen,* Acc. Chem. Res. *4,* 31 (1971).
[96] *G. V. Garner, K. B. Niewiadomski, H. Suschitzky,* Chem. Ind. (London) *1972,* 462.
[97] *R. Garner, E. B. Mullock, H. Suschitzky,* J. Chem. Soc. *C 1966,* 1980.

[98] *R. K. Smalley, H. Suschitzky*, J. Chem. Soc. *1963*, 5571.
[99] *R. K. Smalley, W. A. Strachan, H. Suschitzky*, Tetrahedron Lett. *1974*, 825.
[100] *M. I. Chohan, A. O. Fitton, B. T. Hatton, H. Suschitzky*, J. Chem. Soc. *C 1971*, 3079.
[101] *B. Iddon, H. Suschitzky, D. S. Taylor, M. W. Pickering*, J. Chem. Soc. Perkin Trans. I *1974*, 575.
[102] *E. B. Mullock, H. Suschitzky*, J. Chem. Soc. *C 1968*, 1937.
[103] *R. Garner, H. Suschitzky*, J. Chem. Soc. *C 1967*, 74.
[104] *Ch. L. Zirkle, C. Kaiser* in *A. Burger:* Medicinal Chemistry. 3rd Edit., Part II. Wiley, New York 1970, pp. 1410, 1470.
[105] *Z. U. Khan, E. F. V. Scriven, H. Suschitzky*, unpublished work.
[106] *J. I. G. Cadogan, I. Gosney, E. Henry, T. Naisby, B. Nay, N. J. Stewart, N. J. Tweddle*, J. Chem. Soc. Chem. Commun. *1979*, 189; *J. I. G. Cadogan, N. J. Stewart, N. J. Tweddle, ibid. 1979*, 191.
[107] *A. M. Jeffrey, D. M. Jerina*, J. Am. Chem. Soc. *97*, 4427 (1975).
[108] *F. L. Rose*, Nature *215*, 1492 (1967).

Capto-dative Substituent Effects in Syntheses with Radicals and Radicophiles[**]

New synthetic methods (32)

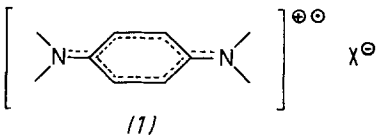
By Heinz Günter Viehe, Robert Merényi, Lucien Stella, and Zdenek Janousek[*]

Dedicated to the double anniversary: 100 years Wurster's salts and 50 years Paneth's radical reactions with metal mirrors

The 100 years old Wurster's salts have long been recognized as compounds with radical cations. Their unusual stabilization derives partly from *capto-dative (cd)* substitution. This principle is now discussed as one factor of radical stabilization and it is applied to simple methine derivatives. *cd*-Substitution has synthetically useful applications: *cd*-substituents on a carbon atom allow its selective dehydrodimerization. Olefins with geminal and thus cross-conjugated *cd*-substituents are "radicophilic" and permit twofold carbon radical addition. *cd*-Substituted olefins are useful antioxidants, polymerization inhibitors and are promising agents in the control of biological radical reactions. Generally, many reactions of *cd*-substituted molecules appear to involve radicals.

1. Introduction

In 1879, Wurster's salts *(1)* were discovered[1] but their radical nature was recognized only about half a century later[2].



(1)

Wurster's salts: 1879

In 1929, the surprising stability of *(1)* as isolable salts with radical cation structure was contrasted with the unstable methyl and phenyl radicals when *Paneth* published his famous mirror experiments[3]. Thus, when tetramethyllead was decomposed thermally in a glass tube it produced ethane, and lead as a deposit. This lead mirror could be dissolved as tetramethyllead when exposed to a stream of methyl radicals generated by thermolysis from other organometallic compounds such as trimethylbismuth (Fig. 1).

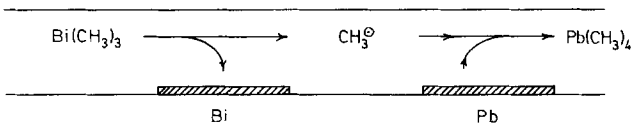


Fig. 1. *Paneth*'s methyl radicals dissolving lead mirrors: 1929.

With these historical events of organic and particularly of radical chemistry in mind, it now appears appropriate to report on a general principle in radical chemistry which partly explains the stability of Wurster's salts: the *capto-dative (cd) substituent effect*[4].

In the past, organic free radicals have been divided into two classes: 1) The long-lived radicals which are stabilized by resonance, and for which, as for Wurster's salts *(1)*, one can formulate several mesomeric forms with the lone electron in different positions. 2) The short-lived radicals like methyl or phenyl which do not enjoy such stabilization and for which only one mesomeric form is possible.

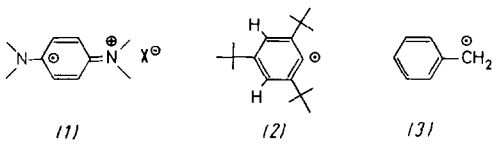
Later, the notion of stabilization was dissociated from that of persistence[5]. The persistence of a radical $R^{\odot}$ refers to its

[*] Prof. H. G. Viehe, Dipl.-Ing. R. Merényi, Dr. Z. Janousek
Université de Louvain, Laboratoire de Chimie Organique
Place Louis Pasteur 1, 1348 Louvain-la-Neuve (Belgium)
Dr. L. Stella
Laboratoire de Chimie Organique B, Université d'Aix-Marseille
Rue Henri Poincaré, F-13397 Marseille Cédex 4 (France)

[**] Capto-dative Substitution Effects, Part 5.—Part 4: [67].

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0917 $ 02.50/0*

lifetime under specified experimental conditions[5], while the stabilization has been defined[6] in terms of dissociation energies of the R—H bond. Thus, a persistent radical is not necessarily stabilized, *e.g.* the 2,4,6-tri-*tert*-butylphenyl radical *(2)*, while a stabilized radical can often be transient, such as the benzyl radical *(3)*.

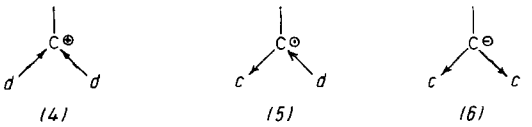


(1) *(2)* *(3)*

(1): Salt with persistent stabilized radical cation
(2): Persistent destabilized radical
(3): Short-lived (transient) stabilized radical

Another definition[7] of radical stabilization is based on equilibrium constants derived from polarographic redox potentials in reversible systems. Spin density delocalization also reflects the thermodynamic stabilization of radicals[8].

The capto-dative *(cd)* substituent effect[4] derives from a logical extension of the principles governing the stabilization of cations and anions: whereas carbocations *(4)* are stabilized by electron donor-substituents, and carbanions *(6)* by electron acceptor-groups, electroneutral radicals *(5)*—formally situated between *(4)* and *(6)*—enjoy particular stabilization when they are substituted simultaneously by a donor and an acceptor group.



(4) *(5)* *(6)*

c = electron acceptor group *("capto")*
d = electron donor group *("dative")*

The *cd*-substitution concept further leads to the notion of *radicophilicity* as a complement to nucleophilicity and electrophilicity. Moreover, this concept represents a practical tool for organic chemistry and biochemistry. Its application enables, *e.g.*, the design of new radical inhibitors, antioxidants and spin-traps. *cd*-Substituent effects can also be useful in polymer chemistry and organic synthesis and appear in many chemical processes where radical reactions are involved. In biochemistry, the *cd*-systems are omnipresent, since they occur, for example, in amino-acids, sugars, and vitamins C and E. In biology and medicine *cd*-substituent effects are linked to photosynthesis, the radioprotection of organisms and to enzymatic dehydrogenation. They appear to play an important role in controlling mutagens[9] and in the processes of ageing.

2. Radical Stabilization by Capto-dative *(cd)* Substitution

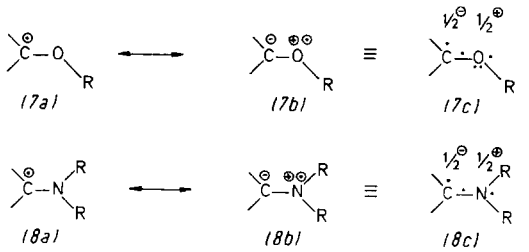
It is well known that free radicals are stabilized by both electron acceptor groups *(c)* and by electron donor groups *(d)*.

c = —CN, —CO—R, —COOR, —CR=$\overset{\oplus}{N}$R$_2$, —NO$_2$, *etc.*
d = —OR, —NR$_2$, —SR, —SeR, —O$^{\ominus}$, *etc.*

Kinetic studies indicate that substituents such as —CN stabilize an adjacent radical to a large extent[10]. Substituents with heteroatoms of the first Period such as —OR have a smaller stabilizing effect[11,12,13], those with heteroatoms of the second Period such as —SR display an intermediate effect[11,12].

Although the data for stabilization energies are derived principally from kinetic experiments, they reflect the substituent effects for the stability of the radical. Bond dissociation energies[14] reveal the same trend. The oxidation of ethers or amines gives an example of selective radical formation in the α-position to the heteroatom [see *(7)* and *(8)*].

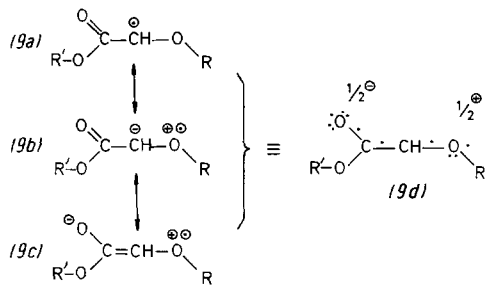
This selectivity can be explained by electronic assistance of the donor group which stabilizes adjacent radicals by resonance, but charge separation in the resonance forms *(7b)* and *(8b)* leads to an increase in energy because it is opposed to the relative electronegativies. The Linnett structures *(7c)* and *(8c)*[15] lead to the same conclusion: spin-delocalization imparts double quartet electron configuration to all atoms, but the polarization is unfavorable.



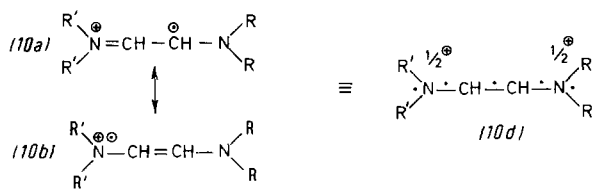
(7a) *(7b)* *(7c)*

(8a) *(8b)* *(8c)*

If these radicals are further substituted by an electron acceptor group, and hence are *cd*-substituted, then the resonance becomes greatly enhanced since the negative charge is delocalized over the electron-acceptor group. Hereby the radicals such as *(9)* and *(10)* with *cd*-substitution derived from alkoxyacetic esters or from 1,2-diaminoethylenes enjoy particular dipolar resonance stabilization and the "right" polarization.



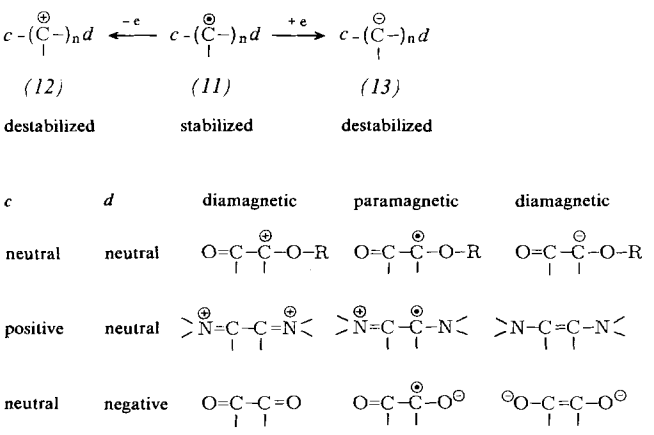
(9a) *(9b)* *(9c)* *(9d)*



(10a) *(10b)* *(10d)*

More generally, the substitution by neutral or charged acceptor *c* and donor *d* groups in *(11)* leads to *cd*-stabilization if *n* is an odd number. Conversely, the diamagnetic species *(12)* and *(13)* obtained from *(11)* by one-electron release or

uptake, respectively, are destabilized by the opposite polarization effect of the two substituents (Scheme 1).

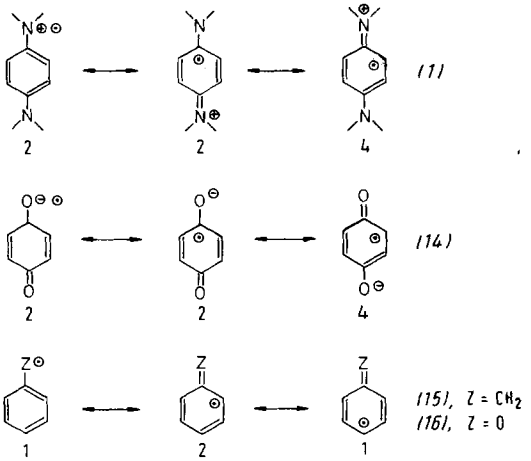


Scheme 1. Stabilization and destabilization by *cd*-substitution.

On the other hand, the species *(11)* in which n is an even number are stable diamagnetic compounds such as amides, esters, *etc.* The groups *c* and *d* act in a synergetic way. Only radicals *(11)*, $n=1$, are dealt with in this article.

Many examples of vinylogous radical ions, like Wurster's salts *(1)* and their oxa-analogues, the semiquinones *(14)*, can be found in a recent review[7].

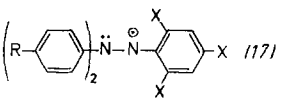
In radical ions of the type *(1)* and *(14)* the *cd*-effect is enhanced by delocalization in the π system of the aromatic ring. Such delocalization is more profound than that in benzyl *(15)* or phenoxyl *(16)* radicals where only alternate carbon atoms are involved. In *(1)* and *(14)*, however, the delocalization effectively takes place over all the six carbon atoms of the benzene ring and thus leads to much greater stabilization (Scheme 2).



Scheme 2. Stabilization of radicals and radical ions by delocalization. The number of resonance structures for different positions of the unpaired electron is given under the formulas.

3. Historical Development

After *Gomberg*'s discovery[16] of triphenylmethyl as the first stabilized free radical great efforts were made to determine the factors governing the stability of radicals. For triphenylhydrazyl radicals *(17)* *Goldschmidt* observed an increase in stabilization with increasing strength of the acceptor group X ($\sim c$)[17].



It should be noted that the stable diphenylpicrylhydrazyl radical (DPPH) *(17)*, R = H, X = NO_2, can be considered as a *cd*-substituted aminyl radical.

Walter tried to interpret the influence of different groups R on the properties of *(17)* and related radicals[18].—The radical nature of Wurster's salts *(1)* was already recognized by *Weitz* in 1925 (cf. [19]).

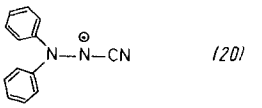
It appears that the first theoretical formulation of the stabilizing effect of a donor and an acceptor substituent, when applied to conjugated alternate odd numbered hydrocarbon radicals, was made by *Dewar* in 1952[20].

Linnett formulated the double quartet rule which explains the stability of radicals and radical ions such as nitrogen monoxide and the nitroxides, semiquinones and Wurster's salts[15].

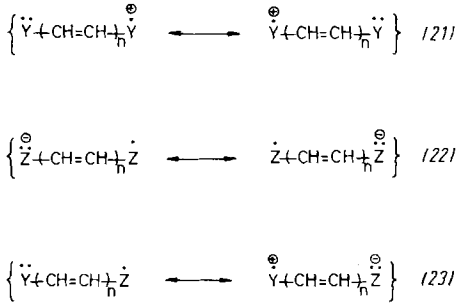
Based on the analogy between merocyanines *(19)* and radicals of the type *(18)*, *Katritzky* developed the principle of merostabilization[21].



Balaban introduced the term push-pull stabilization for nitrogen-centered radicals, like *(20)*[22].



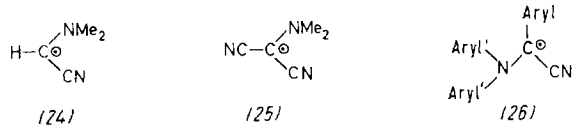
Hünig (cf. [7]) studied the one-electron redox systems which involve a semiquinone (SEM) between the reduced (RED) and oxidized (OX) form. The semiquinones *(21)*, *(22)* and *(23)* correspond to radicals which are stabilized by *c,d*-substitution.



The thermodynamic stabilization is expressed by the equilibrium constant K.

$$K=[\mathrm{SEM}]^2/[\mathrm{RED}][\mathrm{OX}]$$

De Vries[23] detected the radicals *(24)* and *(25)* and *Aurich*[24]

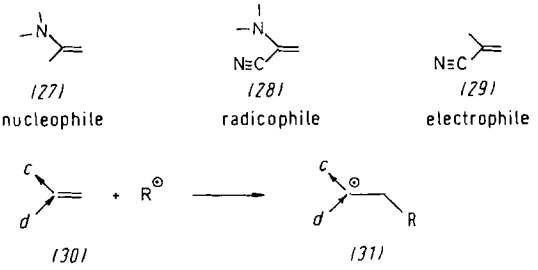


(24) (25) (26)

generated those of type *(26)*; both authors recognized the stabilizing effects discussed by *Katritzky* and *Balaban*.

4. Radicophilicity of Olefins as a Consequence of *cd*-Substitution

Since electron-rich olefins such as enamines *(27)* are nucleophilic and electron-poor ones like acrylonitrile *(29)* are electrophilic, the α-cyano-substituted enamines *(28)* and all *cd*-substituted olefins *(30)* can be considered as radicophilic [4]. The stabilized *cd*-substituted radicals *(31)* formed in the addition step do not undergo typical reactions such as polymerization or hydrogen abstraction but rather they trap another radical $R^{\ominus}$ or dimerize.



(27) nucleophile (28) radicophile (29) electrophile

(30) (31)

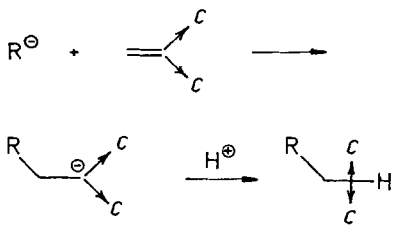
Although this definition of radicophilicity corresponds mainly to the thermodynamic stabilization of the radical adduct *(31)* by capto-dative substitution[4], it is not excluded that the kinetic aspects of addition, which depend primarily on steric and polar factors, may also be favorably influenced by *cd*-substitution[25] (cf. Section 12).

Because of cross conjugation of the *cd*-substituents, the π orbital of the double bond in *(30)* must have a marked degree of dissymetry. "One-electron conjugation" in the adduct *(31)* replaces the original cross conjugation in the *cd*-olefin *(30)*.

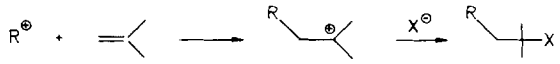
Moreover, radicophilic olefins, because of opposite substituent polarization, should trap any radicals regardless of their polarity.

This concept of radicophilicity is in many ways useful for syntheses. Most obvious is the possibility of twofold carbon radical addition to *cd*-substituted olefins. This is practically impossible for ionic reactions except for polymerization and cycloadditions.

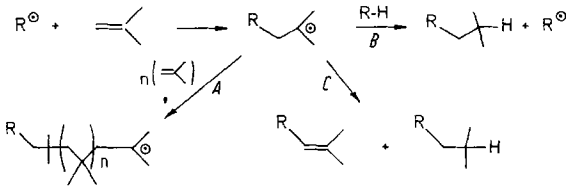
Nucleophilic addition of carbanions (and $H^{\oplus}$) to electrophilic double bonds leads only to C and H addition:



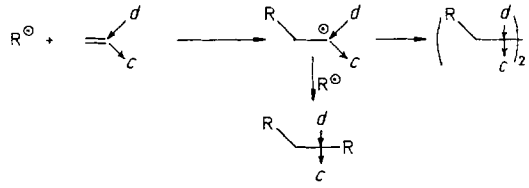
Similarly, electrophilic addition of carbenium ions (and $X^{\ominus}$) to olefins results in both C and X addition:



The adducts of radicals to simple olefins such as propene or isobutene are not sufficiently stabilized or are too polar to be able to couple with themselves or with other radicals. Usual reactions are polymerization (Route A), H-abstraction as chain reaction (Route B) as well as disproportionation and chain termination.



In contrast to simple olefins, a radicophilic olefin can undergo twofold radical addition; the usual chain reactions do not take place.



Variation of the nature of both the groups *c* and *d* should make it possible to establish a scale of radicophilicity of different *cd*-substituted olefins and even a scale of stabilizing effects on radicals. The experimental approach is equally attractive for the organic chemist because of its potential in syntheses.

5. *c,d*-Substituent Effects and Orbital Correlation

5.1. *cd*-Substituent Effects on Radicals

The effect of α-substituents on the stability of radicals has been rationalized in terms of one-electron molecular orbital theory[26]. Interaction of a radical with either an electron-acceptor group (c = –C≡N, –CO–R, –CO_2R *etc.*) or an electron donor group (d = –OR, –NR_2, –SR *etc.*) leads to stabilization (Fig. 2).

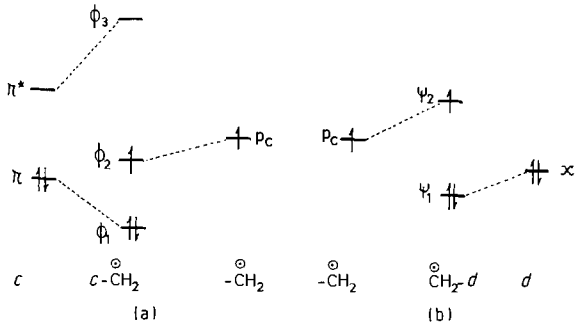


Fig. 2. Orbital interactions involved in the stabilization of a radical by a) an unsaturated group *c*, and b) by a group *d* with an heteroatom of the first or second period.

If we consider a radical $H\overset{\oplus}{C}cd$[27] whose substituents have opposite effects and can interact with the singly occupied atomic orbital p_C we can construct the correlation diagram for $H\overset{\oplus}{C}cd$ by the successive combination of $-\overset{\oplus}{C}H_2$ with *c* and *d*. Considering first the union with *c* (see Fig. 2) and next the union of $H_2\overset{\oplus}{C}c$ with *d* (Fig. 3), the interaction between the two filled orbitals Φ_1 and χ will be antibonding while that between the filled orbital χ and the singly occupied one of $H_2\overset{\oplus}{C}c$ (Φ_2) will be bonding.

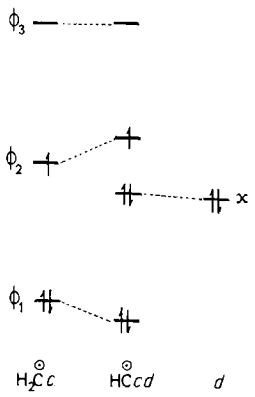


Fig. 3. Orbital interactions involved in the stabilization of a radical by an unsaturated group *c* and a group *d* with an heteroatom.

The net result will depend on the relative magnitudes of these two apparently conflicting effects. The magnitude of the interaction between χ and the two MOs Φ_1 and Φ_2 will then be determined by the orbital coefficients of the carbon atom adjacent to *d*. These in turn will depend on the extent of the coupling between the *c* orbitals π and π^* and the singly occupied atomic orbital p_C.

Comparing for example an allyl radical with a cyanomethyl radical (Fig. 4), it is well known[28] that for the latter there are two main consequences arising from the additional electron-acceptor effect of the nitrogen atom:

1) The energy levels of all the MOs in the cyanomethyl radical are lowered and so the C≡N triple bond affords a stabilization energy greater than that of a C=C double bond. In addition, the SOMO bearing the unpaired electron is lower in energy than in the allyl radical.

2) The orbital coefficients in the bonding MO Φ_1 increase strongly towards the nitrogen atom, and inversely decrease in the nonbonding MO Φ_2[29].

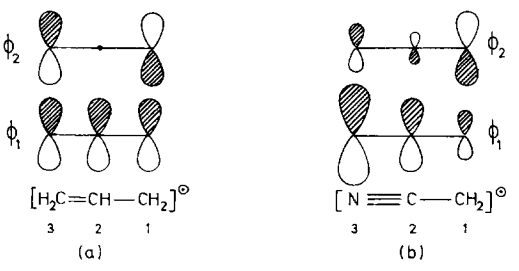


Fig. 4. Orbital coefficients in MOs Φ_1 and Φ_2 of a) the allyl radical and b) the cyanomethyl radical.

This implies that the unpaired electron will be strongly localized on carbon 1, where the orbital coefficient is high[30]. Under these conditions the net interaction resulting from the next union with the heteroatom in the donor substituent *d* will be more bonding because only the singly occupied MO will interact effectively with the orbital of the heteroatom. In addition, the singly occupied orbital Φ_2 of the cyanomethyl radical is lower in energy than $A\overset{\oplus}{O}p_C$ of methyl. Consequently in the construction of $NC{-}\overset{\oplus}{C}H{-}d$ the net stabilizing effect of *d* will be higher than it would be on methyl itself. Under these conditions one substituent augments the effect of the other.

As mentioned above, it should be emphasized that the first theoretical hint of such an effect was already given in 1952[20] (see Section 3).

5.2. *cd*-Substituent Effects in Olefins

The *cd*-substituent effect on frontier orbitals π and π^* of an olefin is now considered. In agreement with qualitative notions of substituent effects on orbital energies[31], electron donating substituents *d* raise both frontier orbital energies, but the HOMO more than the LUMO, and electron accepting substituents *c* lower both frontier orbital energies, in this case the LUMO more than the HOMO (Fig. 5).

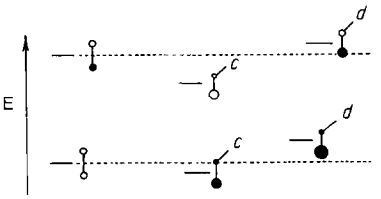


Fig. 5. Frontier orbital energies and coefficients for olefins with electron acceptor (*c*= C—N, CO R, *etc.*) and electron donor (*d*= OR, NR_2, *etc.*) substituents.

Thus geminal *cd*-substitution on olefins reduces the frontier orbital separation.

In general, radicals which have a low-energy SOMO show electrophilic properties and react more easily with nucleophilic olefins which have a high energy HOMO. On the other hand, radicals which have a high energy SOMO show nucleophilic properties and react more easily with electrophilic olefins which have a low energy LUMO[26].

Reducing the frontier orbital separation in *cd* olefins $cdC^1{=}C^2H_2$ makes them radicophilic by drawing the SOMO of the radical near to both the LUMO and the HOMO of the olefin. The relative magnitudes of the coefficients can also be deduced from qualitative considerations[31]. Electron donor groups increase the remote coefficient in the HOMO and the nearby coefficients in the LUMO. Electron acceptor groups have exactly the opposite effect from that of donor groups if they interact only inductively (*e.g.* $-CF_3$), but since most of the substituents of this type are also conjugating, the magnitude of the remote coefficients in the LUMO is strengthened, while the difference in the HOMO coefficient values is diminished or reversed. Consequently, the combined action of

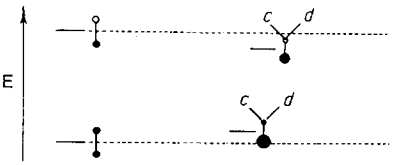


Fig. 6. Frontier orbital energies and coefficients for radicophilic olefins compared with those of ethylene.

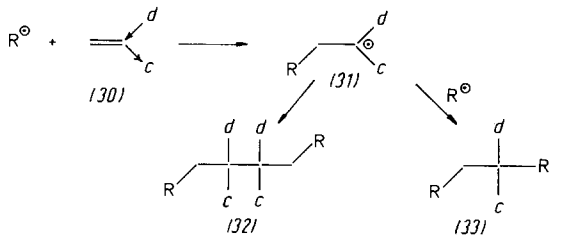
donor and acceptor groups on olefins must lead to an increase of the remote coefficient in both the LUMO and the HOMO (Fig. 6).

In this way it becomes evident that radical addition to the unsubstituted carbon of a *cd* olefin is thus favored by both polar and steric factors.

6. Syntheses by Radical Addition to Radicophilic Olefins

6.1. General Remarks

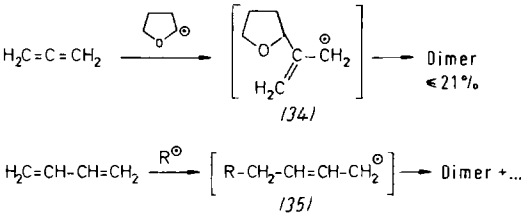
As already explained, geminal *cd*-substituted olefins *(30)* are excellent radical traps over a wide temperature range (see Section 4); the adducts *(32)* and *(33)* can be isolated in good yields. The *meso* and DL forms of the "adduct-dimer" *(32)* are obtained.



(30) *(31)* *(32)* *(33)*

Additive radical dimerizations from monoolefins other than those bearing *cd*-substituents are practically unknown. 1,1-Diphenylethylene behaves as a radicophile towards isobutyronitrile (IBN) radicals giving the bisadduct *(39)* (see Section 6.2).

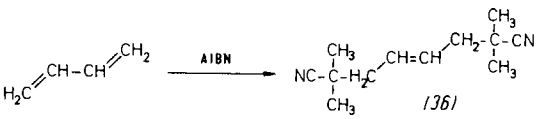
Allene[33] and 1,3-butadiene[34] may occasionally lead to adduct-dimers *via* the corresponding resonance stabilized allyl radicals *(34)* and *(35)*. Butadiene also forms oligomers.



(34) *(35)*

6.2. Addition of Isobutyronitrile (IBN) Radicals

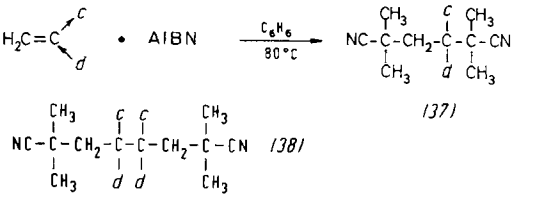
IBN radicals conveniently generated thermally or photochemically from azodiisobutyronitrile (AIBN) are used as initiators of polymerization and as very mild hydrogen abstractors *e.g.* from thiols[35] and trialkyltin hydrides[36]. Homolytic substitutions with IBN radicals are very uncommon[37] and so is their addition to multiple C—C bonds. Thus, 4-vinylcyclohexene reacts with IBN$^{\odot}$ to give a mixture containing addition, substitution and adduct-dimer products in low yield[38]. According to a patent[39] butadiene affords the bisadduct *(36)* in satisfactory yield.



(36)

On the other hand, the radicophilic olefins *(30)* react with AIBN at 80 °C in benzene to form either bisadducts *(37)* or adduct-dimers *(38)*[32], which can be isolated in moderate to very good yields (see Table 1).

Table 1. Formation of bisadducts *(37)* from radicophiles *(30)* and IBN$^{\odot}$.



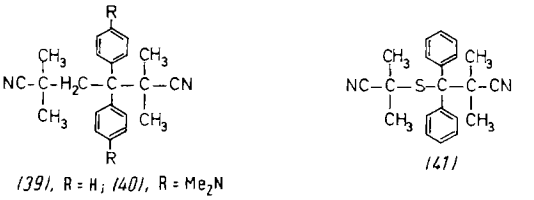
(37) *(38)*

c	*d*	*(37)* Yield [%]	*c*	*d*	*(37)* Yield [%]
CN	*t*BuS	88	CN	Morpholino	68
CO_2Me	*t*BuS	76	CN	Me_2N	38
CO_2Me	MeS	35	CO_2Me	Et_2N	37
CO_2Me	MeO	49	CN	Me_3SiO	33 [40] [a]
$CONMe_2$	Me_2N	40	CN	MeS	18 [b]

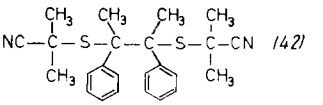
[a] See also *(49)*. [b] Alongside 51% *(38)*, for clarity shown as *meso*-form [cf. *(47a)*].

It should be noted that the bulky IBN$^{\odot}$ adds only to *cd*-olefins bearing a free methylene group.

1,1-Diphenyl- and 1,1-bis(*p*-dimethylaminophenyl)ethylenes behave also as good radicophiles giving 55% and 65% yields, respectively, of bisadducts *(39)* and *(40)*[32,41].



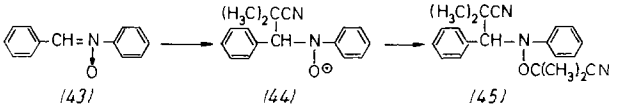
(39), R = H; *(40)*, R = Me_2N *(41)*



(42)

Radicophiles do not have to be olefins. The radicophiles thiobenzophenone and thioacetophenone react exclusively to give the bisadduct *(41)* and the adduct-dimer *(42)*, respectively[42].

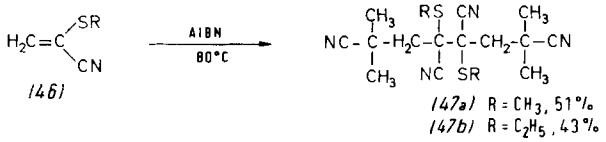
Nitrones *(43)*, the well known spin traps, are necessarily radicophilic and consequently they add to IBN$^{\odot}$ in stoichiometric amounts[43] leading to the bisadduct *(45)* *via* the nitroxide *(44)*. CIDNP signals could be observed during this addition[44].



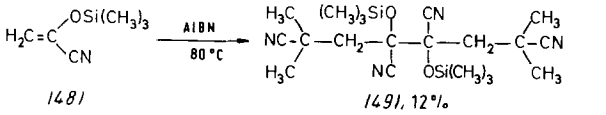
(43) *(44)* *(45)*

Galvinoxyl, which is known as a highly efficient radical scavenger, traps IBN$^{\odot}$ in 63% yield[45]. Radicophilic olefins of type *(46)* and *(48)* afford, besides the bisadduct, the ad-

duct-dimers *(47)* and *(49)* as a mixture of DL and *meso* forms[32,40].

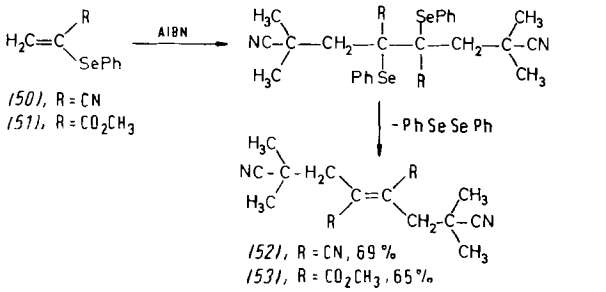


146 → *147a* R = CH_3, 51%; *147b* R = C_2H_5, 43%



148 → *149*, 12%

Yet another feature is encountered with α-(phenylseleno)acrylonitrile *(50)* and the ester *(51)*. The adduct-dimers spontaneously lose diphenyl diselenide to afford olefins *(52)* and *(53)*[32].

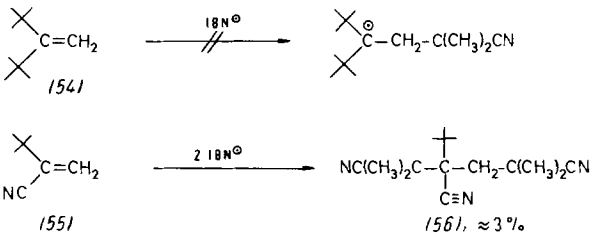


150, R = CN
151, R = CO_2CH_3

152, R = CN, 69%
153, R = CO_2CH_3, 65%

IBN$^{\odot}$ adds only to olefins bearing *cd*-substituents or aryl substituents. Accordingly, electron-rich olefins, namely enamines, vinyl ethers, ketene acetals (O,O-, N,S- and N,O-acetals) fail to react altogether under the above conditions. Electron-poor vinyl compounds, *e.g.* acrylonitrile, acryl esters and methylene malonates lead only to oligo- and polymerization[32]. The latter reaction, however, is prevented by the presence of radicophilic olefins, which demonstrates their usefulness as inhibitors of polymerization and of radical processes in general.

IBN$^{\odot}$ does not react with the olefin *(54)*, and reaction with α-*tert*-butylacrylonitrile *(55)* leads to only very low yields of the bisadduct *(56)*[32]. This indicates that it is the thermodynamic stability of the adduct rather than its persistency which is responsible for radicophilicity.



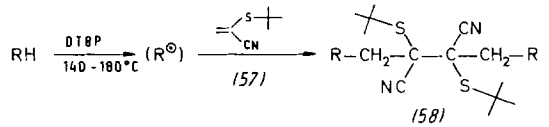
154

155 → *156*, ≈3%

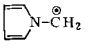
6.3. Addition of Other Radicals to Radicophilic Olefins

The little reactive and highly selective IBN$^{\odot}$ adds preparatively only to radicophilic olefins. These compounds could be anticipated to smoothly add both electrophilic and nucleophilic radicals. This has been borne out in practice, although most of the work was done with α-(*tert*-butylthio)acrylonitrile *(57)* and the radicals were generated thermally by oxidation with di-*tert*-butyl peroxide (DTBP)[46]. Unlike with IBN$^{\odot}$ these additions lead in the majority of cases to adduct-dimers *(58)* which are particularly attractive for synthetic organic chemistry as new valuable highly functionalized intermediates (see Table 2).

Table 2. Radical addition to α-(*tert*-butylthio)acrylonitrile *(57)* [46].

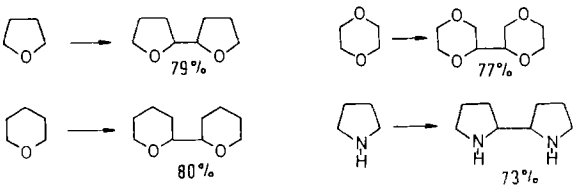


157 → *158*

RH	$R^{\odot}$	*(58)*, Yield [%]
N,N-Dimethylaniline	$PhNMe\overset{\odot}{C}H_2$	50
Trimethylamine	$Me_2N\ \overset{\odot}{C}H_2$	33
Triethylamine	$Et_2N\ \overset{\odot}{C}HMe$	30
N-Methylpyrrole		70
Hexamethylphosphoric triamide	$(Me_2N)_2PONMe\overset{\odot}{C}H_2$	60
p-Methyldimethylaniline	$Me\text{-}C_6H_4\text{-}NMe\ \overset{\odot}{C}H_2$	46
Dimethyl ether	$Me\ O\ \overset{\odot}{C}H_2$	51
Diethyl ether	$Et\ O\ \overset{\odot}{C}HMe$	55
Diisopropyl ether	$MeCHO\overset{\odot}{C}Me_2$	60
THF Tetrahydrofuran		59
Tetrahydropyran		41
1,4-Dioxane		52
[12]Crown-4	$[C_8H_{15}O_4]^{\odot}$	64 [a]
[15]Crown-5	$[C_{10}H_{19}O_5]^{\odot}$	48 [a]
[18]Crown-6	$[C_{12}H_{23}O_6]^{\odot}$	51 [a]

[a] Together with disproportionation products.

In the absence of a radicophile, radical dimers are obtained in very good yields[59], *e.g.*

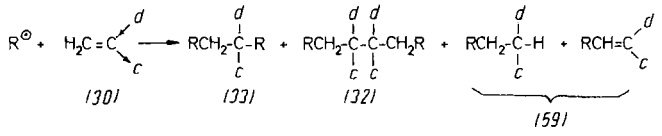


Pyrrolidine adducts of type *(58)* could not be obtained.

The behavior of the *N*-methylanilinomethyl radical towards a number of different radicophilic olefins has been studied in some detail[46]. The results show clearly the influence of substituents on the fate of the intermediate radical. Thus α-aminoacrylonitrile and diphenylethylene[47] adducts tend to undergo exclusively disproportionation. It is puzzling that replacement of the cyano group by an ester group in α-(alkylthio)acrylic derivatives leads to the formation of bisadducts with only a trace of adduct-dimers (Table 3).

Electrochemically generated methyl radicals from the Kolbe reaction could be trapped by α-(*tert*-butylthio)acrylonitrile *(57)* to give a low yield of the adduct-dimer *(60)*[48] which can also be obtained in better yield from the thermal decomposition of DTBP dissolved in *(57)*[49].—The main

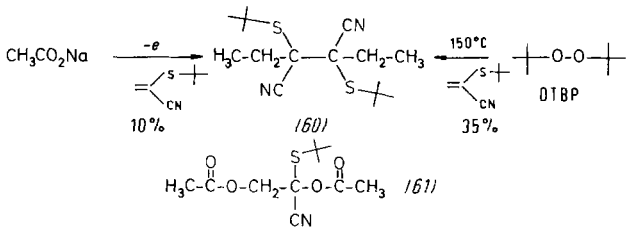
Table 3. Addition of *N*-methylanilinomethyl radicals to radicophilic olefins *(30)*. $R^{\odot} = PhNMe\overset{\odot}{C}H_2$.



(30) *(33)* *(32)* *(59)*

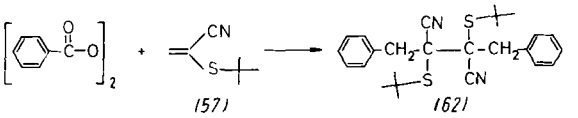
c	d	Yield [%] (33)	(32)	(59)
CN	*t*BuS	—	50	—
CN	EtS	—	45	—
CO_2Me	*t*BuS	30	traces	—
CN	Morpholino	—	—	45
CN	Me_2N	—	—	35
CO_2Me	MeO	12	18	—
Ph	Ph	—	—	50

product (60%) of the electrochemical reaction is the diacetate *(61)*[48].



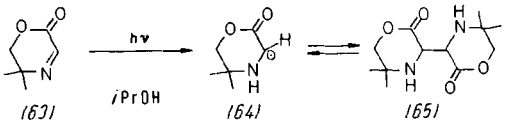
(60) *(61)*

The phenyl radical from the thermal decomposition of dibenzoyl peroxide could also be trapped with α-(*tert*-butylthio)acrylonitrile *(57)* to give the adduct-dimer *(62)*[50].



(57) *(62)*

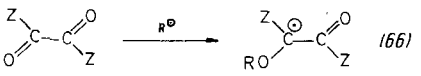
The terminal CH_2 group in radicophilic olefins can be replaced by heteroatoms *e.g.* O, S, and N(R). Thus, when 1,4-oxazin-2-one *(63)* is irradiated in isopropanol as solvent it undergoes reductive dimerization[51] to *(65)*, apparently *via* the *cd*-substituted radical *(64)*.



(63) *(64)* *(65)*

The dimer *(65)* exists in equilibrium with the radical *(64)*; the enthalpy of dissociation in ethanol (11 kcal/mol) is about the same as in the case of the triphenylmethyl dimer[52]. The central C—C bond in *(65)* is unusually long (1.591 Å)[53]. This lengthening and the extremely easy dissociation were attributed to steric strain only, which does not seem to be justified in this case.

The trapping of radicals by α-diketones and 1,2 and 1,4 quinones leads also to *cd*-substituted radicals *(66)*[54,55].



(66)

The 4-pyridine carbonitrile adducts *(67)* of silyl, germyl and stannyl radicals have recently been investigated[56].



(67)

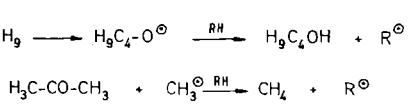
Pyridinyl radicals and their importance in biology have been extensively reviewed[57].

7. Dehydrodimerization of Compounds with *cd*-Substituted Methylene or Methine Groups

Numerous examples of dehydrodimerization, also known as "oxidative dimerization" or "oxidative coupling" reactions have been reported in the literature[58].

$$R' + R^{\odot}H \rightarrow R'H + R^{\odot} \qquad 2R^{\odot} \rightarrow R{-}R$$

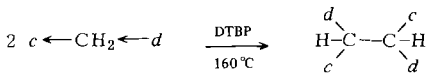
As expected, the hydrogen atom is abstracted mostly, but not necessarily, from a carbon in the α-position to a heteroatom, a cyano or an ester group. Di-*tert*-butyl peroxide (DTBP) has an advantage over other oxidizing species since it forms first very efficient, electrophilic *tert*-butoxy radicals which may further decompose to acetone and (nucleophilic) methyl radicals. The methyl radicals can abstract hydrogen atoms very well, even in the cases where *tert*-butoxy radicals fail, *e.g.* from malonic esters. It is possible to determine which path is operative by measuring the acetone/*tert*-butyl alcohol ratio.



In this review we are concerned only with substrates bearing *cd*-substituents on methylene or methine groups. The available evidence clearly shows that such sites are attacked preferentially and can therefore be considered as "proradical".

This principle is illustrated by the examples given in Table 4[59].

Table 4. Reactions of proradical methylene derivatives *(68)* with di-*tert*-butyl peroxide (DTBP).

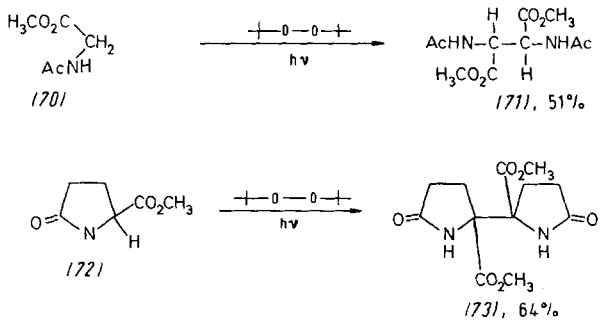


(68) *(69)*

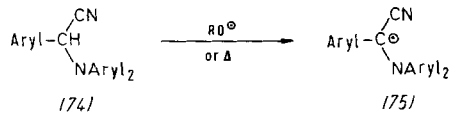
c	d	(69), Yield [%]
CO_2Me	MeO	91
CO_2Me	Me_2N	25
CO_2Me	$MeCO_2$	83
CN	MeO	51
CN	Me_2N	52
$CONMe_2$	Me_2N	31

Even in cases where the yields are low, owing to side reactions, only products arising from attack at the *cd*-substituted site could be isolated.

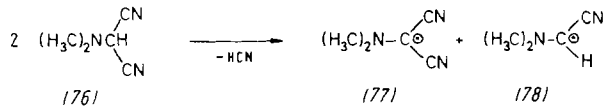
Photochemically generated *tert*-butoxy radicals effected the dimerization of methyl *N*-acetylglycinate *(70)* to *(71)* and of methyl pyroglutamate *(72)* to *(73)*, respectively[60].



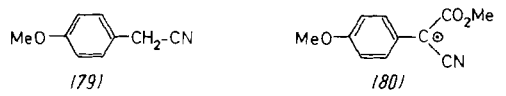
α-Aminobenzyl cyanides *(74)* undergo a very easy hydrogen abstraction with alkoxy and aminyl radicals in benzene; the persistent radicals *(75)* are formed[24] [cf. *(26)*].



Dimethylaminomalononitrile *(76)* decomposes at room temperature to give the persistent radical *(77)*, radical *(78)* and HCN. The abstracting species here is thought to be dimethylamino(cyano)carbene[23].



In another study[61], the relative rates of hydrogen abstraction from substituted phenylacetonitriles by the trichloromethyl radical were measured. This work revealed that *p*-methoxyphenylacetonitrile *(79)*, which can be regarded as *cd*-substituted phenylogous methoxyacetonitrile, reacts three times faster than phenylacetonitrile.



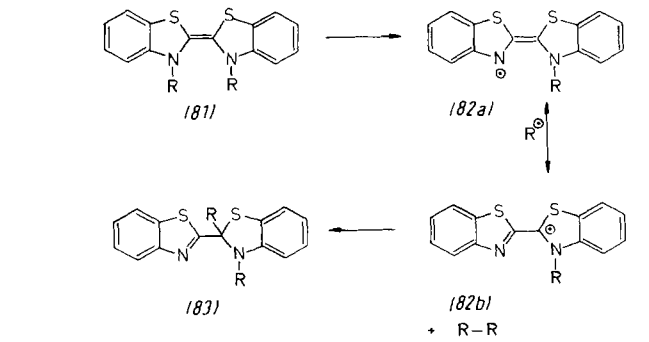
An ESR study disclosed an enhanced spin delocalization in *(80)* owing to the presence of a *p*-methoxy group[21].

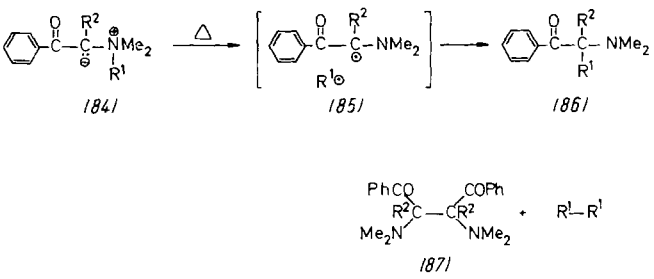
8. Rearrangements Involving *cd*-Substituted Radicals

An increasing number of rearrangements previously thought to be concerted or ionic are now recognized as being of a radical or diradical nature. These rearrangements may proceed with unexpected ease when the radicals involved possess the stabilization imparted by *cd*-substitution.

Thus, the benzothiazoles *(81)*, R = benzyl, are unstable and undergo a [1,3] benzyl shift to give the rearranged product *(83)*. A careful investigation[62] has revealed that the first step involves a dissociation to *(82)* and $R^{\odot}$ followed by recombination to *(83)*. The *cd*-substitution in *(82b)* is obvious.

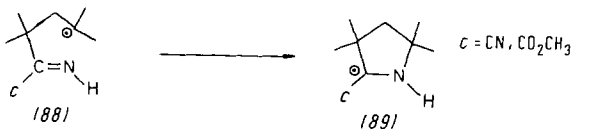
Considerable efforts have been made to establish the mechanism of the Stevens rearrangement and related [1,2] anionic rearrangements[63,64]. The conclusion that such processes proceed *via* radical pair pathways is based on CIDNP results. The isolation of escape products such as *(87)* formed from radical pair intermediates, strong dependence upon solvent viscosity and temperature effects support this mechanism.



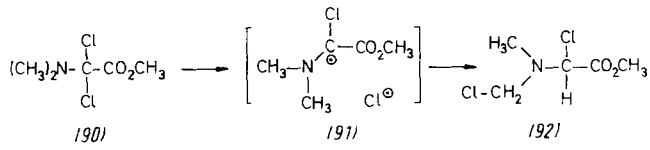


The high degree of stereoselectivity[64] in rearrangements of *(84)* when R^1 is a chiral group seemed at first to be inconsistent with a radical pair process but such stereoselective recombination of radical pairs is now widely accepted. It is a consequence of the limited translational movement required within the radical pair before they recombine to the [1,2] coupling product. More racemization occurs in the competitive [1,3] coupling mode.

An unusual ring-closure of radicals *(88)*, observed recently[65], leads to the more stable *cd*-substituted radicals *(89)*.



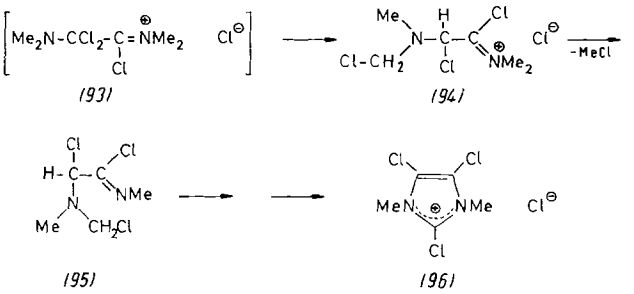
Chlorine attached to a carbon bearing *cd*-substituents as in *(90)* undergoes a peculiar [1,3] migration to the *N*-methyl group[66]:



This reaction might also conceivably proceed through a radical pair *(91)*.

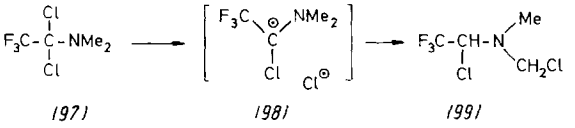
The intermediate *(93)*, which resembles *(90)* and is itself unstable even at low temperatures, apparently rearranges in the same fashion to give *(94)*, which then undergoes loss of

methyl chloride and finally forms the imidazolium chloride *(96) via (95)*[67].



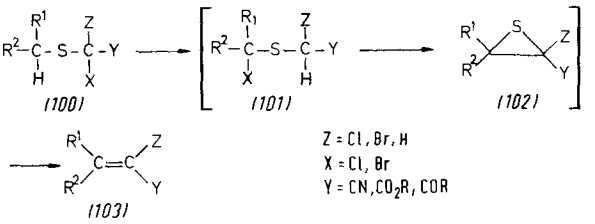
(93) *(94)* *(95)* *(96)*

The covalent amide chloride *(97)* can be isolated, but it rearranges to *(99)* when heated above 100 °C[68].



(97) *(98)* *(99)*

Even more elevated temperatures are necessary for α-haloalkyl sulfides *(100)* bearing various electron acceptor groups. During the flash-pyrolysis, secondary reactions become predominant with accompanying loss of HX and sulfur to give olefins *(103)*[69].



(100) *(101)* *(102)* *(103)*

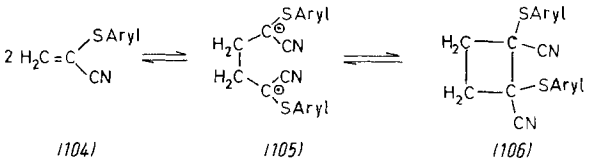
Z = Cl, Br, H
X = Cl, Br
Y = CN, CO_2R, COR

9. Cycloadditions

An understanding of the mechanism of cycloaddition reactions has been one of the most challenging problems in modern organic chemistry. Of particular interest is the question whether cycloadditions, retrocycloadditions and related rearrangements are fully concerted, involve a considerable degree of charge separation in the transition state or involve spin-paired diradicals[70]. Polar intermediates can be readily discounted if there is little change in the rate of reaction in different solvents or if the presence of either electron-donating or withdrawing groups leads to an increase in rate. It is much more difficult to distinguish between a concerted process and one in which a spin-paired diradical is formed. In many cases the solvent and substituent effects found, as well as negative values of $\Delta S^{\neq}$, are consistent with either process[71]. Recent studies[72] discuss the possibility of a "concerted-diradical" mechanism for 1,3 dipolar cycloadditions and it was suggested that a more appropriate term for "1,3-dipolar" compounds would be "zwitterionic diradical hybrid"[72].

No matter how important diradical intermediates may be, it is obvious that cycloadditions (or their reversal) would be more likely to develop radical pairs if the compounds carried *cd*-substituents.

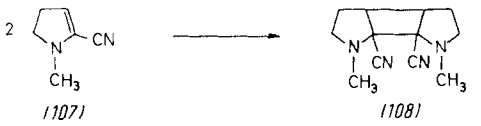
One pertinent example[73] is the spontaneous and reversible dimerization of α-(arylthio)acrylonitriles *(104)* to cyclobutane derivatives *(106)*.



(104) *(105)* *(106)*

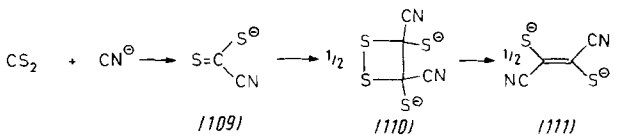
The analogous dimerization of acrylonitrile also involves a radical process because it leads to a head-to-head-dimer[74], but it proceeds at much higher temperatures and the yields are low.

A further example is the dimerization of the α-cyano-substituted enamine *(107)*[75].



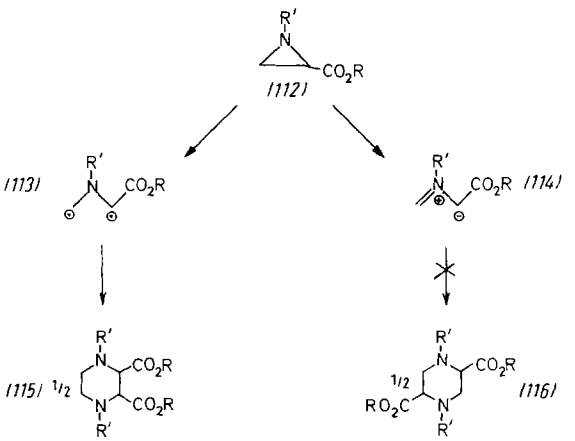
(107) *(108)*

Cyanodithioformate salts *(109)* readily dimerize to fumaronitriles *(111)*[76]. This reaction might also be envisaged as proceeding *via* a 1,4-diradical to give a dithietane *(110)* followed by loss of sulfur.



(109) *(110)* *(111)*

Yet another interesting example[77] is the thermal dimerization of the aziridine ester *(112)* leading to a "head-to-head" adduct *(115)*. The dipolar intermediate *(114)* should lead to the other geometric isomer *(116)* but the observed regiospecific formation of *(115)* is consistent with assumption of the existence of diradical *(113)*.



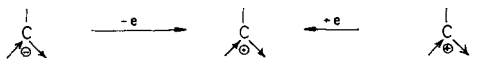
(112) *(113)* *(114)* *(115)* *(116)*

10. Radical Formation by One Electron Transfer Processes Involving *cd*-Substituted Anions and Cations

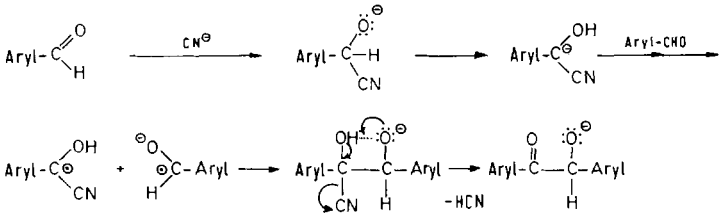
Contrary to radicals, anions are destabilized by *cd*-substitution when the donor groups are amino or alkoxy groups;

cations are destabilized by poor donors such as alkylthio groups in the presence of electron-acceptor groups.

Consequently these very reactive ions should be prone to one-electron transfer reactions:

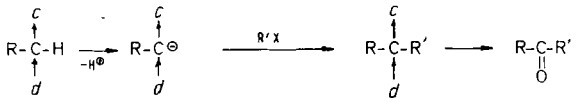


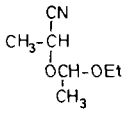
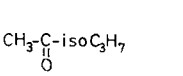
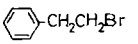
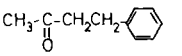
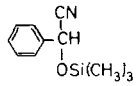
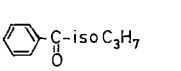
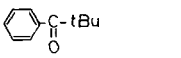
This scheme should enable many classical reactions and certain mechanistic puzzles to be more readily understood. The well known benzoin condensation[78], for example, and its recent extension to vinylogous benzoins[79] are known to pass through *cd*-substituted anions. The high reactivity of these carbanions might be suggestive of one-electron transfer followed by radical coupling.



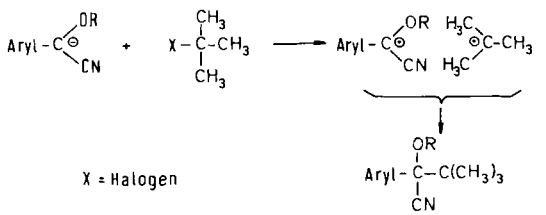
This interpretation is supported by the high nucleophilicity of α-cyano-α-alkoxy substituted anions, even towards tertiary halides[80] (Table 5).

Table 5. Formation of ketones *via cd*-substituted anions.



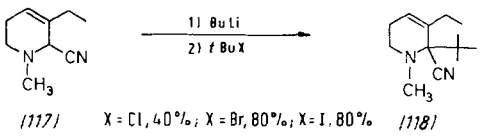
Substrate	Electrophile	Product	Yield [%]	Ref.
	iso C_3H_7-I		80	[81]
			84	[81]
	iso C_3H_7-I		95	[82]
	t Bu-I		85	[82]

One-electron transfer followed by radical coupling could explain this puzzling but highly useful ditertiary carbon-carbon bond formation.



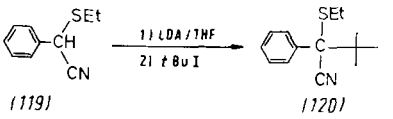
It should be kept in mind that these reactions do not always proceed through radical pairs and there is compelling evidence that strongly polar transition states may develop in some cases[83].

Anions derived from α-aminonitriles[84] or α-aminoesters[85] have also been used successfully as synthetic equivalents to nucleophilic acyl anions, even in cases where dithiane anions[86] do not work[87]. The classical S_N2 mechanism does not suffice to explain some recent results, as for example in the reaction of *(117)*[88].



(117) X = Cl, 40%; X = Br, 80%; X = I, 80% *(118)*

α-Alkylthionitrile anions *(119)*, which have already been used in substitution reactions with alkyl halides[89,90], can also be alkylated in high yield with *tert*-butyl iodide[91] (LDA = lithium diisopropylamide).



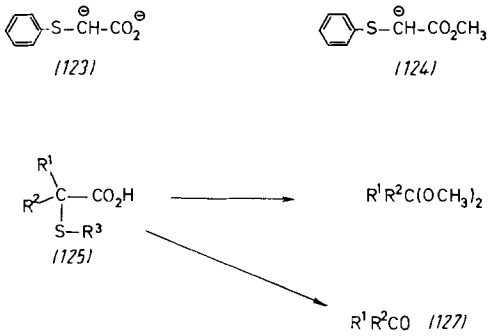
(119) *(120)*

Ethyl 2-lithio-1,3-dithiane-2-carboxylate *(121)*, *Schlessinger's* reagent[92], reacts stereoselectively *via* 1,4-addition with α,β-unsaturated ketones, whereas 2-lithio-1,3-dithiane requires the presence of a copper salt[93]. The alkylation of *(122)* has been described as being very easy and yields are very high even with isopropyl iodide (91%)[94].

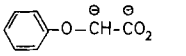


(121) *(122)*

The dianions *(123)* of (phenylthio)acetic acid and the monoanion *(124)* have been reported to react very smoothly with alkyl halides and carbonyl compounds[95]. The resulting α-(alkylthio)carboxylic acids *(125)* can be transformed into ketals *(126)* using the procedure of *Trost*[96], which involves an oxidative decarboxylation. An alternative method involves electrolysis under very mild conditions; the ketones *(127)* corresponding to *(126)* are obtained[97].



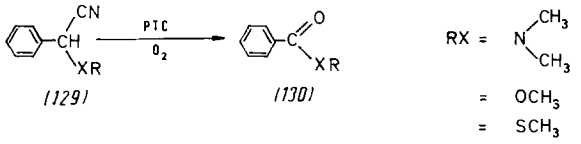
The dianion of phenoxyacetic acid *(128)* also reacts with remarkable ease with alkyl halides and ketones[98].



Furthermore, besides substitution reactions which proceed *via* radical anion intermediates[99], there are only a few well-authenticated examples of S_N2 displacements at a tertiary carbon atom[100].

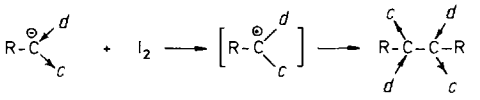
Since the tendency towards reduction of alkyl halides[101] decreases in the order C—I > C—Br > C—Cl, electron transfer reactions from *cd*-anions to alkyl halides must follow the same trend.

The high probability of one-electron-transfer from *cd*-anions is also supported by their great ease of oxidation. Thus α-(dimethylamino)-, α-methoxy- and α-(methylthio)benzyl cyanides *(129)* mostly lead quantitatively *via* phase transfer catalysis (PTC) to the amides, esters and thioesters *(130)*, respectively, under conditions which do not affect phenylacetonitrile[102].



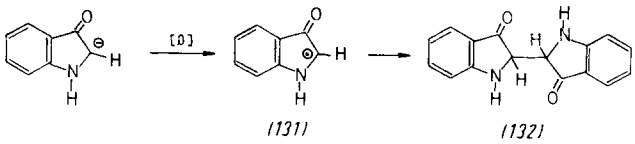
The well known dimerization of carbanions by iodine proceeds either through radicals formed *via* one-electron-transfer or through iodides which couple with the carbanion present in an S_N reaction[103]. The latter path is less probable in the case of *cd*-substituted carbanions and one-electron-transfer is a more realistic alternative (see Table 6).

Table 6. Dimerization of carbanions with iodine.

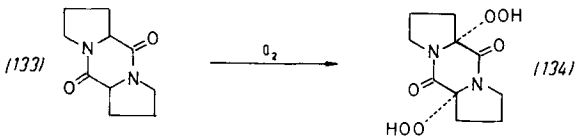


c	*d*	R	Yield [%]	Ref.
CO_2Et	Piperidino	H	71	[46]
Piperidinocarbonyl	Piperidino	H	80	[46]
CO_2Et	EtS	H	55	[46]
$CONMe_2$	Me_2N	H	60	[46]
$PO(OEt)_2$	Me_2N	H	65	[46]
CO_2Et	Me_2N	H	80	[91]
CN	EtS	Me	20	[91]
CO_2Et	Morpholino	CO_2Et	40	[91]
SMe	MeS	SMe	41	[104]
SEt	EtS	SEt	86	[104]
S*i*Pr	*i*PrS	S*i*Pr	50	[104]

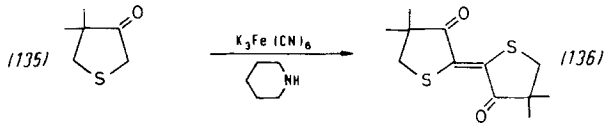
The conversion of indoxyl into indigo by the action of oxygen in basic solution proceeds *via* indoxyl radicals *(131)* followed by coupling to give leucoindigo *(132)*[105].



The oxidation of the piperazinedione *(133)* to *(134)* takes place with exceptional ease at the *cd*-substituted methine position[106].

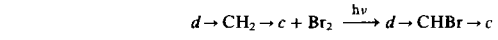


The dihydrothiophen-3(2H)-ones *(135)* can be oxidized directly to thioindigo-like compounds *(136)*[107].



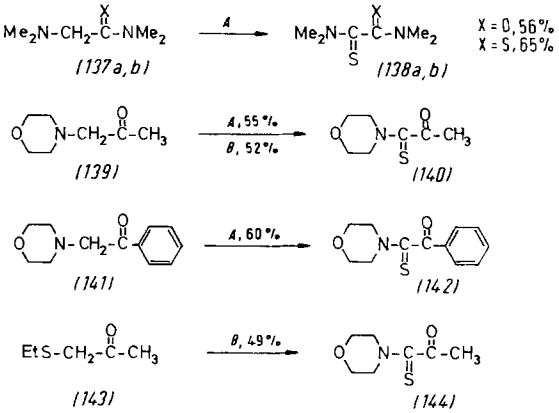
Other oxidizing agents like halogens and sulfur are also very good reaction partners for *cd*-substituted methylene compounds. Photochemical bromination proceeds very smoothly and yields are very good[91], except when *d* is an amino group (see Table 7).

Table 7. Photochemical bromination of *cd*-substituted methylene compounds.



c	*d*	Yield [%]
CO_2Me	MeO	91
CN	MeO	87
CN	MeS	94
CO_2Et	EtS	95
COMe	EtS	92

A number of *cd*-substituted methylene groups have been sulfurated using sulfur in DMF at 150 °C (conditions *A*) or at

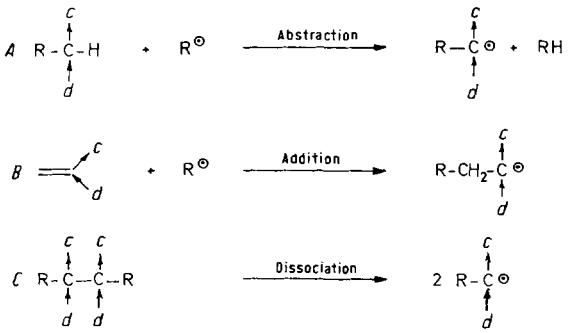


Scheme 3. Reaction of *cd*-substituted methylene compounds with sulfur. *A*, *B* see text.

room temperature with sulfur, DMF and morpholine (Route *B*). The results are summarized in Scheme 3[108].

11. *cd*-Substituted Radicals in ESR Spectroscopy

Three routes have been used for the generation of *cd*-substituted radicals in an ESR cavity:



Thus formed, many *cd*-substituted radicals can be detected by ESR at unusually high temperatures. If $d = NR_2$ or SR, the signal disappears on cooling and reappears reversibly upon heating. ESR data of radicals generated by method *B* are presented in Table 8.

Table 8. ESR data of *cd*-substituted radicals *(145)* in chlorobenzene at 130 °C [4, 109].



	c	*d*	a_N CN	a_N NR_2	β	a_H γ	δ
(145a)	CO_2CH_3	OCH_3	—	—	9.82	2.65	1.19
(145b)	CN	Morpholino	2.94	7.9	10.12	7.12	—
(145c)	CN	$N(CH_3)_2$	3.0	8.0	7.4	6.2	—
(145d)	CN	SCH_3	2.75	—	9.14	3.68	—
(145e)	CO_2CH_3	SCH_3	—	—	7.9	4.1	0.9

If we compare the hyperfine coupling constants on nitrogen atoms of the amino group and of the cyano group in radicals *(145)* with those observed for α-cyano or α-amino radicals (Table 9), it is clear that:

a) Introduction of a donor (morpholino) group on the radical already substituted by a cyano group [*(146)*→*(145b)*], decreases the spin density on the cyano nitrogen atom.

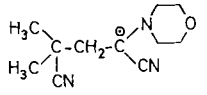
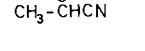
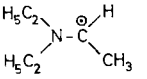
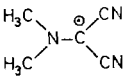
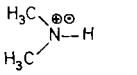
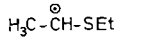
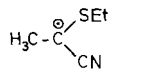
b) Introduction of an acceptor (cyano) group on the radical already substituted by an amino group [*(147)*→*(145b)*] increases the spin density on the amino nitrogen.

c) Introduction of a second cyano group [*(145b)*→*(148)*] on the *cd*-radical again increases the spin density on the amino group nitrogen atom.

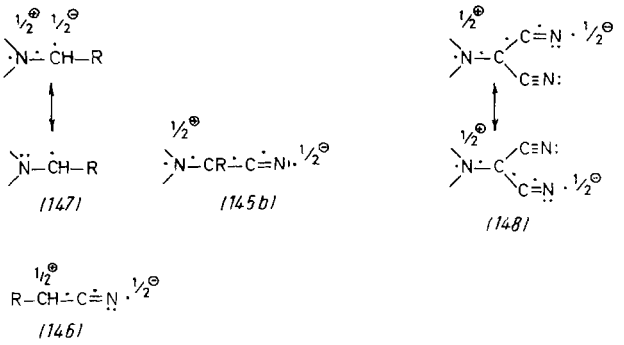
The same trend is observed for *cd*-systems with an alkylthio substituent as donor group (Table 9).

Linnett structures are in agreement with these facts: the stabilization by electron sharing gives an unfavorable polarization in the radical *(147)* and a favorable one in *(146)*. Thus, considering the *cd*-substituted radical *(145b)*, the gain in spin delocalization is more important relative to *(147)* than to *(146)*.

Table 9. ESR data of radicals with α-cyano-, α-amino and α-alkylthio substituents.

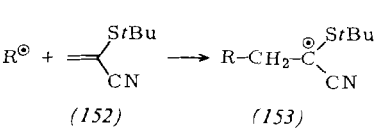
	$R^{\odot}$	a_N^{CN}	$a_N^{NR_2}$	$a_H^{SCH_2}$	Ref.
(145b)		2.94	7.9		[4, 109]
(146)		3.41			[110]
(147)		—	5.2		[111]
(148)		1.99	10.25		[23]
(149)		—	19.28		[112]
(150)				1.6	[113]
(151)		2.6		2.0	[114]

The double-quartet of electrons is realized for each atom in *(145b)*, and the molecule is polarized in the favorable direction. This occurs even more so in radical *(148)*.



According to their radicophilic nature, *cd*-substituted olefins can trap radicals more or less independent of their polarization. Thus, for all of the various types of radicals listed in Table 10, α-(alkylthio)acrylonitriles act as very powerful scavengers[114].

Table 10. ESR data of radical-adducts in chlorobenzene at 130 °C [114].



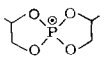
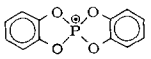
	$R^{\odot}$	$a_\beta^{CH_2}$	a_N^{CN}
(153a)	$(nBu)_3\overset{\oplus}{Sn}$	8.5	2.5
(153b)	$(CH_3)_2\overset{\oplus}{C}$ OH	8.5	2.6
(153c)	$CH_3S^{\odot}$	8.3	2.5
(153d)	$(CH_3)_2\overset{\oplus}{C}$ CN	8.3	2.5
(153e)	$Cl_3C^{\odot}$	7.5	2.5

The use of α-(*tert*-butylthio)acrylonitrile *(152)* in spin trapping studies of transient radicals, where the unpaired electron is located on a non-zero spin nucleus such as phosphorus[114], is complementary to the trapping with nitroso compounds and nitrones in that ^{31}P-couplings can be studied up to 170 °C (Table 11).

Table 11. ESR data of adducts *(154)* from substituted phosphorus radicals and α-(*tert*-butylthio)acrylonitrile *(152)* [114].



(152) *(154)*

	$L_nP^{\odot}$	a_P	a_{H^1}	a_{H^2}	a_N
(154a)	$Et_2\overset{\odot}{P}O$	39.0	10.0	10.0	2.6
(154b)	$Ph_2\overset{\odot}{P}O$	41.0	10.0	9.2	2.6
(154c)	$EtO(Ph)\overset{\odot}{P}O$	46.8	9.7	9.5	2.6
(154d)	$(EtO)_2\overset{\odot}{P}O$	51.5	10.0	10.0	2.6
(154e)	$(Me_3SiO)_2\overset{\odot}{P}O$	57.2	9.2	9.2	2.6
(154f)		63.0	10.0	9.5	2.6
(154g)		75.0	8.7	8.7	2.6

Another aspect of ESR studies of *cd*-substituted radicals concerns the effect of substituents upon the structure[115].

Both the cyano and the alkylthio groups have been shown to induce a planar configuration at a radical center[116,117]. Accordingly, a radical substituted by both these groups should be planar, since electron delocalization gives the C—CN and C—SR bonds some double bond character. This conclusion is supported by the experimental value of $a_{^{13}C}$ for radical *(153d)* and its temperature dependence:

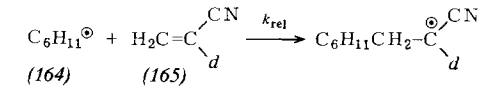
$a_{^{13}C} = [(25.76 \pm 0.02) + (8.0 \pm 0.8) \times 10^{-3} t]$ Gauss ($t = °C$)[114].

The decrease in the spin density at the radical center is a qualitative indication of the radical stabilizing effect of the substituents. The α-CH_3 coupling constants of the radical $CH_3-\overset{\odot}{C}H-X$ are proportional to the spin density on the central carbon atom (*Fischer*'s approach[118]). However, to compare spin densities in a quantitative way, planar configurations of the radical centers are required. This is certainly the case for *cd*-substituted radicals; thus, the decrease in spin density on the radical center, caused by the combined action of an acceptor and a donor substituent, can be deduced from the ESR parameters (Table 12).

The negative difference between the observed and calculated ρ values, for the planar radical *(151)* seems to reflect a certain trend in the mutual interaction of the acceptor and donor groups. This qualitative approach is in good agreement with an enhanced radical stabilization by the *cd*-effect. In contrast, $(\rho_{obs.} - \rho_{calc.})$ is positive for the bis(thioethyl)-substituted radical *(163)*. As far as the known *cd*-substituted ethyl radicals *(159)* to *(162)* are concerned, this difference is negative. Nevertheless, the latter values should be regarded with caution since a planar configuration of these radicals has not been proven.

12. Rates of Addition of Radicals to *cd*-Substituted Alkenes

Alkyl radicals behave like nucleophiles in addition reactions with alkenes. This polar effect has been confirmed by positive ρ^+-values in reactions with styrene derivatives[123]. On insertion of electron-donor groups *d* into electron-deficient alkenes with acceptor groups *c* the rate of reaction depends on the opposing influences of the *d*-substituents on the radical stability and the polar effect. In fact, *Giese et al.*[25,124] found that the strong electron-donor *d* = morpholino hardly changes the reaction rate in additions of cyclohexyl radicals *(164)* to acrylonitriles *(165)*, although unsubstituted enamines react very slowly with alkyl radicals. Thio and seleno groups increase the rate of addition (cf. Table 13).



(164) *(165)*

Table 12. p-Orbital spin density at the center of the radical $R^{\odot}$.

	$R^{\odot}$	$a_{\beta}^{CH_3}$ [Gauss]	$\rho_{obs.}$ [a]	$\rho_{calc.}$ [b]	$(\rho_{obs.} - \rho_{calc.})$	Ref.
(155)	$H_3C\ \overset{\odot}{C}H\ OH$	22.61	0.772			[119]
(156)	$H_3C\ \overset{\odot}{C}H\ NH_2$	20.2	0.689			[116]
(150)	$H_3C\ \overset{\odot}{C}H\ SEt$	19.8	0.675			[113]
(146)	$H_3C\ \overset{\odot}{C}H\ CN$	23.05	0.787			[110]
(157)	$H_3C\ \overset{\odot}{C}H\ COOH$	24.98	0.853			[118]
(158)	$H_3C\ \overset{\odot}{C}H\ COCH_3$	22.5	0.768			[122]
(159)	$H_3C\ \overset{\odot}{C}(OH)\ CN$	17.88	0.610	0.658	−0.048	[110]
(160)	$H_3C\ \overset{\odot}{C}(OH)\ COOH$	17.1	0.584	0.716	−0.132	[120]
(161)	$H_3C\ \overset{\odot}{C}(NH_2)\ COO$	13.92	0.475	0.640	−0.165	[121]
(162)	$H_3\overset{\odot}{C}\ \overset{\odot}{C}(OH)\ COCH$	13.33	0.455	0.591	−0.136	[125]
(151)	$H_3C\ \overset{\odot}{C}(SEt)\ CN$	15.0	0.512	0.577	−0.065	[114]
(163)	$H_3C\ \overset{\odot}{C}(SEt)_2$	17.6	0.601	0.497	+0.104	[109]

[a] $\rho_{obs.} = a_{CH_3}/29.3$. [b] Calculated according to *Fischers* equation $\rho_{calc.} = \Delta\rho_{CH_3} \times \Delta\rho_c \times \Delta\rho_d$. $\Delta\rho_{CH_3} = 0.919$; $\Delta\rho_c$ and $\Delta\rho_d$ were derived from $\rho_{obs.}$ of the monosubstituted ethyl radicals.

Table 13. Relative reaction rates of the addition of cyclohexyl radicals *(164)* to *d*-substituted acrylonitriles *(165)* in CH_2Cl_2 at 293 K.

d	k_{rel} [a]
CH_3	0.56
H	≡1.00
Cl	8.5
CO_2CH_3	86
Morpholino	0.83
$SC(CH_3)_3$	5.0
SeC_6H_5	9.5
C_6H_5	18

[a] Mean error ±5%; for determination cf. [123].

13. Outlook

The *cd*-substituent effect represents a challenge for theoretical chemistry, in particular for quantitative molecular orbital considerations and for *ab-initio* calculations. Spectroscopic studies are necessary to determine the structures and configurations of *cd*-substituted radicals and to measure their life-times and monomer-dimer equilibrium constants.

The concept of *cd*-substitution sets new goals and reveals new possibilities for organic synthesis especially in the fields of cycloadditions, nucleophilic and electrophilic substitutions, and selective reductive or oxidative transformations *via* radicals.

These applications reach far beyond the field of chemistry into everyday life, for example in the design of new inhibitors of polymerization and oxidation. In medicine and generally in biology, there appears a possibility of controlling the ageing of cells. The anticipated control of mutagenicity based upon the concept of radicophilicity has been proven in the Ames Test.

Radicals, afterall, pervade the whole of life: in photosynthesis, growth and ageing. Hence, the synthesis of radicals and control of radical processes represents an exciting research problem both for the present and for the future.

For helpful discussions we thank our colleagues: A. T. Balaban, Sir D. H. R. Barton, J. I. G. Cadogan, R. A. Firestone, B. Giese, R. Huisgen, S. Hünig, K. U. Ingold, A. R. Katritzky, G. Leroy, H. Naarmann, Nguyen-Trong-Anh, Ch. Rüchardt, G. Smets, J. M. Surzur, Lord J. M. Tedder, P. Tordo and J. C. Walton. For their particular assistance we thank our coworkers: T. G. C. Bird, F. Hervens-Gorissen, B. Le Clef, M. Demolder-Marin and L. Vertommen. We gratefully acknowledge generous support from the Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture (IRSIA), BASF A.G. Ludwigshafen, and the Fonds de la Recherche Fondamentale et Collective.

Received: October 17, 1979 [A 298 IE]
German version: Angew. Chem. *91*, 982 (1979)

[1] *C. Wurster, R. Sendtner,* Ber. Dtsch. Chem. Ges. *12*, 1803 (1879).
[2] *E. Weitz, K. Fischer,* Angew. Chem. *38*, 1110 (1925).
[3] *F. Paneth, W. Hofeditz,* Ber. Dtsch. Chem. Ges. *62*, 1335 (1929).
[4] *L. Stella, Z. Janousek, R. Merényi, H. G. Viehe,* Angew. Chem. *90*, 741 (1978); Angew. Chem. Int. Ed. Engl. *17*, 691 (1978).
[5] *D. Griller, K. U. Ingold,* Acc. Chem. Res. *9*, 13 (1976).
[6] *H. E. O'Neal, S. W. Benson* in *J. K. Kochi:* Free Radicals. Wiley, New York 1973.
[7] *K. Deuchert, S. Hünig,* Angew. Chem. *90*, 927 (1978); Angew. Chem. Int. Ed. Engl. *17*, 875 (1978).
[8] *Ch. Rüchardt,* Angew. Chem. *82*, 845 (1970); Angew. Chem. Int. Ed. Engl. *9*, 830 (1970).
[9] *M. Roberfroid, C. de Meester, F. Poncelet, M. Mercier, Z. Janousek, R. Merényi, L. Stella, H. G. Viehe:* "Radicals stabilised by *cd*-substitution act act as antimutagenic agents". 4th International Symposium on Microsomes and Drug Oxidations. University of Michigan, Ann Arbor, Michigan, July 15, 1979.
[10] *J. C. Roy, R. R. Williams, J. R. Nach, W. A. Harnill,* J. Am. Chem. Soc. *78*, 519 (1956).
[11] *J. W. Timberlake, A. W. Garner, M. L. Hodges,* Tetrahedron Lett. *1973*, 309.
[12] *A. Ohno, Y. Ohnishi,* Tetrahedron Lett. *1969*, 4405.
[13] *J. W. Timberlake, M. L. Hodges,* Tetrahedron Lett. *1970*, 4147.
[14] *J. A. Kerr,* Chem. Rev. *66*, 465 (1966).
[15] *J. W. Linnett,* J. Am. Chem. Soc. *83*, 2643 (1961); *R. A. Firestone,* J. Org. Chem. *34*, 2621 (1969).
[16] *M. Gomberg,* J. Am. Chem. Soc. *22*, 757 (1900); cf. *J. M. McBride,* Tetrahedron *30*, 2009 (1974).
[17] *S. Goldschmidt,* Ber. Dtsch. Chem. Ges. *53*, 44 (1920); Justus Liebigs Ann. Chem. *473*, 137 (1929).
[18] *R. I. Walter,* J. Am. Chem. Soc. *88*, 1923 (1966).
[19] *E. Weitz,* Angew. Chem. *66*, 658 (1954).
[20] *M. J. S. Dewar,* J. Am. Chem. Soc. *74*, 3353 (1952).
[21] *R. W. Baldock, P. Hudson, A. R. Katritzky, F. Soti,* J. Chem. Soc. Perkin Trans. I, *1974*, 1422.
[22] *A. T. Balaban,* Rev. Roum. Chim. *16*, 725 (1971).
[23] *L. de Vries,* J. Am. Chem. Soc. *99*, 1982 (1977); *100*, 926 (1978).
[24] *H. G. Aurich, E. Deutschle, W. Weiss,* J. Chem. Res. (S) *1977*, 301; (M) *1977*, 3457.
[25] *B. Giese,* Lecture, ESOC I, Köln, August 20—23, 1979.
[26] *F. Bernardi, N. D. Epiotis, W. Cherry, H. B. Schlegel, M. H. Whangbo, S. Wolfe,* J. Am. Chem. Soc. *98*, 469 (1976); *I. Fleming:* Frontier Orbitals and Organic Chemical Reactions. Wiley, New York 1975, Chap. 5.
[27] *F. Lahousse, M. Bertrand, L. Stella,* unpublished work.
[28] *A. Streitwieser, Jr.:* Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961, Chap. 2.
[29] *C. A. Coulson, H. C. Longuet-Higgins,* Proc. R. Soc. (London) *A 191*, 39 (1947).
[30] *R. O. C. Norman,* Chem. Br. *6*, 66 (1970).
[31] *K. N. Houk,* J. Am. Chem. Soc. *95*, 4092 (1973).
[32] *B. Le Clef, F. Hervens-Gorissen, L. Stella, R. Merényi, Z. Janousek, H. G. Viehe,* to be published.
[33] *E. Montaudon, J. Thepenier, R. Lalande,* C. R. Acad. Sci. Ser. *C 284*, 581 (1977).
[34] *D. D. Coffman, E. L. Jenner,* J. Am. Chem. Soc. *80*, 2872 (1958); *D. D. Coffman, H. N. Cripps, ibid. 80*, 2880 (1958).
[35] *W. A. Pryor, G. Gojon, D. F. Church,* J. Org. Chem. *43*, 793 (1978).
[36] *H. U. Buschhaus, W. P. Neumann,* Angew. Chem. *90*, 74 (1978); Angew. Chem. Int. Ed. Engl. *17*, 59 (1978).
[37] *Y. Ogata, K. Takagi, E. Hayashi,* J. Org. Chem. *44*, 856 (1979).
[38] *J. R. Shelton, E. E. Borchert,* Can. J. Chem. *46*, 3833 (1968).
[39] *F. Druesne, B. Sillion,* Fr. Pat. 2041421; Chem. Abstr. *75*, 117979 (1971).
[40] *S. Hünig, R. Schaller,* Synthesis, in press.
[41] *H. Allaime, B. Le Clef, H. G. Viehe,* unpublished results.
[42] *G. Tsuchihashi, M. Yamauchi, A. Ohno,* Bull. Chem. Soc. Jpn. *43*, 968 (1970).
[43] *M. Iwamura, N. Inamoto,* Bull. Chem. Soc. Jpn. *40*, 702 (1967); *43*, 856, 860 (1970).
[44] *H. Iwamura, M. Iwamura,* Tetrahedron Lett. *1970*, 3723.
[45] *P. D. Bartlett, T. Funahashi,* J. Am. Chem. Soc. *84*, 2596 (1962).
[46] *S. Mignani, H. G. Viehe,* unpublished results.
[47] *T. Miyamoto, Y. Tsujimoto, T. Tsuchinaga, Y. Nishimura, Y. Odaira,* Tetrahedron Lett. *1978*, 2155; *1979*, 373.
[48] *A. Ramboux, G. Minet, H. G. Viehe,* unpublished results.
[49] *B. Le Clef, F. Hervens-Gorissen, H. G. Viehe,* unpublished results.
[50] *F. Hervens-Gorissen, B. Le Clef, H. G. Viehe,* unpublished results.
[51] *T. H. Koch, J. A. Olesen, J. De Niro,* J. Org. Chem. *40*, 14 (1975).
[52] *T. H. Koch, J. A. Olesen, J. De Niro,* J. Am. Chem. Soc. *97*, 7285 (1975).
[53] *R. C. Haltiwanger, T. H. Koch, J. A. Olesen, C. S. Kim, N. K. Kim,* J. Am. Chem. Soc. *99*, 6377 (1977).
[54] *A. Alberti, A. Hudson,* J. Chem. Soc. Perkin Trans. II *1978*, 1098.
[55] *A. Hudson, R. A. Jackson, N. P. C. Simmons,* J. Chem. Soc. Perkin Trans. II *1977*, 1633.
[56] *A. Alberti, G. F. Pedulli,* Tetrahedron Lett. *1978*, 3283.
[57] *E. M. Kosover* in *W. A. Pryor:* Free Radicals in Biology. Academic Press, New York 1976, Vol. II, Chap. 1.
[58] *P. Gouverneur,* Ind. Chim. Belg. *39*, 329, 467 (1974).
[59] *M. Beaujean, J. Collard-Motte, H. G. Viehe,* unpublished results.
[60] *N. Obata, K. Niimura,* J. Chem. Soc. Chem. Commun. *1977*, 238.
[61] *E. K. Chess, B. S. Schatz, G. J. Gleicher,* J. Org. Chem. *42*, 752 (1977).
[62] *J. E. Baldwin, S. E. Branz, J. A. Walker,* J. Org. Chem. *42*, 4142 (1977).

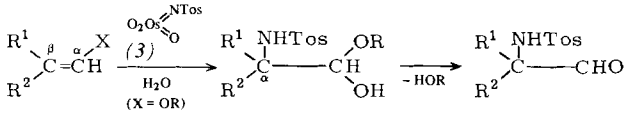
[63] *W. D. Ollis, M. Rey, I. O. Sutherland, G. L. Closs,* J. Chem. Soc. Chem. Commun. *1975*, 543, 545; cf. *J. E. Baldwin, W. F. Erickson, R. E. Hackler, R. M. Scott,* Chem. Commun. *1970*, 576.
[64] *K. Chantrapromma, W. D. Ollis, I. O. Sutherland,* J. Chem. Soc. Chem. Commun. *1970*, 670, 672, 673, 675.
[65] *D. D. Tanner, R. M. Rahimi, J. Org. Chem. 44*, 1674 (1979).
[66] *F. Huys, R. Merényi, Z. Janousek, L. Stella, H. G. Viehe,* Angew. Chem. *91*, 650 (1979); Angew. Chem. Int. Ed. Engl. *18*, 615 (1979).
[67] *Z. Janousek, F. Huys, L. René, M. Masquelier, L. Stella, R. Merényi, H. G. Viehe,* Angew. Chem. *91*, 651 (1979); Angew. Chem. Int. Ed. Engl. *18*, 616 (1979).
[68] *M. Rover-Kevers,* Dissertation, Universität Louvain-la-Neuve, planned for 1980.
[69] *J. C. Pommelet, C. Nyns, F. Lahousse, R. Merényi, H. G. Viehe,* to be published.
[70] *R. A. Firestone,* Tetrahedron *33*, 3009 (1977).
[71] *G. F. Palladino, W. E. McEwen,* J. Org. Chem. *43*, 2420 (1978).
[72] *R. D. Harcourt,* Tetrahedron *34*, 3125 (1978).
[73] *K. D. Gundermann, E. Röhrl,* Justus Liebigs Ann. Chem. *1974*, 1661.
[74] *J. D. Roberts, C. M. Sharts,* Org. React. *12*, 1 (1962).
[75] *J. Toye,* Dissertation, Universität Louvain-la-Neuve 1977.
[76] *G. Bahr, G. Schleitzer,* Chem. Ber. *83*, 1771 (1955); *H. E. Simmons, D. C. Blomstrom, R. D. Vest,* J. Am. Chem. Soc. *84*, 4756 (1962).
[77] *R. Huisgen, W. Scheer, G. Szeimies, H. Huber,* Tetrahedron Lett. *1966*, 397.
[78] *W. S. Ide, J. S. Buch,* Org. React. *4*, 269 (1948).
[79] *H. Stetter,* Angew. Chem. *88*, 695 (1976); Angew. Chem. Int. Ed. Engl. *15*, 639 (1976).
[80] *A. Kalir, D. Balderman,* Synthesis *1973*, 358.
[81] *G. Stork, L. Maldonado,* J. Am. Chem. Soc. *93*, 5286 (1971).
[82] *K. Deuchert, V. Hertenstein, S. Hünig,* Synthesis *1973*, 777.
[83] *S. Hünig, G. Wehner,* Chem. Ber. *112*, 2045 (1979).
[84] *Z. Welwart,* Bull. Soc. Chim. Fr. *1961*, 1653; *D. Seebach,* Angew. Chem. *81*, 690 (1969); Angew. Chem. Int. Ed. Engl. *8*, 639 (1969); *C. R. Hauser, H. M. Taylor, T. G. Ledford,* J. Am. Chem. Soc. *82*, 1786 (1960); *E. Leete, M. R. Chedekel, G. B. Bodem,* J. Org. Chem. *37*, 4465 (1972); *E. Leete, ibid. 41*, 3438 (1976); *J. D. Albright, F. J. McEroy, D. B. Moran,* J. Heterocycl. Chem. *15*, 881 (1978); *E. B. Sanders, H. V. Secor, J. I. Seeman,* J. Org. Chem. *43*, 324 (1978); *H. Ahlbrecht, K. Pfaff,* Synthesis *1978*, 897.
[85] *G. Stork, A. Y. W. Leong, A. M. Touzin,* J. Org. Chem. *41*, 3491 (1976); *P. Bey, J. P. Vevert,* Tetrahedron Lett. *1977*, 1455; see also *R. Lohmar, W. Steglich,* Angew. Chem. *90*, 493 (1978); Angew. Chem. Int. Ed. Engl. *17*, 450 (1978).
[86] *D. Seebach,* Synthesis *1969*, 17; *B. T. Gröbel, D. Seebach, ibid. 1977*, 357.
[87] *G. Stork, A. A. Ozorio, A. Y. W. Leong,* Tetrahedron Lett. *1978*, 5175.
[88] *M. Urrea, D. S. Grierson, H. P. Husson,* personal communication.
[89] *M. Mąkosza, E. Bialecka, M. Ludwikow,* Tetrahedron Lett. *1972*, 2391.
[90] *F. Pochat, E. Levas,* Tetrahedron Lett. *1976*, 1491.
[91] *F. L. Lahousse, L. Stella, H. G. Viehe,* to be published.
[92] *J. L. Herrmann, J. E. Richman, R. H. Schlessinger,* Tetrahedron Lett. *1973*, 2599.
[93] *H. Paulsen, H. Bünsch,* Chem. Ber. *111*, 3484 (1978).
[94] *H. N. Khatri, H. M. Walborsky,* J. Org. Chem. *43*, 734 (1978).
[95] *S. Yamagiwa, N. Hoshi, H. Sato, H. Kosugi, H. Uda,* J. Chem. Soc. Perkin Trans. I *1978*, 214.
[96] *B. M. Trost, Y. Tamaru,* J. Am. Chem. Soc. *99*, 3101 (1977).
[97] *J. Nokami, M. Kawada, R. Okawara,* Tetrahedron Lett. *1979*, 1045.
[98] *W. Adam, H. H. Fick,* J. Org. Chem. *43*, 772 (1978).
[99] *N. Kornblum,* Angew. Chem. *87*, 797 (1975); Angew. Chem. Int. Ed. Engl. *14*, 734 (1975).
[100] See [99], footnote 13.
[101] *S. Bank, D. A. Noyd,* J. Am. Chem. Soc. *95*, 8203 (1973).
[102] *L. Stella, H. G. Viehe,* unpublished results.
[103] *H. Neumann, D. Seebach,* Chem. Ber. *111*, 2785 (1978).
[104] *R. Schlecker, U. Henkel, D. Seebach,* Chem. Ber. *110*, 2880 (1977).
[105] *G. A. Russell, G. Kaupp,* J. Am. Chem. Soc. *91*, 3851 (1969).
[106] *U. Schmidt, J. Häusler, E. Öhler, H. Poisel,* Prog. Chem. Org. Nat. Prod. *37*, 286 (1979).
[107] *P. Yates, Y. C. Toong,* J. Chem. Soc. Chem. Commun. *1978*, 205.
[108] *F. Dutron-Woitrin,* Dissertation, Universität Louvain-la-Neuve 1979.
[109] *R. Merényi, L. Stella, F. Hervens-Gorissen, B. Le Clef, Ph. Dellis, H. G. Viehe,* to be published.
[110] *P. Smith, R. A. Kaba, T. G. Smith, J. T. Pearson, P. B. Wood,* J. Magn. Reson. *18*, 254 (1975).
[111] *D. E. Wood, R. V. Lloyd,* J. Chem. Phys. *52*, 3840 (1970).
[112] *W. C. Danen, R. C. Rickard,* J. Am. Chem. Soc. *94*, 3254 (1972).
[113] *I. Biddles, A. Hudson, J. T. Wiffen,* Tetrahedron *28*, 867 (1972). *B. C. Gilbert, D. K. C. Hodgeman, R. O. C. Norman,* J. Chem. Soc. Perkin Trans. II *1973*, 1748.
[114] *L. Stella, R. Merényi, Z. Janousek, H. G. Viehe, P. Tordo, A. Munoz,* J. Phys. Chem., in press.
[115] *M. J. S. Dewar, R. C. Bingham,* J. Am. Chem. Soc. *95*, 7180, 7182 (1973); *L. Pauling,* J. Chem. Phys. *51*, 2767 (1969); *J. A. Claxton, N. A. Smith, ibid. 52*, 4317 (1970); *A. Begum, J. H. Sharpe, M. C. R. Symons, ibid. 53*, 3756 (1970).
[116] *A. J. Dobbs, B. C. Gilbert, R. O. C. Norman,* J. Chem. Soc. Perkin Trans. II *1972*, 786.
[117] *R. A. Kaba, K. U. Ingold,* J. Am. Chem. Soc. *98*, 523 (1976).
[118] *H. Fischer,* Z. Naturforsch. *A 19*, 866 (1964); *A 20*, 428 (1965); *R. O. C. Norman, B. C. Gilbert,* Adv. Phys. Org. Chem. *5*, 53 (1967).
[119] *P. Smith, J. T. Pearson, R. V. Tsina,* Can. J. Chem. *44*, 753 (1966).
[120] *W. T. Dixon, R. O. C. Norman, A. L. Buley,* J. Chem. Soc. *1964*, 3625.
[121] *H. Paul, H. Fisher,* Ber. Bunsenges. Phys. Chem. *73*, 972 (1969).
[122] *A. L. Buley, R. O. C. Norman, R. J. Pritchett,* J. Chem. Soc. *B 1966*, 849.
[123] *B. Giese, J. Meister,* Angew. Chem. *89*, 178 (1977); Angew. Chem. Int. Ed. Engl. *16*, 178 (1977); *B. Giese, J. Meixner, ibid. 91*, 167 (1979) and *18*, 154 (1979).
[124] *B. Giese, J. Meixner,* unpublished results.
[125] *H. Zeldes, R. Livingstone,* J. Chem. Phys. *47*, 1465 (1967); *H. Paul, H. Fischer,* Helv. Chim. Acta *56*, 1575 (1973).

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

α-Aminoaldehydes from Enamines and Chloramine-T[**]

By *Ingolf Dyong* and *Quan Lam-Chi*[*]

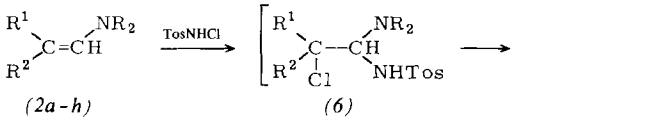
In the search for new synthetic routes to antibiotic sugars with >N–C–R-branching we started from the idea that regioorientation in the vicinal *cis*-hydroxyamination of olefins with OsO_4/Chloramine-T trihydrate[1,2] [reactive species: *(3)*[1]] can be steered by electronic substituent effects[3]. Thus, 1,3-dipolar cycloaddition of *(3)* to β-C branched olefins having an electron donor on the α-C atom [vinyl ethers *(1)* or enamines *(2)*] should lead to α-amino derivatives of type *(4)*, and after cleavage of alcohol or amine to α-(*N*-tosylamino)aldehydes *(5)*, respectively.



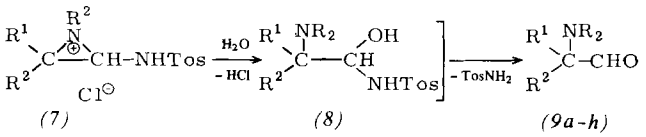
(1), X = OR
(2), X = NR_2

(4) *(5)*

Vinyl ethers *(1)* react, as expected, to give compounds *(5)*. This reaction also takes place with the trihydrate of *N*-chloro-*p*-toluenesulfonamide (Chloramine-T)[4] in absence of OsO_4. Under these conditions, however, the enamines *(2a–h)* afford almost quantitatively (crude products) the *N,N*-dialkylated α-aminoaldehydes *(9a–h)* (Table 1).



(2a–h) *(6)*



(7) *(8)* *(9a–h)*

Table 1. Physical data of the α-aminoaldehydes *(9a–h)*. In the mass spectra the ions with $m/e = M^+ - CHO$ always appear as base fragment. All compounds *(9)* gave correct elemental analyses.

	R^1	R^2	NR_2	Yield [%]	M.p. [°C] B.p. [°C/Torr]	^{1}H-NMR [δ_{CHO}]
(9a)	$-(CH_2)_5-$		Piperidino	70	30	9.32 [a]
(9b)	$-(CH_2)_5-$		$N(CH_3)_2$	50	42/0.1	9.34 [a]
(9c)	CH_3	CH_3	Piperidino	77	40/0.1	9.36 [a]
(9d)	CH_3	CH_3	Morpholino	64	69/4	9.31 [b]
(9e)	C_2H_5	C_2H_5	Piperidino	74	81/3	9.38 [b]
(9f)	C_2H_5	C_2H_5	Pyrrolidino	72	77/5	9.60 [a]
(9g)	C_6H_5	CH_3	$N(CH_3)_2$	83	62/0.01	9.33 [b]
(9h)	C_6H_5	CH_3	Piperidino	84	110/0.01	9.30 [b]

[a] 100 MHz in $CDCl_3$; [b] 60 MHz in $CDCl_3$.

To our knowledge the hitherto best entry to α-aminoaldehydes *(9)* was by reaction of the corresponding α-haloaldehydes proceeding *via* β-haloiminium salts[5,6] to the aziridinium ions, which react with alcohol/triethylamine to give acetals of *(9)*[5] or with bases to give *(9)*[7].

The initial step of the reaction *(2)*→*(9)* is most likely an electrophilic halogenation of the enamines *(2)* by *N*-chloro-*p*-toluenesulfonamide[8]. In the resulting aminals *(6)* the dialkylated nitrogen is the better nucleophile, so that reaction proceeds *via* aziridinium salts of type *(7)* giving *N*-tosylated "*N,O*-semiacetals" *(8)*, which lose tosylamide with formation of the α-dialkylaminoaldehydes *(9a–h)*.

The rearrangement *(6)*→*(8)* proceeds intramolecularly, since only *(9)* is formed, even in the presence of competing amines.

Since the reaction of ketones with *N*-alkylated lithioaminomethylphosphonates leads directly to enamines of α-branched aldehydes[9] and since hexopyranoside-*n*-uloses ($n = 2$–4) are readily accessible the reaction *(2)*→*(9)* with enamines of *C*-formyl branched hexopyranosides could lead to carbohydrates with >N–C–R-branching.

General procedure

A mixture of *(2)* (0.04 mol) and Chloramine-T·$3H_2O$ (0.05 mol) in CH_2Cl_2 (140 ml) is stirred for 3.5–20 h at room temperature (chromatographic monitoring). The filtrate is washed twice with 200 ml 4% NaOCl and once with 200 ml semi-saturated NaCl solution, dried and evaporated down. The residue is distilled under reduced pressure.

Received: July 9, 1979 [Z 336 IE]
German version: Angew. Chem. *91*, 997 (1979)

CAS Registry numbers:
(2a), 6604-81-5; *(2b)*, 16792-75-9; *(2c)*, 673-33-6; *(2d)*, 2403-55-6; *(2e)*, 19394-71-9; *(2f)*, 66685-15-2; *(2g)*, 72087-76-4; *(2h)*, 24401-44-3; *(9a)*, 72087-77-5; *(9b)*, 72087-78-6; *(9c)*, 16042-93-6; *(9d)*, 16042-91-4; *(9e)*, 72087-79-7; *(9f)*, 72087-80-0; *(9g)*, 72087-81-1; *(9h)*, 25076-75-9; Chloramin-T, 127-65-1

[*] Prof. Dr. I. Dyong, Dipl.-Chem. Quan Lam-Chi
Organisch-chemisches Institut der Universität
Orléans-Ring 23, D-4400 Münster (Germany)

[**] This work was supported by the Landesamt für Forschung des Landes Nordrhein-Westfalen and the Fonds der Chemischen Industrie.

[1] *K. B. Sharpless, A. O. Chong, K. Oshima*, J. Org. Chem. *41*, 177 (1976).
[2] *A. O. Chong, K. Oshima, K. B. Sharpless*, J. Am. Chem. Soc. 99, 3402 (1977); *E. Herranz, K. B. Sharpless*, J. Org. Chem. *43*, 2544 (1978).
[3] *I. Dyong, G. Schulte, Q. Lam-Chi, H. Friege*, Carbohydr. Res. *68*, 257 (1979); *I. Dyong, N. Jersch*, Chem. Ber. *112*, 1849 (1979); *I. Dyong, N. Jersch, Q. Lam-Chi, ibid. 122*, 1859 (1979).
[4] *I. Dyong, J. Weigand*, unpublished.
[5] *L. Duhamel, J.-M. Poirier*, Bull. Soc. Chim. Fr. *1975*, 329.
[6] Preparative synthesis of β-haloiminium halides from ketone enamines: *W. Seufert, F. Effenberger*, Chem. Ber. *112*, 1670 (1979).
[7] *L. Duhamel, P. Duhamel, C. Collet, A. Haïder, J.-M. Poirier*, Tetrahedron Lett. *1972*, 4743.
[8] *F. Ruff, A. Kucsman*, J. Chem. Soc. Perkin Trans. 2 *1975*, 509; *K. Tsujihara, N. Furukawa, K. Oae, S. Oae*, Bull. Chem. Soc. Jpn. *42*, 2631 (1969).
[9] *E. K. Fields*, J. Am. Chem. Soc. *74*, 1528 (1952); *S. F. Martin, R. Gompper*, J. Org. Chem. *39*, 2814 (1974).

Structure of the Dicyanophosphide Ion in a Crown-Ether Sodium Salt[**]

By *William S. Sheldrick, Jürgen Kroner, Franz Zwaschka,* and *Alfred Schmidpeter*[*]

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

The dicyanophosphide ion $P(CN)_2^-$ is formed on reduction of phosphorus tricyanide, *e.g.* with [18]crown-6-sodium cation surrounded by a crown ether and situated at a crystallographic inversion center (0.5, 0, 0.5 and 0, 0.5, 0.5, respectively), which takes up two further ligands in the *trans* position, namely two *O*-coordinated tetrahydrofuran molecules or two *N*-coordinated dicyanophosphide ions (Fig. 1)[3]. The latter randomly populate two different sites with occupation factors of 0.42 and 0.58(1), respectively (Fig. 1, *(2)* bottom view). In *(1)*, as in *(2)*, the ligand atoms surround the Na^+ ion in an almost (squat, cf. bond lengths, Fig. 1) hexagonal

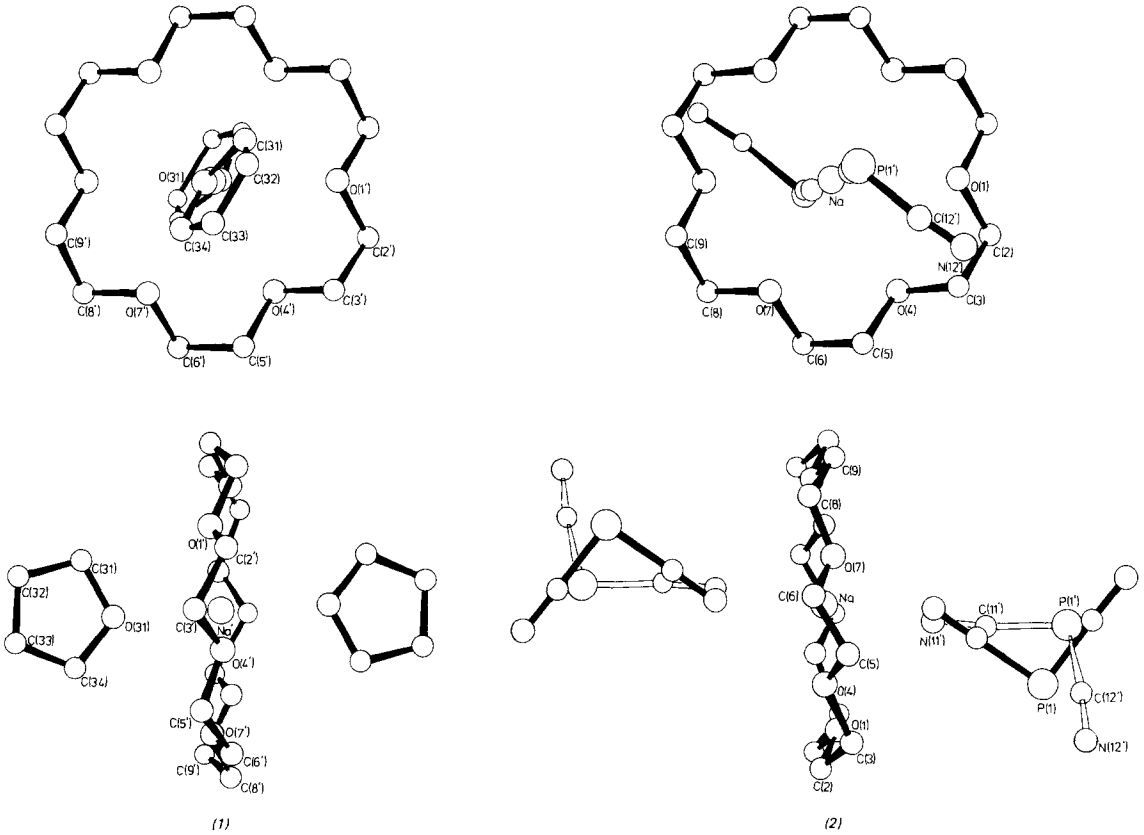


Fig. 1. View of the $\{[18]crown\text{-}6\text{-}Na(tetrahydrofuran)_2^+\}^-$ *(1)* and the $\{[18]crown\text{-}6\text{-}Na[P(CN)_2^-]_2\}^+$-unit *(2)* perpendicular (top) and parallel (bottom) to the crown-ether plane.

Bond lengths [pm]					Apex-(Na or Na')-equator angles [°]			
		Na	N(11)	244(2)				
Na' O(31)	236.4(7)	Na	N(11')	248(2)		O(31)	N(11)	N(11')
Na' O(1')	271.2(5)	Na	O(1)	277.5(2)	O(1 or 1')	88.8(2)	81.9(4)	75.0(5)
Na' O(4')	273.9(5)	Na	O(4)	277.9(6)	O(4 or 4')	92.3(2)	87.5(4)	89.6(5)
Na' O(7')	279.1(4)	Na	O(7)	273.2(7)	O(7 or 7')	83.3(2)	84.9(4)	94.0(6)

diethyl phosphite in tetrahydrofuran[1]. $NaP(CN)_2$ crystallizes with the crown ether and tetrahydrofuran in the molar ratio 1:1:1. The X-ray structure analysis[2] shows that comparable positively *(1)* and negatively *(2)* charged units are present in the crystal. They are each formed from a sodium bipyramidal arrangement. As a result of the alternating deviations of the crown ether oxygen from the mean NaO_6 plane (O(1') −16.3, O(4') 16.2, O(7') −16.1; O(1) −17.2, O(4) 17.0, O(7) −17.4) it is clearly distorted into a scalenohedron, and in *(2)* additionally so by the inclination of the NP axis.

The optimization of all bonding parameters by the STO-3G method[4] predicts a planar molecular skeleton for the $P(CN)_2^-$ ion with the bond lengths and angles shown in Figure 2a. The PCN moieties are bent slightly outwards[5]. The calculated net densities show that the anionic charge is distributed completely over the two cyanide residues while the phosphorus remains free. The high population on N corresponds to the (charge-controlled) *N*-coordination of $P(CN)_2^-$ to Na^+ in the structure described here[6, 7].

[*] Priv.-Doz. Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)
Prof. Dr. A. Schmidpeter, Dr. J. Kroner, Dipl.-Chem. F. Zwaschka
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)

[**] Part 3 of Cyanophosphorus Compounds. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 2: *A. Schmidpeter, F. Zwaschka,* Angew. Chem. *91*, 441 (1979); Angew. Chem. Int. Ed. Engl. *18*, 411 (1979).

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0934 $ 02.50/0

The calculated structure is largely confirmed by the X-ray structure analysis (cf. Fig. 2b). However, the values mea-

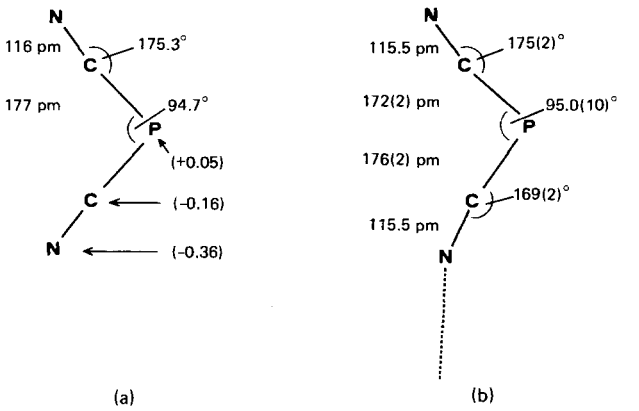


Fig. 2. Bond lengths and angles (and net charge densities) in the cyanophosphide ion: a) calculated [STO-3G], b) from the structure determination (mean values according to the given refinement model [2]).

sured for the $P(CN)_2^-$ ion are subject to larger standard deviations than normal owing to its disorder. In particular the bond lengths P(1)—C(11) [P(1′)—C(11′)] and Na—N(11) [Na—N(11′)] and the angles P(1)—C(11)—N(11) [P(1′)—C(11′)—N(11′)] should be treated with reservation owing to the overlapping of the disordered atoms C(11) and C(11′) and N(11) and N(11′) (for refinement conditions see [2]). Remarkably, the $P(CN)_2^-$ parameters deviate very little from those of $P(CN)_3$ (PC 178, CN 115 pm; CPC 93, PCN 172°)[8]. Only the PC bonds appear somewhat shorter—also compared with the calculated values—and the CPC angle of 95(1)° is not—as would be expected for a phosphide—narrower, but wider than in $P(CN)_3$. Both these findings are consistent with an increased charge delocalization in the cyanide residue. The PCN angles correspond to the calculated value, but they are not coplanar.

Received: May 18, 1979 [Z 321a IE]
Supplemented: July 13, 1979
German version: Angew. Chem. *91*, 998 (1979)

CAS Registry numbers:
(1), 71888-48-7; *(2)*, 71888-47-6

[1] *A. Schmidpeter, F. Zwaschka*, Angew. Chem. *89*, 747 (1977); Angew. Chem. Int. Ed. Engl. *16*, 704 (1977).

[2] Triclinic crystals, $P\bar{1}$, $a=944.2(2)$, $b=1638.1(3)$, $c=815.6(3)$ pm, $\alpha=90.29(3)$, $\beta=92.01(3)$, $\gamma=72.81(2)°$, $V=1204.4(4)\times10^6$ cm³, $Z=2$, $\rho_{calc}=1.22$ g cm^{-3}. The structure was refined to $R=0.083$, $R_w=0.075$ using 1402 independent reflections ($I\geq2.00(I)$, $Mo_{K\alpha}$, Syntex-P2$_1$ diffractometer). Refinement based on the following model for the disordered $P(CN)_2^-$: $d[C\equiv N]=115.5\pm0.1$ pm, $d[P(1)\ C(11)]=d[P(1')\ C(11')]\pm0.1$ pm, $d[P(1)\ C(12)]=d[P(1')\ C(12')]\pm0.1$ pm, $d[C(11)\ldots C(12)]=d[C(11')\ldots C(12')]\pm1$ pm, $d[P(1)\ldots N(11)]=d[P(1')\ldots N(11')]\pm1$ pm, $d[P(1)\ldots N(12)]=d[P(1')\ldots N(12)]\pm1$ pm.

[3] A positively charged (and a neutral) hexagonal-bipyramidal Na complex analogous to *(1)* is found in dibenzo[18]crown-6·$NaBr(H_2O)_2$; a negatively charged complex analogous to *(2)*, on the other hand, has so far not been reported. Cf. *N. A. Bush, M. R. Truter*, J. Chem. Soc. *B 1971*, 1440.

[4] *W. J. Hehre, R. F. Stewart, J. A. Pople*, J. Chem. Phys. *51*, 2657 (1969): 3d orbitals were not considered in the basis set.

[5] The same applies in the case of the isoelectronic $S(CN)_2$; cf. *P. Rosmus, H. Stafast, H. Bock*, Chem. Phys. Lett. *34*, 275 (1975).

[6] SCN is also *N*-coordinated to alkali metal ions, though in this case (again according to STO-3G) the sulfur (net charge density −0.40) has only a slightly smaller portion of the anion charge than the nitrogen (−0.45).

[7] Methylation, on the other hand, takes place at the phosphorus [1].

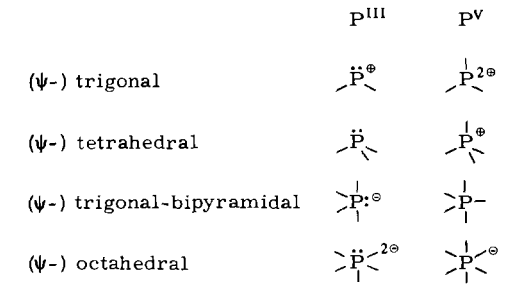
[8] *K. Emerson, D. Briton*, Acta Crystallogr. *17*, 1134 (1964).

Five-coordinate Tervalent Phosphorus in the Tricyanobromo- and -iodophosphate(III) Ion[**]

By *William S. Sheldrick, Franz Zwaschka,* and *Alfred Schmidpeter*[*]

Dedicated to Professor Kurt Issleib on the occasion of his 60th birthday

High-coordination polyhedra are naturally attained more easily for a high oxidation state of an element than for a lower one. In a recent classification of phosphorus compounds[1], of all the reasonable phosphorus coordination possibilities



for P^{III}—in contrast to P^V—only the first two are shown. The third one should be present in the recently prepared cyanohalophosphates(III)[2]. The structure determination of two prototypes, the crown ether alkali metal salts $NaP(CN)_3Br$ and $NaP(CN)_3I$, now surprisingly shows an even higher phosphorus coordination owing to a dimerization of the anion. They provide the first examples of pseudo-(ψ-)octahedral phosphate(III) species[3].

The two compounds crystallize isomorphously in the space group Cmca with four units of the dimer in the elementary cell[4]. The cation shows crystallographic C_h-, the anion C_{2h}-symmetry. The Na^+ cation is eightfold oxygen-coordinated by the [18]crown-6 and perpendicular to its ring by two tetrahydrofuran molecules (as in the case of crown ether complexed $NaP(CN)_2$[5]); one of the tetrahydrofuran ligands is disordered with respect to a plane of symmetry.

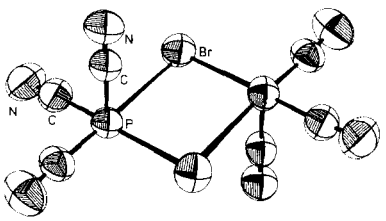


Fig. 1. Structure of the anion $[P_2(CN)_6Br_2]^{2-}$ in the crystal.

The phosphorus coordination in the anion (Fig. 1) can be described as an octahedron, formed by three facial cyano groups, two halogen atoms X, and the lone pair of electrons. Two of these ψ-octahedra are linked by a common X_2-edge with the apical cyano groups in the *trans*-position. The only other examples of edge-linked ψ-octahedra were found in

[*] Prof. Dr. A. Schmidpeter, Dipl.-Chem. F. Zwaschka
Institut für Anorganische Chemie der Universität
Meiserstrasse 1, D-8000 München 2 (Germany)
Priv.-Doz. Dr. W. S. Sheldrick
Gesellschaft für Biotechnologische Forschung mbH
Mascheroder Weg 1, D-3300 Braunschweig-Stöckheim (Germany)

[**] Cyanophosphorus Compounds, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: [5].

$Bi_2Cl_8^{2-}$[6] and as structural unit in the $SbS_{\frac{2}{2}}^{-}$-layer[7]. Here again the apical ligands are *trans* to each other[8].

As expected from electron pair repulsion the phosphorus atom lies below the basal plane of the pyramid (Fig. 1). The basal PCN groups are bent in such a way that their N atoms too are below this plane. The apical PCN group on the other hand is linear and leans somewhat towards the linking edge. Whereas in ψ-octahedra the apical bond is normally shorter than the equatorial ones, the PC-distances here do not differ significantly. In accordance with its synthesis the $P_2(CN)_6X_2^{2-}$ ion can be regarded as two $P(CN)_3$ molecules linked by a halide double bridge. Actually the geometries of the $P(CN)_3$ units therein, for X = Br as well as for X = I, deviate only slightly from free $P(CN)_3$ itself (Table 1). Thus the

Table 1. Bond lengths [pm] and angles [°] of the anion in $[C_{12}H_{24}O_6Na(OC_4H_8)_2]_2[P_2(CN)_6X_2]$ and of $P(CN)_3$ (average values) for comparison [9], deviations [pm] of P and of N from the basal C_2X_2-plane (opposite to the apex direction).

		X = Br	X = I	$P(CN)_3$
PX		305.8(1)	326.2(3)	
PC	basal	182.3(6)	183.5(13)	178.8(28)
	apical	181.0(8)	184.6(18)	
CN	basal	112.5(8)	112.7(13)	114.9(45)
	apical	112.8(10)	110.6(16)	
PXP		80.1(1)	82.0(1)	
XPX		99.9(1)	98.1(1)	
XPC	basal	84.4(2)	85.2(4)	
	apical	83.5(1)	84.3(3)	
CPC	basal	91.0(4)	91.3(8)	93.5(20)
	apical	92.9(2)	92.7(5)	
PCN	basal	173.5(5)	172.3(11)	171.6(30)
	apical	179.8(2)	179.2(15)	
P		8.1	6.6	
N		7.6	10.7	

CPC-angles shrink by only about 1°. On average the PC bonds lengthen by 4 pm and the CN bonds shorten by 3 pm, indicating a weaker bond between P and CN. The distances from P to X are considerably longer than for every known PX bond, being approximately the average of the single bond length in PX_3 (X = Br: 222, X = I: 243 pm) and the sum of the van-der-Waals radii (X = Br: 385, X = I: 405 pm). The coordination number 5, unexpected high for P^{III}, is thus apparently a result of the small reorganization necessary, rather than of strong PX bonds (the ψ-octahedral structure of the dimer with ideal PCP angles of 90° should be more favorable than the ψ-trigonal-bipyramidal one of the monomer with two ideal angles of 90° and one of 120°).

For the solid $P(CN)_3X$ salts we find $\delta^{31}P = -177$ (X = Br) and -168 (X = I); in solution these shifts are almost the same, indicating the dimeric anion to be preserved in solution.

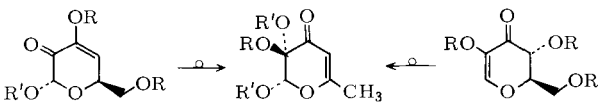
Received: August 3, 1979 [Z 321 b IE]
German version: Angew. Chem. *91*, 1000 (1979)

[1] *G. M. Kosolapoff, L. Maier:* Organic Phosphorus Compounds. Vol. 7, iii. Wiley, New York 1976.
[2] *A. Schmidpeter, F. Zwaschka,* Angew. Chem. *91*, 441 (1979); Angew. Chem. Int. Ed. Engl. *18*, 411 (1979).
[3] *T. C. Waddington, K. B. Dillon,* and *A. W. G. Platt* independently synthesised tetraalkylammonium salts of anions of the same composition (personal communication). As their $\delta^{31}P$ data in solution and in the solid state agree with those of our salts, they should also correspond in the structure of the anions.
[4] Bromo derivative: $a = 1367.9(1)$, $b = 2063.5(1)$, $c = 2227.6(2)$ pm, $\rho_{calc} = 1.31$ g cm^{-3}; 1853 reflections ($Cu_{K\alpha}$, $3.5° \leqq 2\theta \leqq 135.0°$, empirical absorption correction), $R = 0.064$.—Iodo derivative: $a = 1385.0(2)$, $b = 2068.0(2)$, $c = 2238.8(3)$ pm; $\rho_{calc} = 1.32$ g cm^{-3}; 1314 reflections ($Mo_{K\alpha}$, $3° \leqq 2\theta \leqq 50°$), $R = 0.059$.
[5] *W. S. Sheldrick, J. Kroner, F. Zwaschka, A. Schmidpeter,* Angew. Chem. *91*, 998 (1979); Angew. Chem. Int. Ed. Engl. *18*, 934 (1979).
[6] *A. Hershaft, J. D. Corbett,* Inorg. Chem. *2*, 979 (1968).
[7] *K. Volk, H. Schäfer,* Z. Naturforsch. *B 33*, 827 (1978).
[8] AX_4E compounds otherwise display a monomeric ψ-trigonal-bipyramidal structure, a ψ-octahedral structure with shared vertices, or an octahedral structure with shared edges.
[9] *K. Emerson, D. Britton,* Acta Crystallogr. *17*, 1134 (1964).

Novel, Highly Stereoselective Rearrangements of Chiral Dihydropyranones[1]

By *Frieder W. Lichtenthaler, Shigeru Nishiyama,* and *Pan Jarglis*[*]

Dihydropyranones *(1)*[2] are important chiral synthons[3] since the enolone grouping is flanked on each side by chiral centers. A similar synthetic potential attends enediolones *(3)* which hitherto have only been obtained sporadically and in multistep syntheses[4]. We here wish to report on new, facile procedures for the preparation of *(3)* and on the very ready rearrangements of type *(1)*→*(2)* and *(3)*→*(2)*, the latter being remarkable in so far as it comprises a highly stereoselective chirality transfer from one side of the ring to the other.



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

R = Acyl, R' = Alkyl

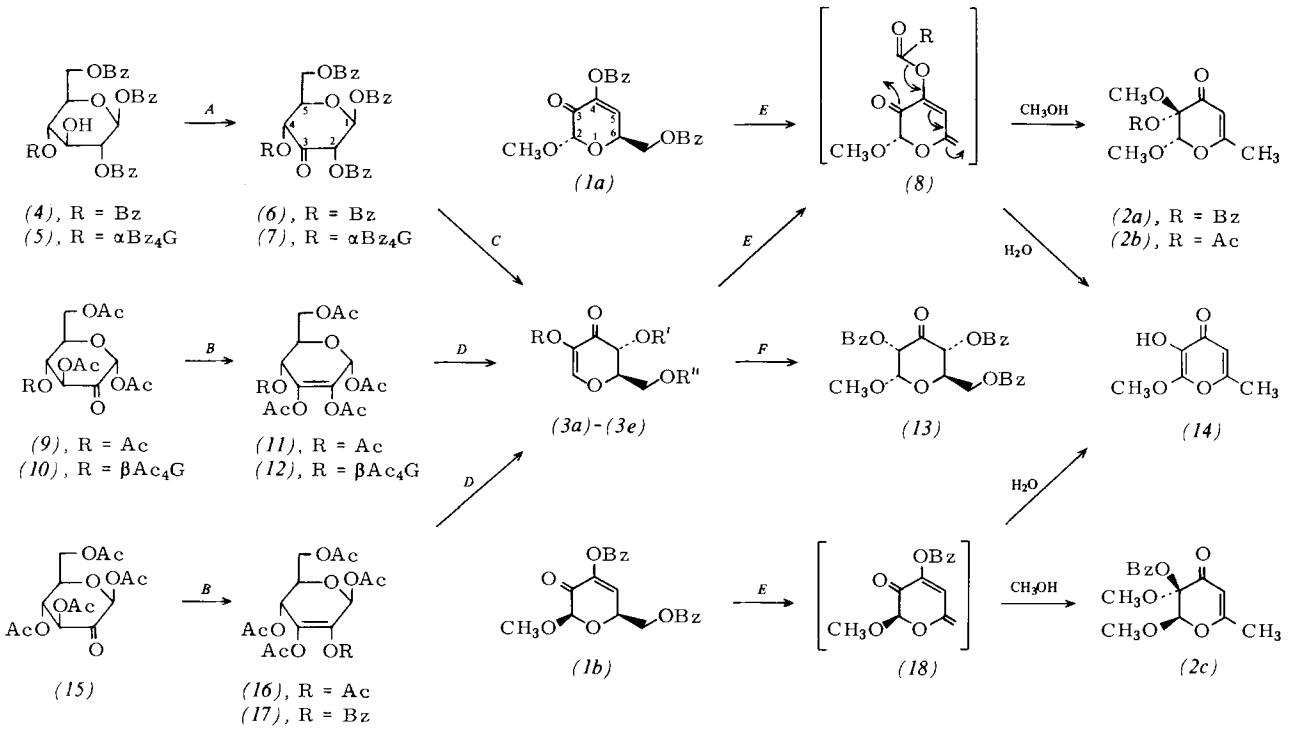
Pyranoid enediolones *(3)* are not only accessible from peracylated hexos-3-uloses by an expectedly[3] facile elimination

Table 1. Synthesis of dihydropyranones *(2)* and *(3)* and their precursors and products; conditions, yields, and physical data [a].

Compd.	Yield [%] (educt [b], conditions [c])	M.p. [°C]	$[\alpha]_D$ in $CHCl_3$ [°]	(*c*, °C)
(2a)	69 (*(1a), E*)	105—106	+263	(0.5, 20)
	64 (*(13), E*)			
	41 (*(3a), (3d), E*)			
(2b)	39 (*(3c), E*)	128—129	+234	(0.5, 21)
(2c)	77 (*(1b), E*)	104—105	−263	(1, 19)
(3a)	86 (*(6), C*)	162—163	+217	(0.8, 20)
	57 (*(4), G*)			
(3b)	67 (*(5), H*)	amorphous	+222	(1, 19)
(3c)	81 (*(16), D*)	75	+218	(1.1, 20)
(3d)	89 (*(17), D*)	111	+212	(0.4, 21)
(3e)	76 (*(12), D*)	150—151	+ 89	(0.8, 20)
(6)	69 (*(4), A*)	152—154	+ 6.4	(1.5, 20)
(11)	60 (*(9), B*)	141	+ 59	(0.4, 23)
(12)	80 (*(10), B*)	174—175	+ 2.6	(1, 23)
(13)	54 (*(3a), F*)	syrup [d]	+124	(1, 23)
(16)	65 (*(15), B*)	85	+165	(0.3, 21)
(17)	55 (*(15), B*)	116	+148	(1, 23)

[a] Values for combustion analysis, molecular weights (MS-FD spectra), as well as ^{1}H-NMR, ^{13}C-NMR, and CD data are in accord with the structures and configurations assigned. [b] Origin of educts already known: *(1a)* [2b, c], *(1b)* [2c], *(4)* [7], *(5)* [6], *(9)*, *(10)* and *(15)* in the form of their monohydrates [2e]. [c] Conditions *A—F*, cf. Scheme 1; *G*, DMSO/$(CF_3CO)_2O$ in CH_2Cl_2 at −60 °C with addition of Et_3N, 4 h at −60 °C, 2 h at 20 °C; H, DMSO/Ac_2O (3:2), 25 °C. [d] Dinitrophenylhydrazone: m.p. 202 °C (dec), $[\alpha]_D^{20} = -180°$ ($c = 1$, $CHCl_3$).

[*] Prof. Dr. F. W. Lichtenthaler, Dr. S. Nishiyama, Dipl.-Ing. P. Jarglis
Institut für Organische Chemie und Biochemie
der Technischen Hochschule
Petersenstrasse 22, D-6100 Darmstadt (Germany)



Scheme 1. Abbreviations: Ac = acetyl, Bz = benzoyl, αBz_4G = tetra-*O*-benzoyl-α-D-glucopyranosyl, βAc_4G = tetra-*O*-acetyl-β-D-glucopyranosyl.—Reaction conditions: *A*, $RuO_2/NaIO_4$ in water/CH_2Cl_2; *B*, acetyl chloride or benzoyl chloride in $CHCl_3$ with controlled amount of pyridine, 0 to −10 °C; *C*, $NaHCO_3$, moist benzene, 3 h, 80 °C; *D*, $AlCl_3$, $CHCl_3$, 20 °C or HBr/acetic acid followed by pyridine; *E*, K_2CO_3, CH_3OH in DMSO, 25 °C; *F*, CH_3OH/BF_3-ether, tetrahydrofuran, 20 °C, followed by purification on silica gel.—*(3a)* R = R′ = R″ = Bz; *(3b)*, R = R″ = Bz, R′ = αBz_4G; *(3c)*, R = R′ = R″ = Ac; *(3d)*, R = Bz, R′ = R″ = Ac; *(3e)*, R = R″ = Ac; R′ = βAc_4G.

of the anomeric substituent, but also from the corresponding hexos-2-uloses *via* a 2→3 shift of the carbonyl group prior to elimination. Thus, the preparatively most convenient method of synthesis is determined by the accessibility of the educt. For instance, the tribenzoyl compound *(3a)* (Scheme 1, Table 1) may be prepared in high yield from tetrabenzoylhexosulose *(6)* by brief heating with $NaHCO_3$ in moist benzene or from the tetrabenzoyl-glucose *(4)* by reaction with dimethyl sulfoxide (DMSO)/acetic anhydride or DMSO/trifluoroacetic anhydride (cf. Table 1). Correspondingly, maltose can be converted into the disaccharide enediolone *(3b)* in 67% yield by benzoylation to the heptabenzoate *(5)*[6] and subsequent reaction with DMSO/acetic anhydride. *O*-Acetylated enediolones such as *(3c)*, *(3d)*, and *(3e)* are most conveniently prepared from the readily accessible[2e,3] peracetylhexos-2-uloses *(9)*, *(10)*, and *(15)* by cautious acylation[8] to the corresponding 2,3-dehydrosugars *(11)*, *(12)*, *(16)*, and *(17)*, and treatment with $AlCl_3$ or $SnCl_4$ in chloroform. The latter step proceeds *via* the 1-chloride and subsequent removal of the elements of acetyl chloride. Alternatively, the enedioldiacetate → enediolone conversion may also be achieved by treatment with HBr/acetic acid (to the 1-bromide) and subsequent treatment with pyridine.

On BF_3 catalysis, enediolones *(3)* add methanol at the anomeric carbon preferentially from the α-side, *e.g.* *(3a)*→*(13)*. Mildly basic conditions, however, such as methanol/potassium carbonate in DMSO, initiate more profound transformations with the elaboration of 5-methyldihydropyranones, as illustrated by the conversions *(3a)*→*(2a)*, *(3d)*→*(2a)*, and *(3c)*→*(2b)*, which proceed with high stereoselectivity[9]. On the other hand, analogously feasible conversions of enolones of type *(1)* are practically stereospecific: *(1b)* yields the 2*R*,3*R*-dihydropyranone *(2c)* in high yield (quantitative conversion, 77% isolated), whilst the anomeric α-enolone *(1a)* is as readily transformed into the 2*S*,3*S* enantiomer *(2a)*.

Structural assignments for dihydropyranones *(2a)* and *(2c)* are based on UV [$\lambda_{max}^{CH_3OH}$ = 233 (11000) and 267 nm (8500)] and ^{1}H-NMR data [δ = 2.06 (C–CH_3), 3.38 and 3.51 ($2OCH_3$), 5.40 (s, 1 anomeric H), 6.18 (s, 1 olefinic H). That the compounds are enantiomers is deduced from identical IR and NMR data and the same magnitude yet opposite sign of their rotations and CD data [*(2a)*: Δε = −1.7 (229 nm), +6.3 (260), +0.6 (290), +2.0 (319)], from which the configuration at the tertiary carbon may also be deduced[10].

The conversion *(1)*→*(2)* is obviously initiated by a known[2b,c] 5,6-elimination of benzoic acid to give the dienolones *(8)* and *(18)*, followed by protonation of the exocyclic double bond and benzoyl migration, and is concluded by addition of the nucleophile ($CH_3O^{\ominus}$), which is stereocontrolled by the anomeric substituent. The elaboration of the γ-pyrone system in the form of methoxyallomaltol *(14)* on replacement of methanol with water is in accord with this view. The conversion *(3)*→*(2)* proceeds *via* analogous intermediates; the 3,2-enolone system *(1)* is primarily formed by preferential α-addition of the alcohol [*e.g.* *(3a)*→*(13)*], *O*-2→*O*-3-acyl migration to the hexosid-2-ulose, and β-elimination of HO-Acyl. This course is substantiated by the observation that peracylated hexosid-3-uloses as readily yield dihydropyranones *(2)* under these conditions [*e.g.* *(13)*→*(2a)*], whereas the 4-*O*-glycosylated enediolones *(3b)* and *(3e)*, lacking a displaceable substituent at C-4, do not undergo these reactions.

These highly stereoselective rearrangements, practically stereospecific in the case of enolones *(1)*, considerably widen the scope of application of pyranoid sugar enolones as chiral synthons, particular with respect to the synthesis of uscharine-type cardiac glycosides and spectinomycin antibiotics.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0937 $ 02.50/0*

Received: September 3, 1979;
revised: October 15, 1979 [Z 337 IE]
German version: Angew. Chem. *91*, 1001 (1979)

CAS Registry numbers:
(1a), 13007-49-3; *(1b)*, 52152-86-0; *(2a)*, 72076-10-9; *(2b)*, 72076-11-0; *(2c)*, 72076-12-1; *(3a)*, 72076-13-2; *(3b)*, 72076-14-3; *(3c)*, 41107-22-6; *(3d)*, 72076-15-4; *(3e)*, 72076-16-5; *(4)*, 72076-17-6; *(5)*, 25018-22-8; *(6)*, 72076-18-7; *(9)*, 61259-53-8; *(10)*, 72076-19-8; *(11)*, 72076-20-1; *(12)*, 72076-21-2; *(13)*, 68325-67-7; *(13)*-DNPH, 72076-25-6; *(15)*, 72076-22-3; *(16)*, 72076-23-4; *(17)*, 72076-24-5

[1] Sugar Enolones, 10th Communication. We gratefully acknowledge support of this work by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 9: [3].

[2] a) *F. W. Lichtenthaler*, Methods Carbohydr. Chem. *6*, 348 (1972); *E. Fischer, F. W. Lichtenthaler*, Angew. Chem. *86*, 590 (1974); Angew. Chem. Int. Ed. Engl. *13*, 546 (1974); b) *F. W. Lichtenthaler, K. Strobel, G. Reidel*, Carbohydr. Res. *49*, 57 (1976); c) *F. W. Lichtenthaler, U. Kraska, ibid. 58*, 363 (1977); d) *F. W. Lichtenthaler, T. Sakakibara, E. Egert*, Chem. Ber., in press; e) *F. W. Lichtenthaler, P. Jarglis, ibid.*, in press.

[3] *F. W. Lichtenthaler*, Pure Appl. Chem. *50*, 1343 (1978).

[4] Aside from the highly instable free enediolone *(3)*, R = H [5a], the 5,7-di-*O*-methyl-3-*O*-acetyl derivative [5b] and the triacetate *(3)*, R = Ac [3, 5c] have been characterized unequivocally. Other derivatives are being discussed in connection with the oxidative degradation of methylated polysaccharides [5d].

[5] a) *O. Theander*, Acta Chem. Scand. *12*, 1887 (1958); b) *G. O. Aspinall, R. R. King, Z. Pawlak*, Can. J. Chem. *51*, 388 (1973); c) *G. O. Aspinall, R. R. King, ibid. 51*, 394 (1973); *J. Weissmüller, H. Kunz*, Tetrahedron Lett. *1978*, 3807; d) *B. Lindberg*, Pure Appl. Chem. *49*, 1089 (1977); *L. Kenne, O. Larm, S. Svensson*, Acta Chem. Scand. *26*, 2473 (1972); *27*, 2797 (1973).

[6] *K. Takeo, S. Okano*, Carbohydr. Res. *59*, 379 (1977).

[7] *K. Freudenberg, H. v. Hochstetter, H. Engels*, Ber. Dtsch. Chem. Ges. *58*, 671 (1925); *K. Freudenberg, E. Plankenhorn*, Justus Liebigs Ann. Chem. *536*, 257 (1938); *M. Bertolini, C. P. J. Glaudemans*, Carbohydr. Res. *15*, 267 (1970).

[8] Excess pyridine causes partial 3,4-elimination to the 3,2-enolone *(1a)*, Ac instead of Bz and CH_3; pyridine/acetic anhydride converts *(9)* quantitatively into di-*O*-acetylkojic acid.

[9] The *(3a)*-derived *(2a)* contains 8—10% of the β-enantiomer *(2c)* as evidenced by its rotation (+236° in $CHCl_3$ *versus* +263° for a product obtained from *(1a)*). The step determining the stereoselectivity of the conversions *(3a)*→*(2a)* and *(3c)*→*(2b)*, in fact, is the addition of methanol at the anomeric carbon, which preferentially (*ca.* 10:1) occurs from the α-side. The α- [*e.g. (13)*] and β-hexosid-3-uloses formed *e.g.* from *(3a)* subsequently yield the respective enediolones *(2a)* and *(2c)* in practically stereospecific reactions.

[10] *Note added in Proof* (Nov. 15, 1979): The structure and configuration of the dihydropyranones *(2)* have meanwhile been corroborated by an x-ray structure analysis of *(2c)*: *H. J. Lindner*, unpublished.

Model System for the Electrochemical Reduction of the Carbon-Halogen Bond[**]

By *Andreas Merz* and *Robert Tomahogh*[*]

Palle Iversen in memoriam

Radicals and carbanions are discussed as intermediates in the reductive electrochemical cleavage of the carbon-halogen bond:

$$\left.\begin{array}{l} R{-}X + e \rightarrow X^{\ominus} + R^{\odot} \\ R^{\odot} \quad + e \rightarrow R^{\ominus} \end{array}\right\} \text{ products} \qquad \begin{array}{l}(a)\\(b)\end{array}$$

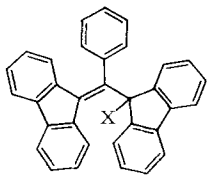
In many cases, however, it is still unclear from which intermediate the products are actually derived; moreover, radicals could be detected neither directly nor by spin-trap methods[1].

We report here on cyclic-voltammetric and coulometric investigations of the model systems 9-fluoro- and 9-chloro-9-[α-(9-fluorenylidene)benzyl]fluorenes *(1a)* and *(1b)*[2], respectively, in which both the carbanion *(2a)*[3a] and the radical *(2b)*[3b] are stable.

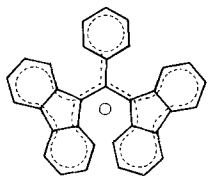
[*] Priv.-Doz. Dr. A. Merz, R. Tomahogh
Institut für Chemie der Universität
Universitätsstr. 31, D-8400 Regensburg (Germany)

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

Figure 1 shows the cyclic voltammograms of *(1a)* (curve b) and *(1b)* (curve a) obtained in anhydrous acetonitrile/0.1 M $Bu_4N^{\oplus}ClO_4^{\ominus}$ (TBAP) with glassy carbon electrodes[4]. The



(1a), X = F
(1b), X = Cl
(1c), X = Br
(3), X = OH
(4), X = H



(2a), O = ⊖
(2b), O = ⊙
(2c), O = ⊕

half-peak potentials (two electron waves) $E_{p/2}$ are −1.35 V for *(1a)* and −0.30 V for *(1b)*. The anodic branch of the voltammogram shows the same maxima for both compounds, those corresponding to the oxidation of the carbanion *(2a)* to the radical *(2b)* and of *(2b)* to the cation *(2c)*.

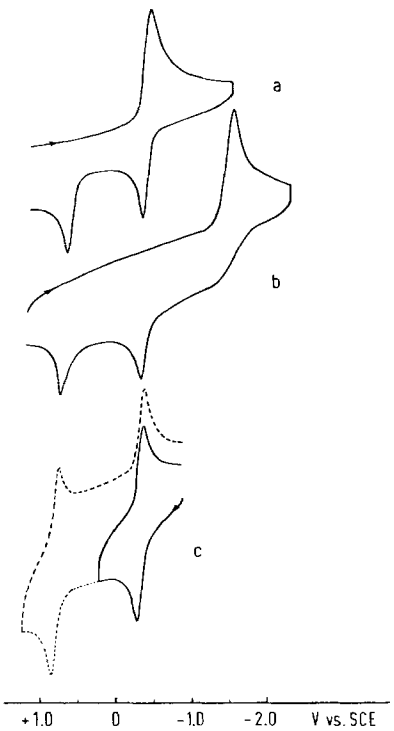


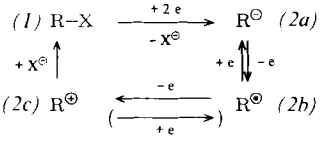
Fig. 1. Cyclic voltammogram in anhydrous acetonitrile/0.1 M $Bu_4N^{\oplus}ClO_4^{\ominus}$ at a carbon disk electrode; 200 mV/s. Curve a: *(1b)*; curve b: *(1a)*; curve c: carbanion *(2a)* after coulometric generation from the radical *(2b)*. The unbroken curve is also obtained directly after coulometric reduction of *(1a)* or *(1b)*. Concentrations *ca.* 5×10^{-4} M.

This interpretation is confirmed by coulometric reduction of *(1a)* and *(1b)* at −1.4 V and −0.4, respectively, which in each case leads with uptake of 2 F/mol to the deep-blue solution of the carbanion *(2a)*. Whereas in the electrolysis of *(1a)* the blue color of the carbanion is stable from the beginning, in the electrolysis of *(1b)* the blue schlieren from the cathode fade with formation of the yellow solution of the radical *(2b)*; the color of *(2a)* persists only after uptake of 1 F/mol. Thus *(2a)* is able to reduce the chloro compound *(1b)*, but not the

fluoro compound *(1a)*, in a homogeneous electron transfer reaction:

$$\underset{(1b)}{R{-}X} + \underset{(2a)}{R^{\ominus}} \rightarrow \underset{(2b)}{2R^{\ominus}} + Cl^{\ominus} \qquad (c)$$

The carbanion *(2a)* can be oxidized coulometrically at 0.0 V (1 F/mol) reversibly to the radical *(2b)* ($E^0 = -0.31$ V). In a further one-electron oxidation at +0.95 V, *(2b)* is transformed into the cation *(2c)*. The latter reaction appears irreversible in the voltammogram; this can be attributed to a rapid back reaction of *(2c)* with the halide ion to give the starting halides *(1a)* and *(1b)*, respectively, whose cyclic voltammograms are observed again after completion of the coulometric cycle (Scheme 1).



Scheme 1

This cycle can be passed through several times without any notable loss in electroactivity. These constitute the first examples of the chemically reversible electroreduction of organic halogen compounds, even though the pathways of the forward and reverse reactions are different[5].

Starting from the isolated radical *(2b)*, in halide-free solution, also the oxidation *(2b)*→*(2c)* is electrochemically reversible, but only on the cyclic voltammetry time scale. Coulometrically generated red *(2c)* reacts with a half-life of a few minutes in an intramolecular Friedel-Crafts reaction[6].

Our results can be discussed in terms of a model for the mechanistic variants of the electroreduction of the carbon-halogen bond: The radical can form at the cathode [eq. (a)][7] only if the reduction potential of the halogen compound is more positive than the redox potential of the radical/carbanion pair [eq. (b)]. This seemingly trivial picture is extended by the electrochemical reduction of the chloro compound *(1b)*, the first well documented example of the "father-son" or "Oedipus" mechanism already postulated by *Elving*[8]. This combination [eq. (a)+(b)+(c)] is possible then, if the redox potential of the radical/carbanion system lies *between* the (unknown) *thermodynamically* and the observed *kinetically* controlled reduction potential of the halogen compound [eq. (a)]. Only in this case the carbanion exclusively formed at the electrodes will be able to reduce the starting compound. As we have found, *(1b)* ($E_{p/2} = -0.30$ V) can be reduced to the radical *(2b)* in homogeneous solution even by ferrocene ($E^0 = +0.42$ V *vs.* SCE, in CH_3CN/TBAP). This proves that the thermodynamic reduction potential is at least 0.7 V more positive than the irreversible half-peak potential at glassy carbon.

The controversy surrounding the mechanism of the electroreduction of the benzyl and allyl halides—carbanion[1c] *vs.* radical mechanism[1d]—is readily settled by this approach, since in the mechanism under discussion both carbanions as well as radicals occur as intermediates, either of which, depending upon the conditions, may be product-determining. Demonstration of such a reaction behavior is afforded by the facile indirect electroreduction of these halides with chromium(II) salts, which proceeds exclusively *via* radical dimerization[9].

Received: July 25, 1979 [Z 338 IE]
German version: Angew. Chem. *91*, 1002 (1979)

CAS Registry numbers:
(1a), 72087-82-2; *(1b)*, 72087-83-3; *(1c)*, 72087-84-4; *(2a)*, 72137-80-5; *(2b)*, 72137-79-2; *(2c)*, 72087-85-5; *(3)*, 72087-86-6; *(4)*, 14750-07-3

[1] a) *A. J. Fry:* Synthetic Organic Electrochemistry. Harper and Row, New York 1972, p. 170ff.; b) *R. Breslow, J. L. Grant*, J. Am. Chem. Soc. *99*, 7745 (1977); c) *A. J. Bard, A. Merz, ibid. 101*, 2959 (1979); d) *D. A. Koch, D. E. Bartak, ibid.*, in press.

[2] *(1b)* was prepared from *(3)* according to the procedure given in [3b]. *(1a)* was obtained by reaction of *(1b)* with KF in anhydrous acetonitrile (80%, m.p. 111 °C). Low yields of *(1c)*, m.p. 135 °C (dec), can also be prepared from *(3)*, in the two-phase system benzene/48% HBr/LiBr.

[3] a) *R. Kuhn, H. Fischer, F. A. Neugebauer, H. Fischer*, Justus Liebigs Ann. Chem. *654*, 64 (1962); b) *C. F. Koelsch*, J. Am. Chem. Soc. *79*, 4431 (1957); c) *K. H. Hausser*, Z. Naturforsch. *A 14*, 425 (1959).

[4] Glassy carbon was also used for the macroelectrodes in the coulometry experiments, so as to eliminate substrate-surface interactions; cf. [1c] and the experimental details cited therein. All values for potentials are referred to the saturated calomel electrode (SCE).

[5] *(2a)* and *(2b)* were identified by their electron excitation spectra and the ESR spectrum of *(2b)*. Further, *(2b)* and *(4)* [protonation product of *(2a)*] were isolated in preparative electrolyses. All the data are in agreement with those given in the literature[3].

[6] *C. F. Koelsch*, J. Am. Chem. Soc. *54*, 1744 (1932).

[7] This would be expected for the bromo compound *(1c)*; *(1c)*, however, ionizes in electrolytic media to *(2c)* and $Br^{\ominus}$ and thus defies measurement.

[8] *P. J. Elving*, Canad. J. Chem. *55*, 3392 (1977).

[9] *J. Wellmann, E. Steckhan*, Synthesis *1978*, 901.

Direct Removal of Functional Groups by Catalytic Hydrogenolysis[**]

By *Wilhelm F. Maier, Peter Grubmüller, Irina Thies, Peter M. Stein, M. Anthony McKervey*, and *Paul von Ragué Schleyer*[*]

The removal of functional groups from organic molecules to yield the parent hydrocarbon often requires multistep procedures; yields may be poor particularly if the functional group is tertiary. For example, the replacement of carboxylic acid, ester, amide, nitrile, ether, alcohol, or amine functions by hydrogen is usually accomplished by indirect methods[2].

Following the discovery that a variety of alkyladamantanes can be dealkylated cleanly and efficiently by gas phase hydrogenolyses on nickel[1,3], we have investigated the gas phase hydrogenolytic removal of functional groups containing heteroatoms. Examples are listed in Table 1 and the course of reaction is apparent from Figure 1. We stress that these reactions are quite general and are not restricted to polycycloalkyl systems such as adamantane.

The experimental procedure involved a flow system in which each substrate was vaporized in a stream of hydrogen at atmospheric pressure (flow rate 20—25 ml/min) and passed through a horizontal catalyst bed consisting of 30% nickel on alumina. Products were collected in a cold trap in high yield and purity[1,2]. The optimum hydrogenolysis temperatures (Table 1) reflect differences in volatility and polarity of the substrates and their rate of passage through the catalyst bed. The results listed in Table 1 show that a wide range of heteroatomic functional groups can be replaced by hydrogen in excellent yields. Previously, synthetically useful catalytic hydrogenolyses were limited largely to carbon-halogen bonds[4] and protecting groups such as benzyl[4]. The direct defunctionalization of unactivated acids and alcohols is feasible

[*] Prof. Dr. P. v. R. Schleyer [+], Dr. W. F. Maier, Dr. P. Grubmüller, Dipl.-Ing. I. Thies, P. M. Stein
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, 8520 Erlangen (Germany)
Prof. Dr. M. A. McKervey
Department of Chemistry, University College, Cork (Ireland)
[+] To whom correspondence should be addressed.

[**] Catalytic Hydrogenolysis, Part 2. This work was supported by the Deutsche Forschungsgemeinschaft and the Deutscher Akademischer Austauschdienst.—Part 1: [1b].

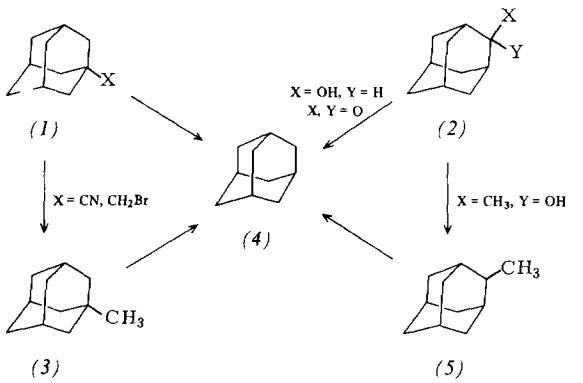


Fig. 1. Hydrogenolytic reactions on a 30% Ni/Al_2O_3 catalyst. Examples of *(1)* and *(2)* are given in Table 1.

Table 1. Summary of hydrogenolyses of adamantane derivatives.

No.	Reactant X	Y	T [°C]	Product	Yield [%]
(1a)	Br		200	*(4)*	97
(1b)	NH_2		240	*(4)*	99
(1c)	OH		180	*(4)*	97
(1d)	$OSiMe_3$		150	*(4)*	99
(1e)	CH_2OH		200	*(4)*	99
(1f)	COOH		240	*(4)*	90
(1g)	$COOCH_3$		240	*(4)*	71
(1h)	COCl		260	*(4)*	86
(1i)	CN		180	*(3)*	99
(1k)	CH_2Br		180	*(3)*	99
(1l)	$CO_2Si(CH_3)_3$		220	*(4)*	55
(3)			280	*(4)*	80
(2a)	=O		220	*(4)*	93
(2b)	OH	H	170	*(4)*	99
(2c)	CH_3	OH	150	*(5)*	99
(5)			235	*(4)*	99

only in special cases, whereas the direct defunctionalization of esters and ethers appears to be unknown, at least as a synthetically useful procedure. The reductive hydrogenolyses of a nitrile group to a methyl group has been observed in solution with a platinum catalyst[5]. However, the present gas-phase method using nickel allows product control by temperature variation; either 1-methyladamantane *(3)* or adamantane *(4)* can be obtained from 1-adamantanecarbonitrile *(1i)*. Similarly, the sterically crowded hydroxyl group in 2-methyl-2-adamantanol *(2c)* can be removed cleanly at 150 °C; at 235 °C the resulting 2-methyladamantane *(5)* is demethylated to give adamantane.

Particularly noteworthy is the quantitative conversion of 1-(trimethylsiloxy)adamantane (I, $X=OSiMe_3$) into adamantane at only 150 °C. The conversion of adamantanone *(3a)* into adamantane using the gas-phase hydrogenolytic procedure is superior to conventional solution methods[6]. Interesting differences in behavior are observed with closely related systems. Thus 1-adamantanemethanol *(1e)* suffers hydrogenolysis with loss of the carbon and oxygen atoms of the CH_2OH group whereas 1-bromomethyladamantane *(1k)* is converted into 1-methyladamantane *(3)* exclusively. Although hydrogenolysis of halogen-containing substrates leads efficiently to hydrocarbon, the catalyst is deactivated in the process and is no longer effective in dealkylation of methyladamantane. Such deactivation is not observed with oxygen containing functional groups. These observations may be relevant to the mechanism of catalytic defunctionalization.

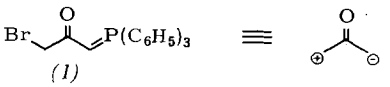
Received: August 6, 1979 [Z 339 IE]
German version: Angew. Chem. *91*, 1004 (1979)

[1] a) *P. Grubmüller, P. v. R. Schleyer, M. A. McKervey,* Tetrahedron Lett. *1979*, 181; b) *P. Grubmüller, W. F. Maier, P. v. R. Schleyer, M. A. McKervey,* Chem. Ber., in press.
[2] *T. Clark, M. A. McKervey,* Comprehensive Organic Chemistry. Pergamon Press, New York 1978, Vol. 1, p. 37.
[3] *P. Grubmüller,* Dissertation, Universität Erlangen-Nürnberg 1979.
[4] *M. Freifelder:* Catalytic Hydrogenolysis in Organic Synthesis, Procedures and Commentary. Wiley-Interscience, New York 1978; *A. P. G. Kieboom, F. v. Rantwijk:* Hydrogenation and Hydrogenolysis in Synthetic Organic Chemistry. Delft University Press, Rotterdam 1977; *M. Freifelder:* Practical Catalytic Hydrogenation. Wiley-Interscience, New York 1971.
[5] *K. Kindler, K. Lührs,* Chem. Ber. *99*, 227 (1966); Justus Liebigs Ann. Chem. *707*, 26 (1976).
[6] *J. W. Larsen, L. W. Chang,* J. Org. Chem. *44*, 1168 (1979).

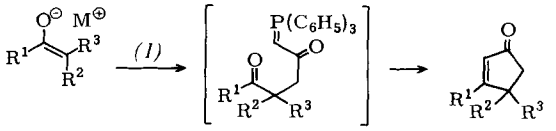
(Bromoacetylmethylene)triphenylphosphorane—A Novel Cyclopentannelating Agent

By *Hans-Josef Altenbach*[*]

Application of the principle of Robinson annelation for the preparation of cyclohexenones to the synthesis of cyclopentenones requires suitable electrophilic C_3 synthons. Since 1-haloacetones undergo smooth alkylation only in exceptional cases a series of electrophilic acetonyl systems has been developed in recent years[1], in which the ketone function is latent. In most cases, however, drastic conditions are necessary for liberation of the ketone. A potential alternative agent for the cyclopentannelation is the already known (bromoacetylmethylene)triphenylphosphorane *(1)*[2].

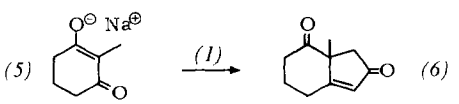


This easily accessible, stabilized ylide has a readily substitutable bromine atom[2b], while the keto group should not react even with hard nucleophiles such as enolates. Moreover, in the intermediate *(3)*, formed by alkylation of an enolate *(2)*, the ylide function should also cause cyclization by intramolecular Wittig reaction[3].



(a), $R^1 = CH_3$, $R^2 = H$, $R^3 = CO_2CH_2CH_3$, $M = Na$

In fact, *(1)* fulfills this expectation: Reaction with the sodium salt of ethyl acetoacetate *(2a)* in ethanol (3 h, 0 °C; 14 h reflux) affords the cyclopentenone *(4a)*[4], which after aqueous workup is isolated by distillation (b.p. 70—72 °C/0.4 torr; yield 39%). The anion of *(5)* prepared by reaction of 2-methyl-1,3-cyclohexanedione with sodium hydride likewise reacts with *(1)* in dimethylformamide (3 h, 0 °C, 16 h, 80 °C), to give the annelated product *(6)*[5] directly (m.p. 74—75 °C; yield 31%).



[*] Dr. H.-J. Altenbach
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0940 $ 02.50/0

This example demonstrates the advantage of ring closure by Wittig reaction: under the usual conditions 2-acetonyl-1,3-cyclohexanedione does not cyclize to *(6)* but undergoes fragmentation[5].

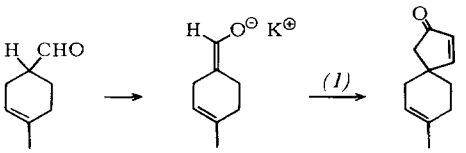
Cyclopentannelation with (bromoacetylmethylene)triphenylphosphorane *(1)* is not restricted to stabilized enolates. Reaction of the anion *(7a)*, generated by treatment of cyclohexanone with lithium diisopropylamide in tetrahydrofuran, with one equivalent of *(1)* at −20 °C affords, after 2 hours' stirring at 0 °C, 14 hours' boiling under reflux, and aqueous workup with pentane, the annelated cyclopentenone *(8a)*[6] (b.p. 50—52 °C/0.02 torr; yield 29%).



(a), R^1 = H, R^2 = H
(b), R^1 = H, R^2 = CH_3
(c), R^1 = CH_3, R^2 = H

(1) is sufficiently reactive towards the enolates *(7b)* (generated by reaction of 2-methyl-1-cyclohexenyl acetate with methyllithium[7]) and *(7c)* (obtained by reaction of 2-methylcyclohexanone with lithium diisopropylamide in tetrahydrofuran[7]) to form regioselectively *(8b)*[8] (yield 25%) and *(8c)*[2f] (yield 22%; mixture of diastereomers), respectively.

The method is also applicable to potassium enolates of aldehydes. If the aldehyde *(9)*[9] is deprotonated with potassium hydride in tetrahydrofuran[10] and the enolate is allowed to react with *(1)*, the spirocyclic compound *(10)*[11] can be isolated (b.p. 54—56 °C/0.1 torr; yield 14%).



(9) *(10)*

Received: August 13, 1979 [Z 341 IE]
German version: Angew. Chem. *91*, 1005 (1979)

[1] a) *P. T. Lansbury*, Acc. Chem. Res. *5*, 311 (1972); b) *R. B. Miller*, Synth. Commun. *2*, 267 (1972); c) *M. Miyano, C. R. Dorn*, J. Org. Chem. *37*, 268 (1972); d) *G. Stork, M. E. Jung*, J. Am. Chem. Soc. *96*, 3682 (1974); e) *S. F. Martin, T. S. Chou, C. W. Payne*, J. Org. Chem. *42*, 2520 (1977); f) *M. Miyashita, T. Yanami, A. Yoshikoshi*, J. Am. Chem. Soc. *98*, 4679 (1976); g) *R. M. Jacobson, R. A. Raths, J. H. McDonald*, J. Org. Chem. *42*, 2545 (1977).

[2] a) *K. Issleib, R. Lindner*, Justus Liebigs Ann. Chem. *713*, 12 (1968); b) *M. Le Corre*, C. R. Acad. Sci. *C 273*, 81 (1971).

[3] Stabilized ylides readily undergo the Wittig reaction only intramolecularly: *C. A. Hendrick, E. Böhme, J. A. Edwards, J. H. Fried*, J. Am. Chem. Soc. *90*, 5926 (1968).

[4] *L. J. Dolby, C. A. Elliger, S. Esfandiari, K. S. Marshall*, J. Org. Chem. *33*, 4508 (1968).

[5] *W. G. Dauben, D. J. Hart*, J. Org. Chem. *42*, 3787 (1977).

[6] *A. M. Islam, R. A. Raphael*, J. Chem. Soc. *1952*, 4086; *P. A. Grieco, C. S. Pogonowski*, J. Org. Chem. *39*, 732 (1974); *C. H. Heathcock, R. D. Clark*, Tetrahedron Lett. *1974*, 1713; *A. De Boer, R. E. Ellwanger*, J. Org. Chem. *39*, 77 (1974).

[7] *M. Gall, H. O. House*, Org. Synth. *52*, 39 (1972).

[8] *R. Fraisse-Jullien, C. Frejaville*, Bull. Soc. Chim. Fr. *1968*, 4449.

[9] *E. F. Lutz, G. M. Bailey*, J. Am. Chem. Soc. *86*, 3899 (1964); *G. I. Fray, R. Robinson, ibid. 83*, 249 (1961).

[10] *P. Groenewegen, H. Kallenberg, A. van der Glen*, Tetrahedron Lett. *1978*, 491.

[11] *D. A. McCrae, L. Dolby*, J. Org. Chem. *42*, 1607 (1977); *S. F. Martin, T. Chou, ibid. 43*, 1027 (1978); *E. Wenkert, B. L. Buckwalter, A. A. Craveiro, E. L. Sanchez, S. S. Sathe*, J. Am. Chem. Soc. *100*, 1267 (1978).

Dithiiranes and Thiosulfines as Reactive Intermediates[**]

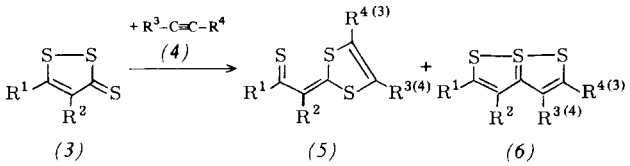
By *Alexander Senning*[*]

Little has hitherto been reported about the dithiiranes *(1)* and the isomeric thiosulfines *(2)*. The molecular geometry of the hypothetical dithiirane *(1a)* has, however, been calcu-



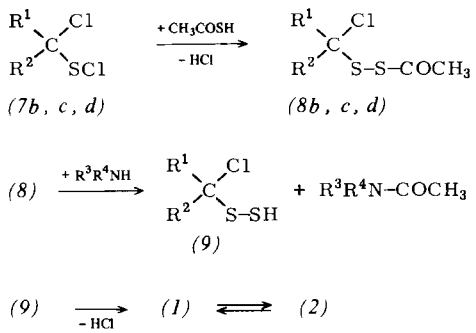
(a), $R^1 = R^2 = H$; *(b)*, $R^1 = R^2 = Cl$;
(c), $R^1 = C_6H_5S$, $R^2 = 4\text{-}CH_3C_6H_4SO_2$; *(d)*, $R^1 = R^2 = C_6H_5CO$

lated[1]. The formation of adducts *(6)*, together with *(5)*, on reaction of 1,2-dithiol-3-thiones *(3)* with alkynes *(4)*[2] can, in our opinion, be readily explained in terms of a preceding



(3) *(5)* *(6)*

rearrangement of *(3)* into *(2)*. Finally, in the mass spectra of some sulfur compounds, fragments occur which derive from *(1)* and/or *(2)*, *e.g. (1a)/(2a)* and *(1b)/(2b)*[3].

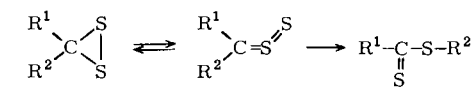


(7b, c, d) *(8b, c, d)*

(9)

We have developed a "wet" synthetic route starting from *(7)*, which conveniently leads *via (8)* (see Table 1) to the unstable α-chloroalkyldisulfanes *(9)* as precursors of *(1)* and/or *(2)*.

The intermediate *(1b)/(2b)* obtained from *(8b)*[4] and morpholine cannot be trapped with either alkynes or strained alkenes (*e.g.* norbornadiene) by cycloaddition, but rearranges



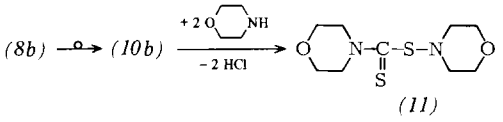
(1b, c) *(2b, c)* *(10b, c)*

to the dithioester *(10b)*, which on reaction with morpholine gives the stable product *(11)*[5]. Reaction of *(8c)* with morpholine analogously leads *via (10c)* to the stable products *(12)*[6] and *(13)*.

[*] Lektor fil. lic. A. Senning
Kemisk Institut, Aarhus Universitet
DK-8000 Århus C (Denmark)

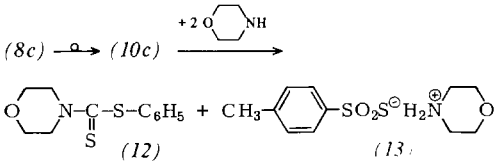
[**] Delivered in part as a lecture at the ACS/CSJ Congress in Honolulu, April 1979; Abstract ORGN 347.

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0941 $ 02.50/0*



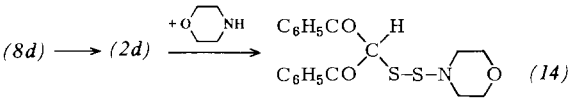
(11)

This novel rearrangement is analogous to the rearrangement of oxiranes into aldehydes or ketones[7] and to the hypothetical rearrangement of dioxiranes into esters (cf. [8]).



(12) (13)

The intermediate *(8d)* does not rearrange to *(10d)*. The end-product is formed immediately by addition of morpholine to *(2d)*.



(14)

Table 1. New compounds of type *(7)* and *(8)*.

Product	Yield [%]	M.p. [°C]
(7d) [a]	≥53	oil
(8c) [b]	74	85—87 (ethanol)
(8d) [b]	53 [c]	107—108 (ethanol)

[a] From $(C_6H_5CO)_2CH$ S S $CH(COC_6H_5)_2$, m.p. 162—166 °C [9]. [b] Synthesized by analogy with [4]. [c] Based on the disulfide [9].

Procedure

A solution of morpholine (0.6 mol) in ether or benzene (50 ml) is added dropwise to a stirred solution of *(8)* (0.1 mol) in 100 ml of the same solvent at such a rate that the temperature does not increase noticeably. The reaction mixture is extracted three times with water and the organic phase is dried over $CaCl_2$ and evaporated to dryness in a rotary evaporator. The crude product crystallizing on trituration in ether is recrystallized from ethanol [*(8b)*→*(11)*[5], yield 22%; *(8c)*→*(12)*[6], yield 60%; *(8d)*→*(14)*, m.p. 121—122 °C, yield 25%].

Received: August 16, 1979 [Z 343 IE]
Supplemented: September 10, 1979
German version: Angew. Chem. *91*, 1006 (1979)

CAS Registry numbers:
(7b), 594-42-3; *(7c)*, 59534-02-0; *(7d)*, 72087-87-7; *(8b)*, 72087-88-8; *(8c)*, 72087-89-9; *(8d)*; 72087-90-2; *(10b)*, 72087-91-3; *(10c)*, 72087-92-4; *(11)*, 13752-51-7; *(12)*, 51861-57-5; *(13)*, 72087-93-5; *(14)*, 72087-94-6; ethanethioic acid, 507-09-5; morpholine, 111-91-8; 2,2'-dithiobis(1,3-diphenyl-1,3-propanedione), 72087-95-7

[1] *J. P. Snyder, L. Carlsen*, J. Am. Chem. Soc. *99*, 2931 (1977); cf. *S. J. Arnold, W. G. Brownlee, G. H. Kimbell*, J. Phys. Chem. *74*, 8 (1970); *G. Calzaferri, R. Gleiter*, J. Chem. Soc. Perkin Trans. II *1975*, 559; *J. W. Hudgens, J. T. Gleaves, J. D. McDonald*, J. Chem. Phys. *64*, 2528 (1976).

[2] *A. Dibo*, Dissertation, Université de Caen 1978.

[3] *K. Morita, S. Kobayashi*, Tetrahedron Lett. *1966*, 573; *H. D. Hartzler*, J. Am. Chem. Soc. *95*, 4379 (1973); *H.-J. Kyi, K. Praefcke*, Tetrahedron Lett. *1975*, 555; *S. Kaae, A. Senning*, Acta Chem. Scand. *22*, 159 (1968); *N. R. Zack, J. M. Shreeve*, J. Fluorine Chem. *5*, 153 (1975).

[4] *R. S. Hawley, A. R. Kittleson*, US-Pat. 2553777 (1951), Standard Oil Development; Chem. Abstr. *45*, 7742 (1951).

[5] *R. D. Taylor*, US-Pat. 3985743 (1976), *B. F. Goodrich*; Chem. Abstr. *86*, 30837 (1978).

[6] *K. Matsushima, A. Kudamatsu, M. Miyamoto*, Noyaku Seisan Gijutsu *14*, 31 (1966); Chem. Abstr. *67*, 43534 (1967).

[7] *G. Dittus* in Houben-Weyl-Müller: Methoden der Organischen Chemie. Thieme, Stuttgart 1965, Vol. VI/3, p. 435.

[8] *W. v. E. Doering, E. Dorfman*, J. Am. Chem. Soc. *75*, 5595 (1953).

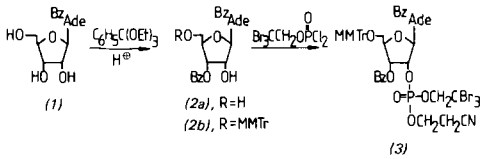
[9] *A. Senning*, unpublished work.

Directed Synthesis of the Trimeric Isoadenylate A2′p5′A2′p5′A

By *Joachim Engels* and *Ute Krahmer*[*]

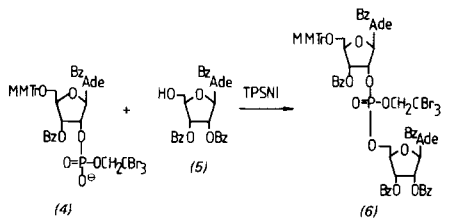
A trimeric oligoadenylate with the "unnatural" linkage 2′-5′ has been isolated from interferon-treated cells[1]. This so-called isoadenylate A2′p5′A2′p5′A inhibits protein biosynthesis in sub-nanomolar concentrations and promises to give new impetus to virus therapy[2].

We report here on a novel directed synthesis of A2′p5′A2′p5′A *(9)* according to the triester method, which enables preparation of the compound on the gram scale. Reaction of the readily accessible N^6-benzoyladenosine *(1)*[3] with orthobenzoic triethyl ester[4] (CCl_3COOH in dioxane) and hydrolysis of the resulting orthoester with 4% aqueous acetic acid afforded dibenzoyladenosine *(2a)* (m.p. 194 °C).



(1) (2a), R=H (2b), R=MMTr (3)

Subsequent reaction of *(2a)* with monomethoxytrityl chloride (MMTrCl) in pyridine at room temperature led to the 5′-substituted derivative *(2b)* in 96% yield, which on phosphorylation with (tribromoethyl)phosphoric dichloride in the presence of triazole and *N*-propylimidazole, followed by 3-hydroxypropionitrile, gave, after chromatography on silica gel ($CHCl_3$/MeOH 25:1), the fully protected nucleoside 2′-phosphate *(3)* in 82% yield. The triester *(3)* could be quantitatively converted with NEt_3 in pyridine/H_2O (1:2:1) into the diester *(4)*, which was condensed with tribenzoyladenosine *(5)* (m.p. 185 °C) and TPSNI (triisopropylbenzenesulfonylnitroimidazolide)[5] to give the dinucleoside phosphate *(6)* in 90% yield.



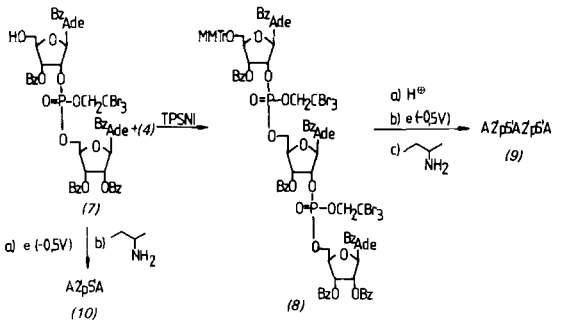
(4) (5) (6)

For proof of the structure, *(6)* was converted with BF_3/MeOH in CH_2Cl_2 into *(7)* (91% yield) and reduced electrochemically (Hg cathode, CH_3CN, $+Bu_4NBF_4$, lutidine)[6]. After extraction of the supporting electrolyte with $CHCl_3$ the aqueous phase was freeze-dried and debenzoylated with *sec*-butylamine in MeOH to A2′p5′A *(10)* (90% yield). The identity of *(10)* with authentic A2′p5′A (Serva) was confirmed chromatographically on PEI-cellulose (NH_4HCO_3) and by liquid chromatography (Polygosil 60-10 $N(CH_3)_2$ from Macherey-Nagel with 0.03 M NH_4HCOO (pH = 6.2) and 3% CH_3CN). According to the liquid chromatogram, less than 2% A3′p5′A is formed.

The dinucleoside phosphate *(7)* was converted with the diester *(4)* and TPSNI into the completely protected trimer *(8)* in 84% yield. For conversion into the native trimeric isoadenylate *(9)* the triester *(8)* was first detritylated (BF_3/MeOH in CH_2Cl_2) and then electrolyzed (Hg cathode, CH_3CN, $LiClO_4$, lutidine)[6]. The diester recovered by ex-

[*] Priv.-Doz. Dr. J. Engels, U. Krahmer
Fachbereich Chemie der Universität
Universitätsstrasse 10, D-7750 Konstanz (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0942 $ 02.50/0



traction with $CHCl_3$ was debenzoylated with *sec*-butylamine in MeOH. Purification [DEAE-cellulose column (0.1—0.3 M NEt_3HCO_3) and RP 8 (H_2O)] afforded crystalline *(9)* as the triethylammonium salt in 70% yield. The ^{1}H-NMR spectrum [D_2O, adenine-H: 7.76, 7.90, 7.95, 7.97, 8.08, 8.17; H1' (doublet): 5.82, 5.92, 6.17] and chromatogram [PEI-cellulose (NH_4HCO_3)] are consistent with the data in the literature[7]. As expected *(9)* is cleaved enzymatically by phosphodiesterase from snake venom but not by phosphodiesterase from spleen[8].

Received: August 1, 1979 [Z 346 IE]
German version: Angew. Chem. *91*, 1007 (1979)

[1] *I. M. Kerr, R. E. Brown*, Proc. Nat. Acad. Sci. USA *75*, 256 (1978); *A. Zilberstein, A. Kimchi, A. Schmidt, M. Revel, ibid. 75*, 4734 (1978).
[2] *L. Carrasco*, Nature *272*, 694 (1978).
[3] *R. H. Hall*, Biochemistry *3*, 6 (1964).
[4] *C. B. Reese*, Tetrahedron *34*, 3143 (1978).
[5] *J. H. van Boom, P. M. J. Burgers, G. van der Marel, C. H. M. Verdegaal, G. Wille*, Nucl. Acids Res. *4*, 1047 (1977).
[6] *J. Engels*, Angew. Chem. *91*, 155 (1979); Angew. Chem. Int. Ed. Engl. *18*, 148 (1979).
[7] *E. M. Martin, N. J. M. Birdsall, R. E. Brown, I. M. Kerr*, Eur. J. Biochem. *95*, 295 (1979).
[8] *K. K. Ogilvie, N. Y. Theriault*, Tetrahedron Lett. *1979*, 2111.

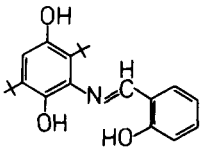
Detection of Heavy Metal Ions by ESR Spectroscopy[**]

By *Hartmut B. Stegmann, Martin Schnabel,* and *Klaus Scheffler*[*]

The high sensitivity and the pronounced selectivity of ESR spectroscopy have prompted us to examine the potential of this method for the detection of heavy metal ions. The proposed technique requires ligands which form complexes with cations and can subsequently be transformed into paramagnetic systems. Moreover, both the complex and the free ligand should be insoluble in water in order to permit two-phase reactions. These requirements are satisfied, for example, by 3,6-di-*tert*-butyl-2-(2-hydroxybenzylidenamino)hydroquinone *(1)*[1].

The ligand *(1)* reacts in pyridine with $Pb^{2\oplus}$, $Zn^{2\oplus}$, or $Cd^{2\oplus}$ to form chelates which are oxidized to paramagnetic complexes by atmospheric oxygen, silver oxide, or lead dioxide. Some experimental values are listed in Table 1.

The spectra of two paramagnetic species can be observed simultaneously in the *(1)*/$Et_2Tl^{\oplus}$ system[2]. The complex *(5)* shows the metal splitting given while the other signal consists merely of a doublet due to a proton. We assign this signal to



(1)

Table 1. ESR data of the heavy metal complexes formed from *(1)* and various cations in pyridine at room temperature.

Complex	Cation	a_H [G]	a_{Metal} [G]	ΔH [G]	g
(2)	$Pb^{2\oplus}$	3.95	7.3	0.45	1.9993
(3)	$Zn^{2\oplus}$	4.00	—	0.45	2.0046
(4)	$Cd^{2\oplus}$	3.90	^{111}Cd 3.95 [a] ^{113}Cd 4.13 [a]	0.35	2.0044
(5) [b]	$Et_2Tl^{\oplus}$	3.25	11.75	0.60	2.0035
(6)	"free"	2.35	—	0.35	2.0048

[a] Determined by spectral simulation. [b] Diethylthallium hydroxide was provided by *U. Bergler*.

the free ligand *(6)*. Its proton coupling constant is considerably smaller and thus reveals the failure of complex formation to take place.

As a result of the different g factors and metal splitting it is possible to detect several ions simultaneously. Figure 1 shows the hyperfine structure observed on reaction of *(1)* with $Cd^{2\oplus}$ and $Pb^{2\oplus}$ ions in pyridine. The lines marked × correspond to the chelate *(4)*, whereas the unmarked lines are assigned to the chelate *(2)*.

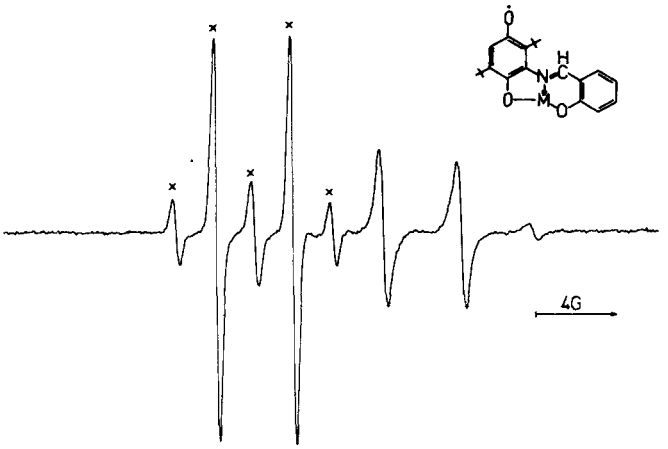


Fig. 1. ESR spectra of the $Cd^{2\oplus}$ chelate *(4)* (×) and the $Pb^{2\oplus}$ chelate *(2)* in pyridine at room temperature.

The above cations can also be detected if they are present in aqueous phase. The aqueous solution is shaken with a benzene solution of the ligand *(1)* in the presence of 10% of pyridine. After separation, the organic phase is dried over sodium sulfate and transferred directly to the ESR sample tube. Some lead dioxide may be added as oxidizing agent. The ESR parameters of the resulting complex agree with the values listed in Table 1. Working in this way with a 10^{-6} molar solution of zinc acetate and a 10^{-2} mol/l concentration of the ligand *(1)* in the organic phase the signal of *(3)* can be recognized without difficulty with a signal to noise ratio of 15:1. This sensitivity can be increased by two orders of magnitude on computerized spectral accumulation.

[*] Prof. Dr. H. B. Stegmann [+], Prof. Dr. K. Scheffler, M. Schnabel
Institut für Organische Chemie der Universität
Auf der Morgenstelle 18, D-7400 Tübingen 1 (Germany)
[+] To whom correspondence should be addressed.

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

Received: August 6, 1979 [Z 347 IE]
German version: Angew. Chem. 91, 1007 (1979)

[1] The compound *(1)* is formed by reaction of 2-amino-3,5-di-*tert*-butylhydroquinone with 2-hydroxybenzaldehyde.

[2] *K. B. Ulmschneider, H. B. Stegmann, K. Scheffler, G. Viertel*, Z. Naturforsch. *B 33*, 237 (1978).

Structure and Reactions of Methylenesulfur Tetrafluoride[**]

By *Hans Bock, James E. Boggs, Gert Kleemann, Dieter Lentz, Heinz Oberhammer, Eva Maria Peters, Konrad Seppelt, Arndt Simon,* and *Bahman Solouki*[*]

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

$H_2C{=}SF_4$ is easily prepared by reaction of $SF_5{-}CH_2Br$ and n-C_4H_9Li at $-110\,^{\circ}C$[1]. This methylene compound is thermally more stable than all known phosphorus and sulfur ylides and metal carbene complexes. In the gaseous state at 10^{-2} torr, it is stable up to 650 °C. The vibrational spectra[2] and the ^1H-, ^{13}C-, and ^{19}F-NMR spectra[1] are in agreement with an ylidic double bond.



The resonance formula with the double bond, however, is much more important than in other ylides: the spectroscopic bond order is 1.8[2]; the charge on the carbon atom is −0.6, as calculated by *ab initio* methods[3].

These findings are supported by the photoelectron spectrum (Fig. 1). This shows a single band at 10.65 eV which is assigned to π_{CS} ionization. Compared with phosphorus ylides, which have first ionization potentials below 7 eV[4], in $H_2C{=}SF_4$ the energy difference to the radical cationic state is increased by the fluorine substitution.

Formal addition of (excited[4b]) CH_2 to the F_4S sulfur electron pair (cf. Fig. 1) generates the π_{CS}- and σ_{CS} bonds[4]; the radical cationic states of the type n_F and σ_{SF} remain nearly unchanged[5].

The IR, Raman, NMR, or PE spectra do not readily indicate the orientation of the methylene group or its possible axial ⇌ equatorial interchange, *e.g.* by pseudorotation of the trigonal bipyramidal F_4SC skeleton. The NMR data, however, indicated that the probably planar H_2C group must be oriented either axially (a) or equatorially (e).

[*] Priv.-Doz. Dr. K. Seppelt [+], Dipl.-Chem. G. Kleemann, Dr. D. Lentz
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)
Prof. Dr. H. Bock, Dr. B. Solouki
Institut für Anorganische Chemie der Universität
Niederurseler Hang, D-6000 Frankfurt am Main 50 (Germany)
Prof. J. E. Boggs
Department of Chemistry, University of Texas
Austin, Texas 78712 (USA)
Prof. Dr. H. Oberhammer
Institut für Physikalische und Theoretische Chemie der Universität
Auf der Morgenstelle 8, D-7400 Tübingen 1 (Germany)
Prof. Dr. A. Simon, Dipl.-Chem. E. M. Peters
Max-Planck-Institut für Festkörperforschung
Heisenbergstrasse 1, D-7000 Stuttgart 80 (Germany)
[+] To whom correspondence should be addressed.

[**] This work was supported by the Fonds der Chemischen Industrie, the Deutsche Forschungsgemeinschaft, and the Robert A. Welch Foundation.

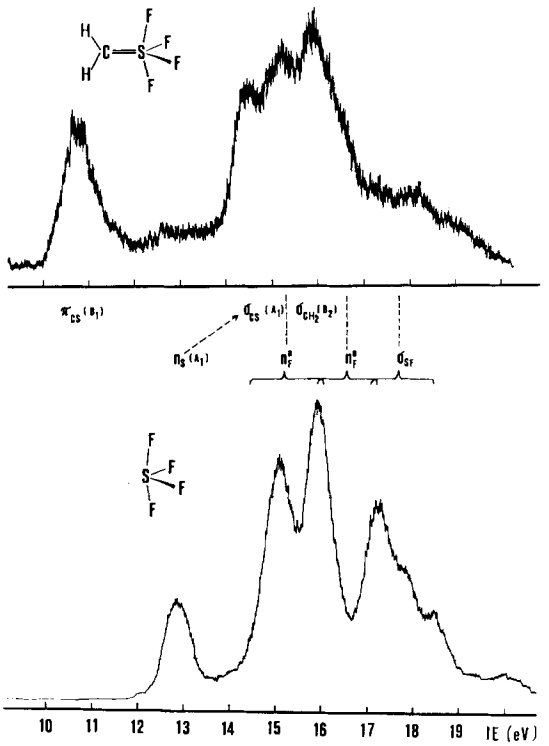


Fig. 1. He(I) PE spectrum of $H_2C{=}SF_4$ with qualitative assignment by comparison with SF_4.

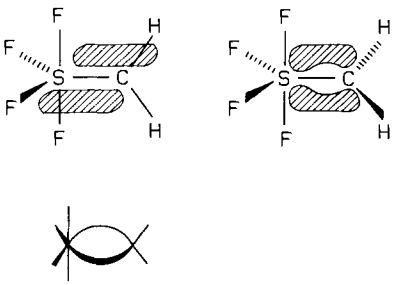


Fig. 2. Structural possibilities of $H_2C{=}SF_4$. According to the valence shell electron pair repulsion model the observed "axial" position of the protons is preferred. Qualitatively the observed structure (left) may be rationalized by linking a tetrahedron with an octahedron through two bent bonds.

Low temperature crystal structure analysis[6], electron diffraction[8], and an *ab initio* calculation (Table 1) all resulted in a trigonal bipyramidal structure similar to that of SF_4, but with a much smaller equatorial angle FSF. The methylene group is oriented in the plane of the axial fluorine atoms. This can be explained by the valence shell electron pair repulsion model: Only in this configuration can the π_{CS} electron density easily be accommodated, and the equatorial

Table 1. Structural data of $H_2C{=}SF_4$.

		Crystal structure [6]	Electron diffraction [7]	*ab initio* SCF [3]
Distances [pm]	S–F_a	159.2, 159.4	159.5 (15)	159.1
	S–F_e	156.0, 156.1	157.5 (15)	156.2
	S=C	155.3	155.0 (20)	154.2
	C–H	(82.2, 92.2)	108 [a]	106.6
Angles [°]	F_aSF_a	170.44	170.0 (2.0)	169.9
	F_eSF_e	96.44	97.0 (2.0)	98.8
	HCH	120.91	122.0 [a]	123.3

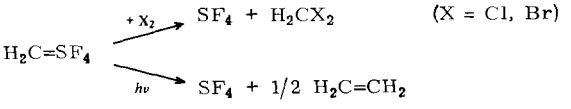
[a] Estimated.

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0944 $ 02.50/0

fluorine atoms are brought closer together (see Fig. 2). The distance between the axial fluorine atoms and the hydrogen atoms is only 240 pm; however, no evidence of H...F bridges is apparent from the spectroscopic data.

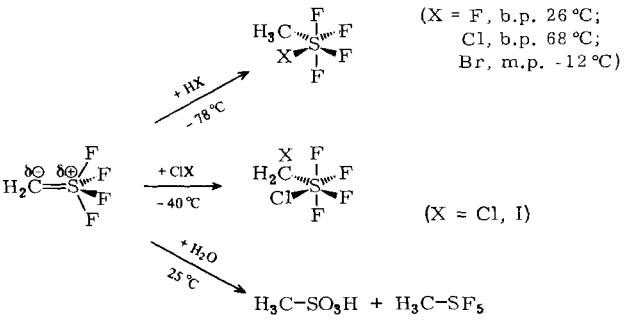
The SCF geometrical optimization shows that the isomer with an equatorially oriented CH_2 group is unstable, and that a high torsional barrier exists, with an estimated value of 77 kcal/mol[3].

In spite of its thermal stability, $H_2C{=}SF_4$ is very reactive. Reactions with halogens or photolysis yield SF_4.

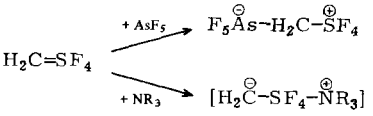


Free carbene has not yet been detected as an intermediate in these reactions (however irradiation of diluted diazomethane also yields large amounts of ethylene[8]).

With polar reagents, addition to the C=S bond occurs.



The addition products are hydrolytically stable liquids having an octahedral *cis*-configuration. The polarity of the C=S bond is indicated by two further reactions: Lewis acids interact with the carbon atom, while Lewis bases attack the sulfur atom:



The trimethylamine adduct is unstable at room temperature. The AsF_5 adduct, however, is stable enough to be characterized by the usual analytical and spectroscopic methods.

Received: July 24, 1979 [Z 334 IE]
German version: Angew. Chem. *91*, 1008 (1979)

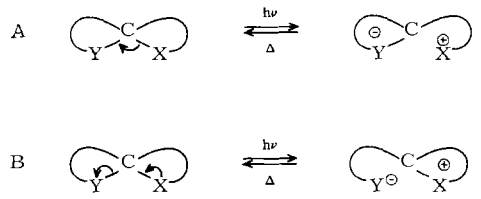
CAS Registry numbers:
Methylenesulfur tetrafluoride, 66793-25-7; sulfur fluoride (SF_4), 7783-60-0; dichloromethane, 75-09-2; dibromomethane, 74-95-3; ethene, 74-85-1; pentafluoromethylsulfur, 753-79-7; chlorotetrafluoromethylsulfur, 72161-32-1; bromotetrafluoromethylsulfur, 72161-33-2; chloro(chloromethyl)tetrafluorosulfur, 72161-34-3; chlorotetrafluoro(iodomethyl)sulfur, 72161-35-4; methanesulfonic acid, 75-75-2; arsenic pentafluoride, 7784-36-3; methylenesulfur tetrafluoride adduct with arsenic pentafluoride (1:1), 72152-12-6

[1] *G. Kleemann, K. Seppelt*, Angew. Chem. *90*, 547 (1978); Angew. Chem. Int. Ed. Engl. *17*, 516 (1978).
[2] *S. Sunder, H. H. Eysel, G. Kleemann, K. Seppelt*, Inorg. Chem., im Druck.
[3] The SCF program Texas by *P. Puley* (Theor. Chim. Acta, in press) was used for the geometrical optimisation. The basis set (F: 4-21, C: 4-21, S: 3-3-21) was enlarged by $3d_s$ functions.
[4] a) *H. Bock*, Pure Appl. Chem. *44*, 343 (1975) and references cited therein; b) *K. A. Ostoja Starzewski, H. Bock*, J. Am. Chem. Soc. *98*, 8486 (1976).
[5] *N. Rösch, V. H. Smith, M. H. Whangbo*, Inorg. Chem. *15*, 1768 (1976) and references cited therein.
[7] Measurement at −160 °C, space group $P2_12_12_1$, $a = 814.6$ (5) pm, $b = 856.0$ (5) pm, $c = 563.3$ (4) pm, $Z = 4$.
[8] In addition to the electron diffraction a microwave investigation is being performed by *W. Zeil* and *H. Krämer*.
[8] *H. M. Frey*, J. Am. Chem. Soc. *82*, 3947 (1960).

1,8a-Dihydroindolizines as Components of Novel Photochromic Systems

By *G. Hauck* and *H. Dürr*[*]

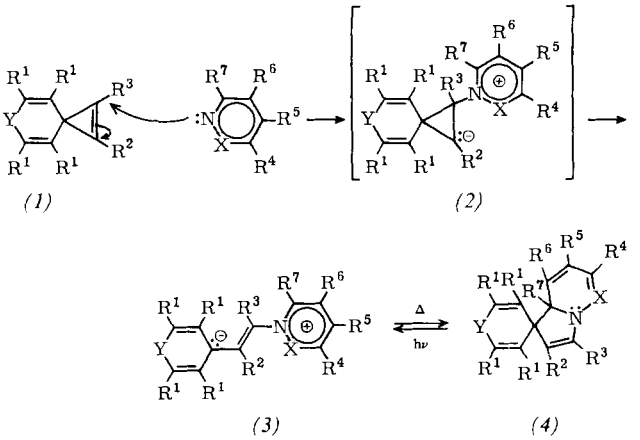
Photochromic systems are currently attracting a great deal of interest. The light-induced formation of colored products can be utilized in silver-free photography (*inter alia* "microimaging systems"), in the production of light-filtering tinted glasses or in data display systems (*e.g.* in computers)[1]. Of topical interest is the potential use of reversible photochromic substances as solar energy storage systems[2]. We describe here a novel photochromic system based on 1,8a-dihydroindolizines (Scheme 1, type A) whose photochromism arises from bond heterolysis[1]. The essential difference between A and the photochromic spiropyrans or rhodamine derivatives[3] (type B) is apparent from Scheme 1.



Scheme 1. Comparison of the photochromic systems of type A (1,8-dihydroindolizines) and type B (spiropyrans or rhodamine derivatives). X = electron donor, Y = electron acceptor.

In case B the electron acceptor Y can only be a heteroatom, whereas in A it can also be a substituted C-atom.

For the synthesis of the photochromic 1,8a-dihydroindolizines *(4)* we allowed cyclopropenes *(1)*[4] to react with *N*-heterocycles in ethereal solution at room temperature. As a rule quantitative yields of colorless to yellow[5] 1:1 adducts were formed, which, on the basis of ^{1}H-NMR, IR, UV and mass spectroscopic data, were assigned the structure 1,8-dihydroindolizines *(4)* (Table 1)[6], a class of compound hitherto rarely taken into consideration because of alleged instability[7]. The synthesis of *(4)* proceeded *via* the intermediate *(2)* and the deep-colored zwitterionic intermediate *(3)*. Only in very few cases (see Table 1) could *(3)* be isolated since it spontaneously reacts further to give *(4)*. The betaine *(3)* was decolorized on addition of acid, a reaction which is reversible with bases.



As demonstrated by the examples *(3g,f)*→*(4g,f)* the cyclization is regiospecific. However, the alternative possibility of

[*] Prof. Dr. H. Dürr, Dipl.-Chem. G. Hauck
Institut für Organische Chemie der Universität
D-6600 Saarbrücken (Germany)

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0945 $ 02.50/0*

Table 1. Data of the betaines *(3)* and the 1,8a-dihydroindolizines *(4)*, $R^2 = R^3 = CO_2CH_3$. Of the betaines *(3f)* and *(3k)* could be isolated.

	Y [a]	R^1	X	R^4	R^5	R^6	R^7	*(4)* M.p. [°C]	*(4)* Yield [%]	*(4)* λ_{max} [nm] (ε)	*(3)* λ_{max} [nm] ($CHCl_3$)	*(3)* k (20 °C) [s^{-1}] ($CHCl_3$)
a	—	CH=CH	CH	H	H	H	H	135	63	384 (10500)	586	4.88×10^{-3}
b	—	CH=CH	CD	D	D	D	D	138	73	383	586	3.4×10^{-3}
c	—	CH=CH	CH	H	OCH_3	H	H	145–147	73	376 (7730)	552	11.0×10^{-3}
d	H, H	CH=CH	CH	H	CH=CH	CH=CH	H	162	52	385 (13380)	572	1.2×10^{-5}
e	—	CH=CH	CH	H	CH=CH	CH=CH	H	162	78	378 (14390)	600	40 [b]
f	—	CH=CH	CCH_3	H	H	H	H	130	31	383 (11100)	570	2.21×10^{-3}
g	—	CH=CH	N	H	H	H	H	146	74	389 (9480)	505	14×10^{-3}
h	—	CH=CH	C CH=CH	CH=CH	H	H	H	192	84	360 (15400)	724	2.7 [b]
i	—	CH=CH	C CH=CH	CH=CH	H	H	CH_3	236	40	363 (12250)	726	0.1 [b]
j [d]	—	CH=CH	CH	H	H	H	H	184	12	376 (10600)	694	832 [b]
k	—	Ph	CH	H	H	H	H	194	89	392 (11300)	629	27.7 [b, c]
l	C=O	CH=CH	CH	H	H	H	H	183	61	388 (8260)		

[a] A dash signifies direct linkage. [b] Determined flash photolytically by Dr. *Hermann*, Mülheim/Ruhr (Germany). [c] Cyclization in two partial steps; the values given are based on the fast step which is neither 1st order nor 2nd order. [d] $R^3 = H$.

ring closure can be brought about if a position is blocked by benzoannelation. This has been proven by the synthesis of the benzo derivative *(4i)* methylated on C-8a. The thermal back reaction *(3)*→*(4)* is of first order, with rate constant k depending on the polarity of the solvent medium and on the resonance and inductive effects of the substituents.

The destabilization of the positive charge by annelated benzene rings is especially effective in *(3)*. But also lack of stabilization of the carbanion by removal of an electron acceptor substituent leads to a drastic reduction in the rate constant k. The longwave absorption maxima of *(3)* show a remarkably strong hypsochromism, thus indicating that an intramolecular charge-transfer—as is observed in the case of the vinylogous pyridinium cyclopentadienylides[8]—is responsible for the color of the betaine *(3)*. The activation parameters of the thermal cyclization *(3a)*→*(4a)* in benzene are: $\Delta G^{\ddagger} = 6.3$ kcal/mol, $E_A = 15.9$ kcal/mol, $\Delta S^{\ddagger} = -32$ cal K^{-1} mol^{-1} (determined UV spectroscopically). The 1,2,3,8a-tetrahydroindolizines accessible by hydrogenation of *(4)* are also photochromic[9], even if to a lesser degree than *(4)*.

Procedure

Synthesis of *(4c)*: 0.52 g (4.80 mmol) of 4-methoxypyridine is added with stirring at room temperature and in the absence of light to a suspension of dimethyl spiro[cyclopropene-1,9′-fluorene]-2,3-dicarboxylate (1.47 g, 4.80 mmol) in anhydrous diethyl ether (40 ml). After 24 h some of the solvent is removed and, on cooling the solution, bright yellow crystals begin to separate out. These are filtered off and washed with pre-cooled ether; yield 1.74 g. IR: 1740 and 1700 (C=O) cm^{-1}; ^{1}H-NMR ($CDCl_3$): $\delta = 3.10$ (s, 3H, OCH_3), 3.27, 4.00 (s, each 3H, CO_2CH_3), 3.35 (mc, 8-H), 5.08 (dd, $J_{6,5} = 8$ Hz, 6-H), 5.63 (s, 8a-H), 6.49 (d, $J_{5,6} = 8$ Hz, 5-H), 7.3—7.9 (8 aromatic-H); MS: $m/e = 415$ (M^+), 356 ($M^+ - CO_2CH_3$).

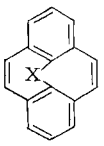
Received: August 27, 1979 [Z 342 IE]
German version: Angew. Chem. *91*, 1010 (1979)

[1] *G. H. Brown* in: Photochromism. Wiley-Interscience, New York 1971.
[2] *T. Laird*, Chem. Ind. (London) *1978*, 186.
[3] *K.-H. Knauer, R. Gleiter*, Angew. Chem. *89*, 116 (1977); Angew. Chem. Int. Ed. Engl. *16*, 113 (1977).
[4] *H. Dürr, B. Ruge*, Angew. Chem. *84*, 215 (1972); Angew. Chem. Int. Ed. Engl. *11*, 225 (1972); *L. Schrader*, Chem. Ber. *104*, 941 (1971); *G. Ege*, Tetrahedron Lett. *1963*, 1667; *H. Reimlinger*, Chem. Ber. *100*, 3097 (1967).
[5] On shortening the chromophore by benzoannelation colorless 1,8a-dihydroindolizines are formed; cf. λ_{max} of *(4h)* and *(4i)*.
[6] *M. L. Deem*, Synthesis *1972*, 675.
[7] *E. Pohjola*, Tetrahedron Lett. *1972*, 2585; *N. S. Basketter, A. O. Plunkett*, J. Chem. Soc. Chem. Commun. *1975*, 594; *E. Winterfeldt*, Chem. Ber. *98*, 3537 (1965).
[8] *E. M. Kosower, B. G. Ramsey*, J. Am. Chem. Soc. *81*, 856 (1959).
[9] *H. Dürr, K.-D. Zils, G. Hauck*, unpublished work.

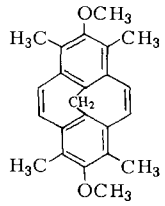
8,16-Methano[2.2]metacyclophane-1,9-diene. A Valence Isomer of 10b,10c-Methano-*cis*-10b,10c-dihydropyrene[**]

By *Kazuhiro Nakasuji, Masanori Katada*, and *Ichiro Murata*[*]

Although much attention has recently been focused on *trans*-10b,10c-dihydropyrenes and their photoisomerization to the corresponding metacyclophane valence isomers[2], little is known about *cis*-10b,10c-dihydropyrene/metacyclophane isomers. The only previous examples known are the bridged and/or highly substituted derivatives *(1)*[3a], *(2)*[3b], and *(4)*[3c]. We now report the preparation of the methano-bridged [2.2]metacyclophane-1,9-diene *(3)*, a valence isomer of 10b,10c-methano-*cis*-10b,10c-dihydropyrene *(3a)*.



(1), X = O
(2), X = NR
(3), X = CH_2



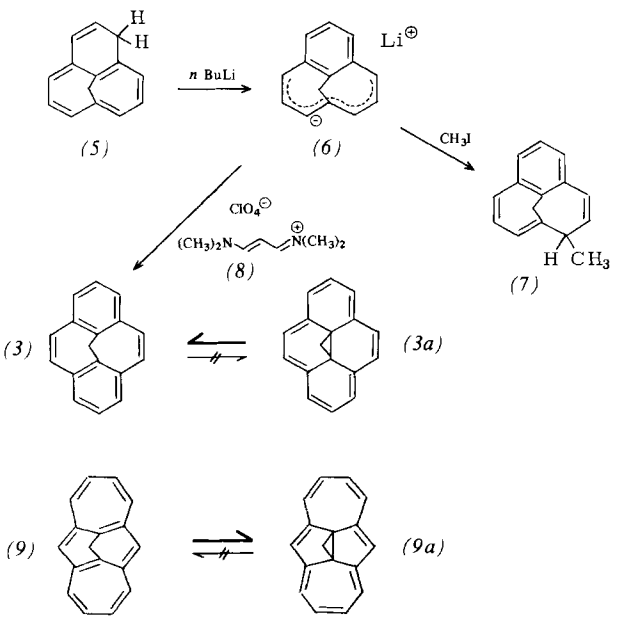
(4)

10,11-Homophenalene *(5)* readily undergoes proton abstraction with *n*-butyllithium to give anion *(6)* which upon reaction with methyl iodide gives the methylated hydrocarbon *(7)*[1]. Thus, it could be expected that *(5)* would undergo six-membered ring annelation in analogy to the formation of pyrene from phenalene as reported by *Jutz*[4]. This was found to be the case. Treatment of a tetrahydrofuran solution of *(5)* with 1.5 eq. of *n*-butyllithium in the presence of hexamethylphosphoramide gives a deep green solution of the anion *(6)*. On treatment with dimethyl(3-dimethylaminopropenyli-

[*] Dr. K. Nakasuji, M. Katada, Prof. Dr. I. Murata [†]
Department of Chemistry, Faculty of Science, Osaka University
Toyonaka, Osaka 560 (Japan)
[†] Correspondence should be addressed to this author.

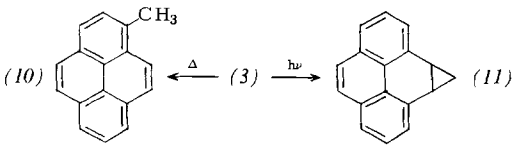
[**] The Chemistry of the Phenalenium System, Part 28.—Part 27: [1].

dene)ammonium perchlorate *(8)*[5] at −55 °C for 0.5 h this solution yields an intermediate fulvene which was not isolated. In order to effect cyclization of the fulvene to *(3)*, the solvent is replaced by quinoline and the solution is heated at 170 °C for 12 h. After the usual work-up the crude product is purified by column chromatography over alumina with hexane. The desired compound *(3)* was obtained as colorless needles, m.p. 140 °C (sealed capillary), in 35% yield[6]. Its structural assignment is supported by its NMR spectrum [singlets at $\delta = 2.53$ (2H) and 7.29 (4H); AB_2 pattern at $\delta = 6.83$ (A part) and 7.30 (B part) with $J_{AB} = 8.7$ Hz]. The UV absorption spectrum of *(3)* is very similar to those of *(1)*[3a] and *(2)*[3b] [λ_{max} (cyclohexane) = 223 nm ($\varepsilon = 28\,800$), 236 (27 400), 246 (28 200), 305 (14 700)]. In the mass spectrum of *(3)* [$m/e = 216$ (M^+, 100%), 215 ($M^+ - H$, 75%)] a peak due to loss of the bridged methano group, though very weak, was also observed [$m/e = 202$ ($M^+ - CH_2$, 3%)]. These spectral findings indicate that, of the two valence isomers *(3)* and *(3a)*, only the metacyclophane structure *(3)* exists at room temperature.



In contrast to our compound *(3)*, an isomeric hydrocarbon synthesized recently by *Vogel*, exists solely as cyclopropanediylidene[14]annulene with a 14π periphery *(9a)* rather than in a cyclophane structure *(9)*[7].

Heating of *(3)* in a quartz tube (500 °C/4 torr/0.5 h) gives 1-methylpyrene *(10)* as colorless plates of m.p. 66–68 °C in quantitative yield[8] (identified by comparison with an authentic sample[4,9]). In contrast, pyrolysis of *(4)* gives the corresponding hexasubstituted pyrene by loss of the methano bridge[3c]. Attempts to effect a photoisomerization of *(3)* to *(3a)* have been unsuccessful. However, irradiation of a cyclohexane solution of *(3)* (6-W low-pressure Hg lamp, N_2, 2 h) led to quantitative conversion of the cyclophane into a single product which was identified as 4,5-cyclopropano-4,5-dihydropyrene *(11)*[10] by spectroscopic comparison with authentic material.



Thus the metacyclophane derivative *(3)* does not rearrange to the dihydropyrene derivative *(3a)* at room temperature. However, the thermal and photochemical isomerizations of *(3)* are most reasonably explained by postulating *(3a)* as an intermediate.

Received: April 26, 1978 [Z 344 IE]
German version: Angew. Chem. *91*, 1011 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(3) 20453-46-7; *(5)*, 68712-47-0; *(7)*, 68712-53-8; *(8)*, 1611-78-5; *(9a)*, 38801-41-1; *(10)*, 2381-21-7; *(11)*, 2978-80-5

[1] *K. Nakasuji, M. Katada, I. Murata*, Tetrahedron Lett. *1978*, 2515.
[2] For a review, see *V. Boekelheide* in *T. Nozoe, R. Breslow, K. Hafner, S. Ito, I. Murata:* Topics in Nonbenzenoid Aromatic Chemistry. Hirokawa Publ. Co., Tokyo 1973, Vol. 1, pp. 47 ff.
[3] a) *B. A. Hess, Jr., A. S. Bailey, V. Boekelheide*, J. Am. Chem. Soc. *89*, 2746 (1967); *B. A. Hess, Jr., A. S. Bailey, B. Bartusek, V. Boekelheide, ibid. 91*, 1665 (1969); b) *B. A. Hess, Jr., V. Boekelheide, ibid. 97*, 1672 (1969); c) *H. B. Renfroe, ibid. 90*, 2199 (1968).
[4] *Ch. Jutz, R. Kirchlechner, H.-J. Seidel*, Chem. Ber. *102*, 2301 (1969).
[5] *S. S. Malhotra, M. C. Whiting*, J. Chem. Soc. *1960*, 3812.
[6] The compound *(3)* gave satisfactory elemental analysis.
[7] *E. Vogel*, personal communication.
[8] We are indebted to Dr. *K. Yamamoto* for his help in the pyrolysis of *(3)*.
[9] *H. Vollmann, H. Becker, M. Corell, H. Streck*, Justus Liebigs Ann. Chem. *531*, 1 (1937); *L. K. Keefer, L. Wallcave, J. Loo, R. S. Peterson*, Anal. Chem. *1971*, 1411.
[10] *E. Müller, H. Kessler*, Tetrahedron Lett. *1965*, 2673.

Synthesis and Reactions of Diazoacetyl Chloride—Detection of Diazoketene

By *Hans Jürgen Bestmann* and *Fouad M. Soliman*[*]

The reaction of diazomethane *(2)* with acyl chlorides to give diazoketones has long been known as a standard reaction[1]. Surprisingly, however, no report has yet appeared concerning the reaction of phosgene *(1)* with *(2)*.

On reacting phosgene *(1)* with diazomethane *(2)* in a molar ratio of 1:2 we were able to isolate the hitherto unknown compound diazoacetyl chloride *(3)* (94%) alongside chloroacetyl chloride *(4)* (2%) and 1,3-dichloroacetone *(6)* (4%). Reaction of *(3)* with liberated HCl gives *(4)*, which in turn reacts with *(2)* to afford 1-chloro-3-diazoacetone *(5)* from which *(6)* is formed with HCl.

On reaction of *(1)* and *(2)* in a molar ratio of 1:4 both *(6)* and the diazoketone *(5)* are obtained. The same reaction in the presence of triethylamine (1:4:1) gives only *(5)*.

Compound *(3)* is a yellow liquid which boils at 15 °C/0.5 torr and decomposes only slowly below 0 °C; IR: 2120 (CH—N_2), 1720 cm^{-1} (CO); MS: $m/e = 104/106$ (M^+), 76/78 ($M^+ - N_2$), 69 ($M^+ - Cl$), 68 ($M^+ - HCl$), *etc.* The last-named fragment suggests formation of diazoketene *(10)* in the gas phase. The ^{1}H-NMR spectrum of *(3)* (in CCl_4) is dependent on temperature[2]; at room temperature it shows two signals at $\delta = 5.2$ and 5.5. The coalescence temperature is 33 °C.

Compound *(3)* is an excellent diazoacetylation reagent. Addition of a tertiary base to a solution of *(3)* and *(7)* (X = R—O, R—S, R—NH) in aprotic solvents (molar ratio 1:1:1) leads to a diazoacetic ester derivative *(8)* in high yield; the hydrochloride precipitates. Table 1 shows some examples.

[*] Prof. Dr. H. J. Bestmann, Dr. F. Soliman [**]
Institut für Organische Chemie der Universität Erlangen-Nürnberg
Henkestrasse 42, D-8520 Erlangen (Germany)
[**] Alexander von Humboldt Fellow. Present address: National Research Center Dokki, Cairo (Egypt)

Reaction of *(3)* with deuterated alcohol R—OD in the presence of a tertiary base gives not only deuterated base but a third of the compound *(8)* appears in deuterated form as

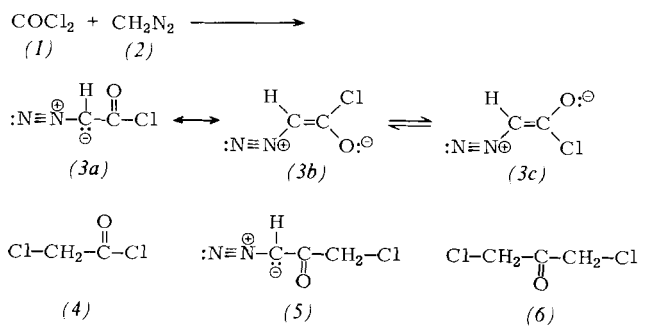
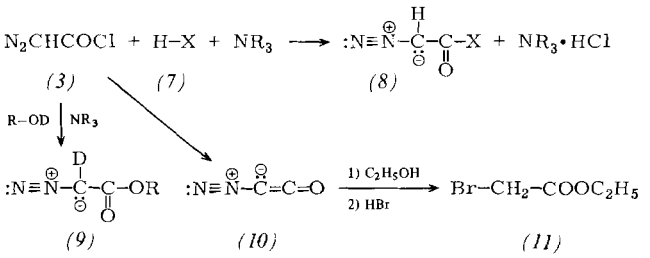


Table 1. Diazoacetic ester derivatives *(8)* from *(3)* and *(7)* with triethylamine in ether; phosphazines $(C_6H_5)_3P{=}N\ N{=}CHCOOR$ *(12)* from *(8)* and triphenylphosphane.

	X	*(8)* Yield [%]	*(8)* B.p. [°C/torr] M.p. [°C]	*(12)* M.p. [°C]
a	C_6H_5 O	90	40/0.01	129 (dec.)
b	*p*-NO_2 C_6H_4 O	92	94	125 (dec.)
c	C_6H_5 S	86	[a]	112 (dec.)
d	$C_{10}H_7$ NH	94	140	

[a] Purified by chromatography since *(8c)* decomposes on distillation.

(9). We cannot yet say for certain whether the long-sought diazoketene *(10)*[3] is involved as intermediate.



We were able to generate and identify the diazoketene *(10)* in the following way: an ethereal solution of diazabicyclooctane was added dropwise to a boiling solution of *(3)* in ether from which the solvent distilled colorless at a bath temperature of 40 °C. The distillate immediately turned pale yellow. It was collected with ethanol in a receiver. After evaporation of the ether from the distillate the IR spectrum of the residue showed the typical band of diazoacetic ester *(8)*, X = OC_2H_5, at 2100 cm^{-1}. Addition of HBr to the distillate liberates nitrogen, and the bromoacetic ester *(11)* (yield 4%) can be unequivocally identified by gas chromatography. The diazoacetic ester *(8)*, X = OC_2H_5, formed in the receiver cannot have arisen from distilled *(3)* and ethanol since any HCl liberated in this reaction would transform the diazoacetic ester into chloroacetic ester.

Received: August 16, 1979 [Z 348 IE]
German version: Angew. Chem. *91*, 1012 (1979)

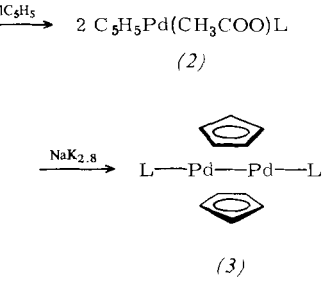
[1] Cf. *M. Regitz:* Diazoalkane. Thieme, Stuttgart 1977.
[2] *F. Kaplan, G. K. Meloy*, J. Am. Chem. Soc. *88*, 950 (1966).
[3] Cf. remark by *H. Gilman*, Adv. Organomet. Chem. *7*, 2 (1968).

Synthesis and Structural Dynamics of Bis(cyclopentadienyl)phosphanepalladium Complexes[1]

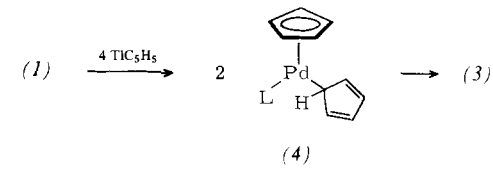
By *Helmut Werner* and *Hans-Jürgen Kraus*[*]

Dedicated to Professor André S. Dreiding on the occasion of his 60th birthday

Palladocene $Pd(C_5H_5)_2$ has so far not been reported in the literature[2]. Recently, however, we were able to synthesize the dinuclear sandwich complex *(3)*, L = $P(iPr)_3$, *via* the *in situ* intermediate *(2)*[3]:



On attempting to isolate *(2)* we observed that *(3)* is also formed directly from *(1)* and cyclopentadienylthallium. This "one-pot synthesis" of the dinuclear complex should proceed *via (4)* as intermediate, which then reacts—probably *via* a $C_5H_5Pd(L)$ radical—to give *(3)*:



We have now been able to isolate compounds of type *(4)* and to demonstrate that they have a fluxional structure, at least in solution.

Reaction of *(1)* [L = PMe_3, $P(iPr)_3$, PPh_3] with TlC_5H_5 (molar ratio ≈ 1:4.4) in benzene at room temperature leads within a few minutes to a dark-green solution from which, after removal of solvent and extraction with pentane, green crystals of *(4)* are obtained (yield 60—85%). These are only slightly air-sensitive and can be stored almost indefinitely at −20 °C. They react at 25 °C in toluene slowly to give *(3)*; for L = PMe_3, the reaction to $(\mu\text{-}C_5H_5)_2Pd_2(PMe_3)_2$ is complete after about nine days. Reaction of *(4)* and $CHCl_3$ affords the compounds $(\eta^5\text{-}C_5H_5)Pd(L)Cl$[4].

The composition of the complexes *(4a)* [L = PMe_3], *(4b)* [L = $P(iPr)_3$] and *(4c)* [L = PPh_3] is confirmed by elemental analysis and mass spectra. The mass spectra (70 eV; inlet temperature 60—120 °C) show the molecular ion with relatively high intensity and consistently PdL^+ as the most intense fragment. The room-temperature ^{1}H-NMR spectra show a *single* sharp signal for the 10 protons of the two cyclopentadienyl ligands. On cooling, this signal broadens to a flat hump (*e.g.* at −23 °C in the case of *(4b)*). At −47 °C *two* signals of different width but *equal intensity* appear in the C_5H_5 region in the case of *(4b)* (see Fig. 1). On further cooling the signal at δ = 5.04 becomes increasingly sharper and at −80 °C a PH-coupling of 1.6 Hz can be observed; the signal at δ = 6.20, on the other hand, becomes broader below −50 °C and coalesces at *ca.* −80 °C. From the chemical shift the former signal can be unequivocally assigned to the $\eta^5\text{-}C_5H_5$ protons and the latter to the $\eta^1\text{-}C_5H_5$ protons.

[*] Prof. Dr. H. Werner, Dipl.-Chem. H. J. Kraus
Institut für Anorganische Chemie der Universität
Am Hubland, D-8700 Würzburg (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0948 $ 02.50/0

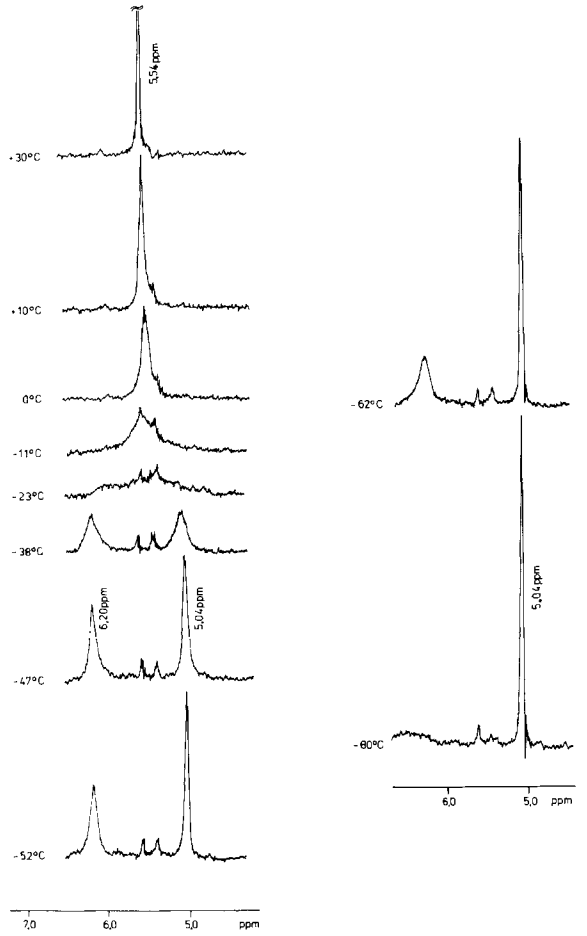


Fig. 1. ^{1}H-NMR spectra of (π-Cp)Pd(σ-Cp)P(iPr)$_3$ *(4b)*.

We conclude from the changes in the NMR spectra that *two dynamic processes take place simultaneously* at higher temperatures (above about $-25\,^\circ$C in the case of *(4b)*): that with the higher activation energy is a π/σ-(η^5/η^1) exchange of the two differently bound cyclopentadienyl ligands; that with the lower activation energy, which for the phosphanes employed can be frozen-in only below $-80\,^\circ$C, is a metallotropic rearrangement of the cyclopentadiene derivative C_5H_5X, *i.e.* a migration of the group $X = Pd(PR_3)(\eta^5\text{-}C_5H_5)$ around the ring. The rate, both of the ring exchange as well as of the metallotropic rearrangement, depends upon the size of the phosphane ligand. Hence, for example, the coalescence temperature for the process with the higher activation energy decreases along the series $PR_3 = P(i\text{Pr})_3$ (*ca.* $-25\,^\circ$C) > PPh_3 (*ca.* $-30\,^\circ$C) > PMe_3 (*ca.* $-65\,^\circ$C).

The ^{13}C-NMR spectrum of *(4b)* confirms the above discussed dynamics for this molecule. At $+35\,^\circ$C (in [D$_8$]toluene) a sharp signal is observed in the region of the ring C-atoms at $\delta = 106.31$, which on cooling to $-30\,^\circ$C splits into two signals of different width. At $-80\,^\circ$C the signal at higher field ($\delta = 100.63$) becomes a sharp doublet with $J_{PC} = 6.6$ Hz, while that at lower field ($\delta \approx 110.4$ at $-35\,^\circ$C) disappears into the background.

To our knowledge, in addition to *(4a)—(4c)* there are two further compounds having the composition $(C_5H_5)_2Mo(NO)(S_2CNR_2)$ [R = Me, *n*Bu][5] which contain one η^5- and one η^1-C_5H_5 ligand and in which π/σ ring exchange (besides a metallotropic rearrangement) takes place[6]. *Cotton* assumes that the ring exchange in these complexes is made possible by the transition of one of the ligands NO or S_2CNR_2 from a 3-electron donor into a 1-electron donor[7]. The η^1-C_5H_5 ligand could then undergo stronger interaction with the metal involving an η^4-C_5H_5 coordination in an intermediate of the exchange. Such a mechanism is out of the question in the case of the ring exchange in *(4a)—(4c)*. We assume that during the transition from (η^5-C_5H_5)(η^1-C_5H_5')PdL to (η^1-C_5H_5)(η^5-C_5H_5')PdL an intermediate is formed in which *both* rings are η^3-bonded. The number of the electrons in the valence shell of the palladium would thus remain unchanged *vis-a-vis* in *(4a)—(4c)*.

Received: August 13, 1979 [Z 349 IE]
German version: Angew. Chem. *91*, 1013 (1979)

[1] Structurally Dynamic Organometal Complexes, Part 1.
[2] *P. M. Maitlis:* The Organic Chemistry of Palladium. Academic Press, New York 1971, Vol. I, p. 254.
[3] *H. Werner, H. J. Kraus,* J. Chem. Soc. Chem. Commun. *1979*, 814.
[4] For the formation of (η^5-C_5H_5)Ni(L)Cl from the postulated intermediate (η^5-C_5H_5)Ni(η^1-C_5H_5)L see: *Yu. A. Ustynyuk, T. I. Voevodskaya, N. A. Zharikova, N. A. Ustynyuk,* Dokl. Akad. Nauk SSSR *181*, 372 (1968); *V. Harder, H. Werner,* Helv. Chim. Acta *56*, 1620 (1973).
[6] In the most well-known compound containing *one* η^5- and *one* η^1-C_5H_5 ligand, $(C_5H_5)_2Fe(CO)_2$, only a metallotropic rearrangement is detectable, but no π/σ ring exchange [7].
[7] *F. A. Cotton* in *F. A. Cotton, L. M. Jackman:* Dynamic Nuclear Magnetic Resonance Spectroscopy. Academic Press, New York 1975, p. 423.

New Pathways to Trinuclear Complexes—Structure of the Tetra-decker Sandwich Complex Bis(η-thiadiborolenecobalt-μ,η-thiadiborolene)iron[1]

By *Walter Siebert, Wilfried Rothermel, Christian Böhle, Carl Krüger,* and *David J. Brauer*[*]

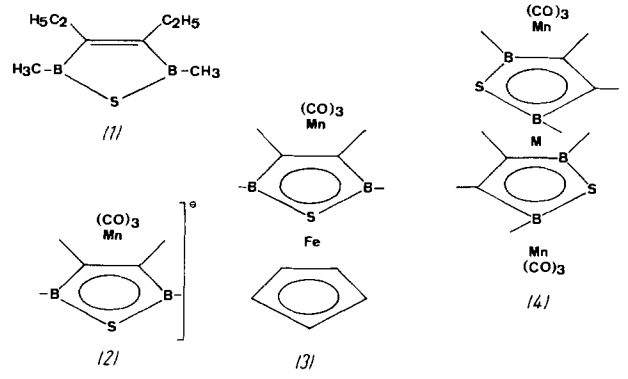
Dedicated to Professor Gerhard Fritz on the occasion of his 60th birthday

Triple-decker sandwich complexes are prepared by reacting dinuclear metal carbonyl compounds with Lewis-acidic boron heterocycles[2] as well as by the nearly quantitative "stacking" of sandwich compounds[3] with fragments of metal complexes [(C_5H_5)M, ($CO)_3$M']. Several preparative routes to tetra-decker complexes are conceivable, of which the thermolysis of the triple-decker salt [(C_6H_6)Fe·*(1)*·Mn($CO)_3$]$^{\oplus}$$AlCl_4^{\ominus}$ giving low yields of centrosymmetric *(4)*, M = Fe, was the first to be reported[1]. Earlier attempts[4] to prepare *(4)* from the tricarbonylmanganese-η-thiadiborolene anion *(2)* and $FeCl_2$ failed since the anion *(2)* cannot be obtained from $(CO)_5$MnNa and *(1)*. We now report the cleavage of triple-decker compounds with cyclopentadienide and conversion of the anionic mononuclear complexes thus formed into trinuclear complexes.

The reaction of *(3)*[1] with $C_5H_5^{\ominus}$ gives ferrocene and *(2)*. Combination of the latter with MCl_2 affords the tetra-decker complexes *(4)* (M = Fe, Co, and Ni) in 23, 45, and 2% yields, respectively. The ^{1}H-NMR spectrum of the iron complex *(4)* contains broad, weakly structured signals indicating the presence of conformational isomers. The ESR spectrum of the 43

[*] Prof. Dr. W. Siebert, Dr. W. Rothermel, Dipl.-Chem. C. Böhle
Fachbereich Chemie der Universität
Lahnberge, D-3550 Marburg 1 (Germany)
Priv.-Doz. Dr. C. Krüger
Max-Planck-Institut für Kohlenforschung
Lembkestrasse 5, D-4330 Mülheim-Ruhr 1 (Germany)
Dr. D. J. Brauer
Gesamthochschule, FB 9—Anorganische Chemie
Gaussstrasse 20, D-5600 Wuppertal-Elberfeld (Germany)

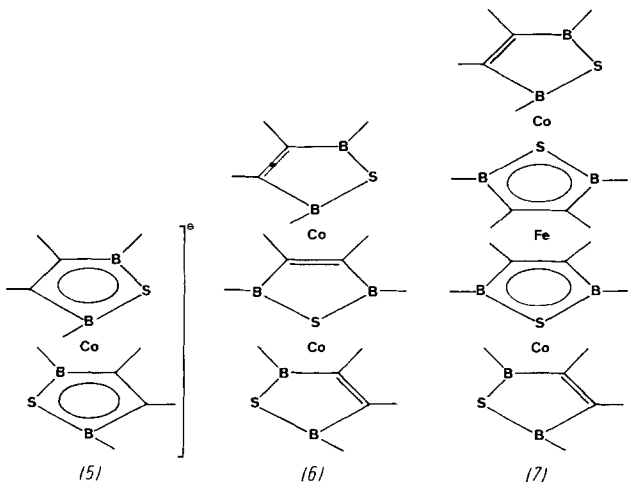
 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0949 $ 02.50/0*



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

valence-electron, paramagnetic cobalt complex *(4)* contains 8 lines [$\langle g\rangle = 2.099$, $\bar{a}(^{59}Co) = 39.7(2)$ G] caused by $I = 7/2$ of ^{59}Co. The black complexes *(4)* (M = Fe, Co, Ni) give analogous MS fragmentation patterns and the IR absorptions $\nu(CO) = 2022$ (s), 1957 (s), 1946 (s) cm^{-1} (in C_2Cl_4).

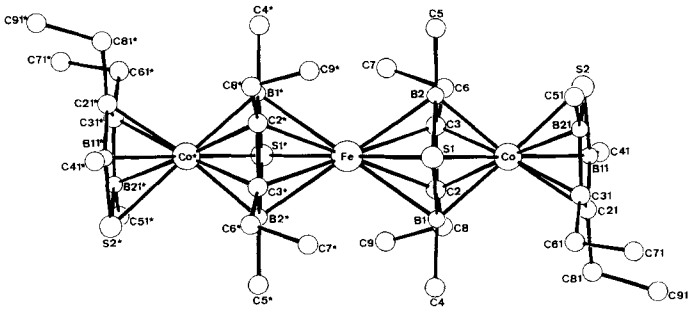
On attempting to replace the thiadiborolenecobalt fragment in the triple-decker sandwich complex *(6)* by $(CO)_3Mn$, the complex *(4)*, M = Co, was unexpectedly formed in 9% yield. Apparently [*(1)*·Co·*(1)*·$Mn(CO)_3$], which is isoelectronic with the 30 valence-electron complex [*(1)*·Co·*(1)*·$Co(CO)_2$][5], is stacked by excess $[Mn_2(CO)_{10}]$ to give tetra-decker *(4)*, M = Co.



(5) (6) (7)

Like *(3)*, compound *(6)* is split by $C_5H_5^{\ominus}$ into [(C_5H_5)Co·*(1)*] and the anion *(5)*, which was isolated as the tetraphenylphosphonium salt (yield 96%) [$\delta^1H = 7.2$—8.0 (M, 20), 1.85 (M, 8), 0.86 (T, 12), 0.22 (S, 12) (in CH_2Cl_2); $\delta^{11}B = 24.7$ (in CH_2Cl_2)]. *(5)* reacts with $FeCl_2$ to give the black tetra-decker sandwich complex *(7)* in 29% yield. The ^{1}H-NMR spectrum of this 42 valence-electron complex is similar to that of *(4)*, M = Fe, with overlapping signals [$\delta = 2.2$ (M, 6), 1.09 (S, 6), 1.04 (T, 12), 0.99 (T, 12), 0.96 (S, 6)] indicating different conformers in solution. On the basis of analytical and mass spectroscopic evidence we proposed a tetra-decker sandwich structure for *(7)*[6a]. This structure has been confirmed by an X-ray structure analysis[7] (Fig. 1).

The Fe···Co distance [3.5370(4) Å] is longer than the corresponding Fe···Mn separation [3.400(7) Å] in *(4)*. As in the latter complex, the Fe atom is located at an inversion center with the μ-rings mutually *trans*. The η-ligands are nearly parallel to the μ-rings and are rotated axially through 102.2°. Comparison of the distances between the best planes of the μ-ligands (D) and the bonded metal atoms in *(4)* and *(7)* reveals a lengthening of about 0.16 Å for Mn/Co [Mn—D *(4)* 1.757 Å; Co—D *(7)* 1.601 Å] but a 0.3 Å shortening for Fe—D [Fe—D *(4)* 1.631 Å; Fe—D *(7)* 1.934 Å]. In agreement with previous investigations of triple-decker complexes[8], we observe in *(7)* a Co-η-D distance [1.691 Å]



which is 0.090 Å longer than the Co-μ-D length. Following the cluster rules, *(7)* may be described by two *nido* and two *closo*-structures with a total of $2\times16+2\times16=64$ skeleton electrons as opposed to 42 valence electrons in the π^6/d^6 description. Further tetra-decker sandwiches have recently been reported[6].

Experimental

A mixture of *(6)* (0.66 g, 1.07 mmol) and C_5H_5Na (0.14 g, 1.60 mmol) in THF (50 ml) was stirred for 20 h. After addition of excess $FeCl_2$, stirring was continued for a further 20 h and the mixture then filtered. After evaporation of the filtrate, ferrocene and [(C_5H_5)Co·*(1)*] were removed from the residue by sublimation. The remainder was treated repeatedly with 30 ml portions of toluene from which black rods of *(7)* crystallize on cooling (0.13 g, 29%); m.p. 210—212 °C (decomp.).

Received: July 16, 1979 [Z 350 IE]
German version: Angew. Chem. *91*, 1014 (1979)

[1] Part 2 of Tetra-decker Complexes. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. Part 1: *W. Siebert, C. Böhle, C. Krüger, Y.-H. Tsay*, Angew. Chem. *90*, 558 (1978); Angew. Chem. Int. Ed. Engl. *17*, 527 (1978).

[2] *W. Siebert*, Nachr. Chem. Techn. Lab. *25*, 597 (1977) and references cited therein; *W. Siebert*, Adv. Organomet. Chem. Vol. *18*, in press.

[3] *H. Werner, A. Salzer*, Synth. Inorg. Met.-Org. Chem. *2*, 239 (1972); *W. Siebert, J. Edwin, M. Bochmann*, Angew. Chem. *90*, 917 (1978); Angew. Chem. Int. Ed. Engl. *17*, 869 (1978).

[4] *C. Böhle*, Diplomarbeit, Universität Marburg (1977).

[5] *W. Rothermel*, Dissertation, Universität Marburg (1979).

[6] a) *W. Siebert*, Lecture at the Autumn Meeting 1978, Chem. Soc. Warwick, England; b) *R. N. Grimes*, Lecture at the Autumn Meeting 1978, Chem. Soc. Warwick, England.

[7] Crystal data: $a = 10.102(2)$, $b = 12.309(2)$, $c = 9.0448(8)$ Å, $\alpha = 94.805(5)$, $\beta = 111.657(9)$, $\gamma = 89.89(1)°$, space group $P\bar{1}$, $Z = 1$, $\rho_{calc} = 1.335$ g cm^{-3}; 7275 reflections, of which 4188 considered observed; $R = 0.039$.

[8] *W. Siebert et al., C. Krüger et al.*, J. Organometal. Chem., in press.

A Stable 2-Adamantyl Cation in the Gas Phase[**]

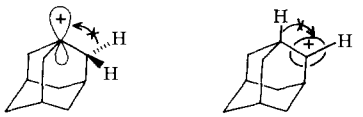
By *Chrysostomos Wesdemiotis, Marita Schilling*, and *Helmut Schwarz*[*]

Under suitable conditions, 1- and 2-adamantyl cations *(1)* and *(2)*, respectively, should be detectable as stable species since the steric relationship between the vacant orbital at the cationic center and the orbital of the migrating group pre-

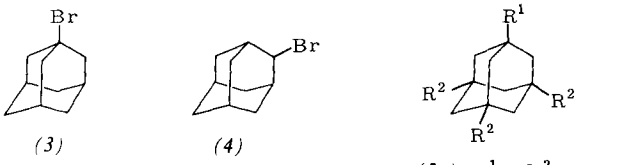
[*] Prof. Dr. H. Schwarz, Dipl.-Chem. C. Wesdemiotis, M. Schilling
Institut für Organische Chemie der Technischen Universität Berlin
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie and the Gesellschaft von Freunden der Technischen Universität Berlin.

cludes an intramolecular 1,2 hydride shift[1]. However, only *(1)* has hitherto been detected as a stable cation in a superacid medium and in the gas phase[2]; all attempts to isolate *(2)* or to identify it by spectroscopy failed[1e,3].



(1) *(2)*



(3) *(4)*

(5a), $R^1 = R^2 = H$
(5b), $R^1 = R^2 = D$
(5c), $R^1 = H$, $R^2 = D$

We have generated the $[M-Br]^+$ ions from 1- and 2-bromoadamantane *(3)* and *(4)*, respectively, by dissociative ionization in the gas phase and recorded their collision activation (CA) spectra[4]. In spite of certain common features, the CA spectra of the $[M-Br]^+$ ions of *(3)* and *(4)* differ to such a degree (for example, see the section between $m/e=65$ and $m/e=81$ shown in Fig. 1[5]) that we have to assign the ions *different* structures (fingerprint criterion).

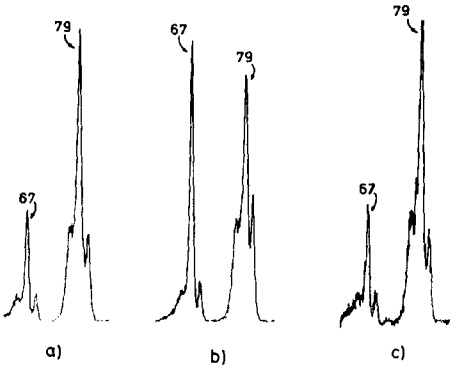


Fig. 1. Section from the CA spectra of the ions $C_{10}H_{15}^+$: a) from *(3)*, $[M-Br]^+$; b) from *(4)*, $[M-Br]^+$; c) from *(5a)*, $[M-H]^+$; the numbers are the m/e values of the collision-induced fragments.

Exothermic isomerization of the $C_{10}H_{15}^+$ ions before or during elimination of Br$^\cdot$ can be ruled out since the kinetic energy liberated on unimolecular decomposition of *(3)* and *(4)*, *i.e.* $T^{1/2}$, and also the line shape of the transition signals[6], are identical: for $[(3)]^{+\cdot} \rightarrow [M-Br]^+$ we obtain $T^{1/2}=0.25$ kcal mol^{-1} and for the decomposition of $[(4)]^{+\cdot}$ a value of $T^{1/2}=0.26$ kcal mol^{-1}.

Since the decomposition of *(3)* can certainly be regarded as a simple dissociation to form the stable 1-adamantyl cation *(1)*, we deduce from the CA and T results that bromine is eliminated from the radical cation of *(4)* in a mechanistically analogous reaction (*i.e.* without rearrangement or σ-neighboring group participation), thus giving the long-sought 2-adamantyl cation *(2)*.

Remarkably, the CA spectrum of the $[M-H]^+$ ion of adamantane *(5a)* and that of *(1)* are identical. This means that either the tertiary C–H bond dissociates specifically or the cation subsequently isomerizes to *(1)* following nonspecific H elimination. The latter alternative can be ruled out because deuterium is exclusively eliminated from the tetradeuterated adamantane *(5b)*. The trideuterated species *(5c)* loses both H$^\cdot$ and D$^\cdot$; after correcting for the statistical probability of H/D elimination the experimental data afford a kinetic isotope effect of $k_H/k_D=1.9$.

Received: May 15, 1979;
supplemented: June 15, 1979 [Z 352a IE]
German version: Angew. Chem. *91*, 1017 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(1), 2819-03-6; *(2)*, 21517-94-2; *(3)*, 768-90-1; *(4)*, 7314-85-4; *(5a)*, 281-23-2; *(5b)*, 19215-02-2; *(5c)*, 72152-35-3

[1] a) *P. v. R. Schleyer*, Angew. Chem. *81*, 539 (1969); Angew. Chem. Int. Ed. Engl. *8*, 529 (1969); b) *P. v. R. Schleyer, L. K. M. Lam, D. J. Raber, J. L. Fry, M. A. McKervey, J. R. Alford, B. D. Cuddy, V. G. Keizer, H. W. Geluk, J. L. M. A. Schlatmann*, J. Am. Chem. Soc. *92*, 5246 (1970); c) *D. M. Brouwer, H. Hogeveen*, Rec. Trav. Chim. Pays-Bas *89*, 211 (1970); d) *M. L. Sinnott, M. C. Whiting*, J. Chem. Soc. Perkin Trans. II *1975*, 1446; e) *P. Vogel, M. Saunders, W. Thielecke, P. v. R. Schleyer*, Tetrahedron Lett. *1971*, 1429.

[2] *P. v. R. Schleyer, R. C. Fort, Jr., W. E. Watts, M. B. Comisarow, G. A. Olah*, J. Am. Chem. Soc. *86*, 4195 (1964); *G. A. Olah, M. B. Comisarow, C. A. Cupas, C. U. Pittman, Jr., ibid. 87*, 2997 (1965); *G. A. Olah, J. Lukas, ibid. 90*, 933 (1968); *R. H. Staley, R. D. Wieting, J. L. Beauchamp, ibid. 99*, 5964 (1977).

[3] *P. v. R. Schleyer*, personal communication. We thank Prof. *Schleyer*, Erlangen, for suggestions concerning this work.

[4] Concerning the method: *K. Levsen, H. Schwarz*, Angew. Chem. *88*, 589 (1976); Angew. Chem. Int. Ed. Engl. *15*, 509 (1976); *R. G. Cooks:* Collision Spectroscopy. Plenum Press, New York 1978; *F. W. McLafferty* in *M. L. Gross:* High Performance Mass Spectrometry: Chemical Applications. ACS Symp. Ser. *70*, American Chemical Soc., Washington, D. C., 1978; *K. Levsen:* Fundamental Aspects of Organic Mass Spectrometry. Verlag Chemie, Weinheim 1978.

[5] No attempt has been made to reproduce the complete space-consuming spectra here.

[6] See: *D. H. Williams*, Acc. Chem. Res. *10*, 280 (1977); *D. H. Williams, B. J. Stapleton, R. D. Bowen*, Tetrahedron Lett. *1978*, 2919; *R. D. Bowen, D. H. Williams, H. Schwarz*, Angew. Chem. *91*, 484 (1979); Angew. Chem. Int. Ed. Engl. *18*, 451 (1979).

Ion Cyclotron Resonance Studies on *tert*-Butyl, 2-Norbornyl, and 1- and 2-Adamantyl Cations[**]

By *Raymond Houriet* and *Helmut Schwarz*[*]

The relative stability of carbocations $R^\oplus$ in the gas phase can be determined by ion cyclotron resonance (ICR) spectroscopy[1]; in this technique the direction of anion transfers and the position of the equilibrium are established [eq. (a), X = F, Br]. The heterolytic bond dissociation energy $D(R^\oplus - X^\ominus)$, which can be regarded as a measure of the relative stability of $R^\oplus$[2,3] and is defined by eq. (b), can be calculated from the equilibrium constant of reaction (a)[3].

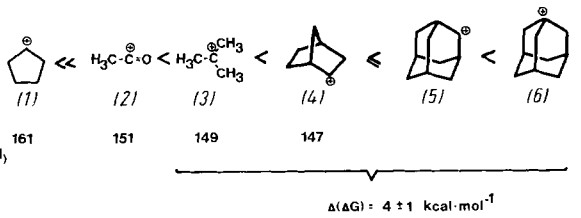
$$R'^\oplus + R''X \rightleftarrows R'X + R''^\oplus \quad (a)$$

$$RX \rightarrow R^\oplus + X^\ominus; \quad \Delta H_r = D(R^\oplus - X^\ominus) \quad (b)$$

We have examined the bromide transfer between the cations *(1)*—*(6)* (Fig. 1[4]) and obtained the stability sequence given in Scheme 1 from the position of the equilibria. These agree both quantitatively and qualitatively with the sequence given by *Beauchamp et al.*[3b] in the case of *(1)*—*(4)*, while qualitative agreement was found for *(6)*. However, we found

[*] Prof. Dr. H. Schwarz
Institut für Organische Chemie der Technischen Universität Berlin
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Dr. R. Houriet
Physikalisch-chemisches Institut
der Eidgenössischen Technischen Hochschule
CH-1015 Lausanne (Switzerland)

[**] This work was supported by the Fonds der Chemischen Industrie and by the Schweizer Nationalfonds zur Förderung der wissenschaftlichen Forschung. – *H. S.* is grateful to the ETH Lausanne for a Visiting Professorship (1979) and to Prof. T. Gäumann, Lausanne, for his hospitality.



Scheme 1. Stability sequence of cations *(1)* to *(6)*; $D(R^{\oplus}\ X^{\ominus})$ values taken from [3b].

that the $\Delta(\Delta G)$ values for the pair *(3)/(6)*, and hence also the differences in the bond dissociation energies, to be ≤ 4 kcal mol^{-1}[5]. This means that, with regard to its stability, *(6)* must be regarded as a normal tertiary carbocation[7], and not, as frequently assumed, as a highly stabilized carbocation.

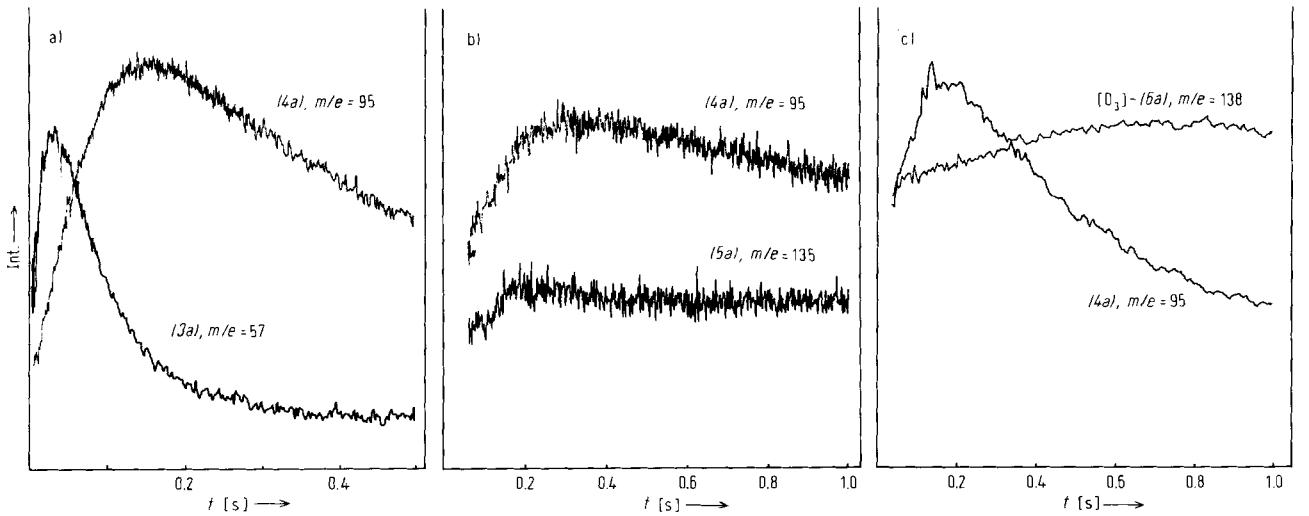
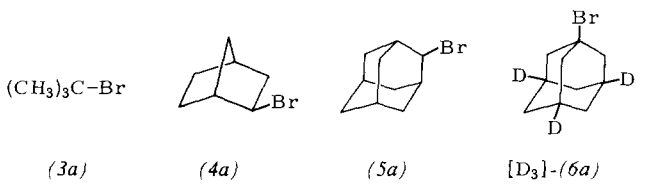


Fig. 1. Ion intensities as function of time in binary mixtures of a) *exo*-2-norbornyl bromide *(4a)* (2.3×10^{-6} torr) and *tert*-butyl bromide *(3a)* (8×10^{-6} torr), b) *(4a)* and 2-adamantyl bromide *(5a)* (1:1 mixture, total pressure: 5.5×10^{-6} torr), and c) *(4a)* and $[D_3]$-*(6a)* (1:1 mixture, total pressure: 7.2×10^{-6} torr).

The situation is completely different in the 2-adamantyl cation *(5)*, which has recently been detected for the first time as



(3a) *(4a)* *(5a)* $[D_3]$-*(6a)*

a stable ion in the gas phase[8]. The stability difference of *ca.* 16 kcal mol^{-1}[2] to be expected for classical *sec/tert* cations is not present; *(5)* and *(6)* differ by 4 kcal mol^{-1} at most. The analogy with the controversial[9] system 2-norbornyl/2-methyl-2-norbornyl cation cannot be overlooked.

Received: October 3, 1979 [Z 352b IE]
German version: Angew. Chem. *91*, 1018 (1979)

CAS Registry numbers:
(1), 3889-74-5; *(2)*, 3170-69-2; *(3)*, 1605-73-8; *(3a)*, 509-19-7; *(4)*, 30967-37-4; *(4a)*, 2534-77-2; *(5)*, 21517-94-2; *(5a)*, 7314-85-4; *(6)*, 2819-03-6; $[D_3]$-*(6a)*, 72152-34-2

[1] Selected literature: a) *J. L. Beauchamp*, Annu. Rev. Phys. Chem. *22*, 527 (1971); b) *T. A. Lehman, M. M. Bursey:* Ion Cyclotron Resonance Spectrometry. Wiley-Interscience, New York 1976.
[2] *W. Kirmse*, Top. Curr. Chem. *80*, 125 (1979).
[3] a) *R. J. Blint, T. B. McMahon, J. L. Beauchamp*, J. Am. Chem. Soc. *96*, 1269 (1974); b) *R. H. Staley, R. D. Wieting, J. L. Beauchamp, ibid. 99*, 5964 (1977).
[4] In order to ensure internal consistency, a total of eleven pairs was examined (some under double resonance conditions). $Br^{\ominus}$ transfer for the pairs *(3)/(4)*, *(4)/(5)*, and *(4)/(6)* are reproduced in Fig. 1. In cases of equal mass, as with *(5)/(6)*, deuterated compounds were used.—The ICR spectrometer built at the ETH Lausanne and used for the measurements contains a Varian V 7300 magnet; the experiments were performed in a flat four-section cell under trapped ion conditions [*T. B. McMahon, J. L. Beauchamp*, Rev. Sci. Instrum. *43*, 509 (1972)]. The dissociative ionization of the bromides was accomplished by a 2.5-ms pulse of 20-eV electrons. All compounds were introduced *via* a dual inlet system.
[5] The data reported in [3a] yield a difference of 10 kcal mol^{-1} for *(3)/(6)*. However, it is emphasized in that publication that the value for *(6)* is attended by considerable uncertainty. On using data from the literature, our measurements yield the enthalpy of formation of *(6)* as $\Delta H^{\circ}_{f(6)} = 159 \pm 3$ kcal mol^{-1}. This value is in excellent agreement with the results obtained by other methods, *e.g.* 160.7 [6a] or 160 kcal mol^{-1} [6b].
[6] a) *J. Allison, D. P. Ridge*, J. Am. Chem. Soc. *101*, 4998 (1979); b) *R. C. Fort, Jr.* in *G. A. Olah, P. v. R. Schleyer:* Carbonium Ions. Vol. IV. Wiley, New York 1973.
[7] This view has already been voiced: *P. Vogel, M. Saunders, W. Thielicke, P. v. R. Schleyer*, Tetrahedron Lett. *1971*, 1429.—*Note added in proof* (Nov. 19, 1979): Recently published STO-3G calculations [*D. E. Sunko, S. Hirši-Starčevič, S. K. Pollack, W. J. Hehre*, J. Am. Chem. Soc. *101*, 6163 (1979)] show *(6)* to be only 4.1 kcal mol^{-1} more stable than *(3)*. However, the stability difference *(5)/(6)* is predicted by these calculations [*M. Kausch, P. v. R. Schleyer*, personal communication of Nov. 11, 1979] to be about 11.7 kcal mol^{-1}.
[8] *C. Wesdemiotis, M. Schilling, H. Schwarz*, Angew. Chem. *91*, 1017 (1979); Angew. Chem. Int. Ed. Engl. *18*, 956 (1979).
[9] *H. C. Brown* (commentary by *P. v. R. Schleyer*): The Non-Classical Ion Problem. Plenum Press, New York 1978.

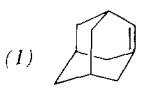
Adamantene in the Gas Phase[**]

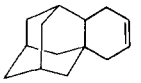
By *Helmut Schwarz, Manfred T. Reetz, Wilhelm F. Maier, Chrysostomos Wesdemiotis, Ioannis Chatziiosifidis,* and *Marita Schilling*[*]

Adamantene *(1)* occupies a special place among the bridgehead olefins[1]. So far, however, the intermediacy of *(1)* has only been established indirectly by trapping experiments [such as cycloaddition to give *(2)*][2]. If the reaction is

[*] Prof. Dr. H. Schwarz, Dipl.-Chem. C. Wesdemiotis, M. Schilling
Institut für Organische Chemie der Technischen Universität
Strasse des 17. Juni 135, D-1000 Berlin 12 (Germany)
Prof. Dr. M. T. Reetz, Dr. W. F. Maier, Dipl.-Chem. I. Chatziiosifidis
Institut für Organische Chemie und Biochemie der Universität
Gerhard-Domagk-Strasse 1, D-5300 Bonn (Germany)

[**] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We are grateful to Prof. Dr. *H. Vorbrüggen*, Schering AG Berlin, for chemicals.

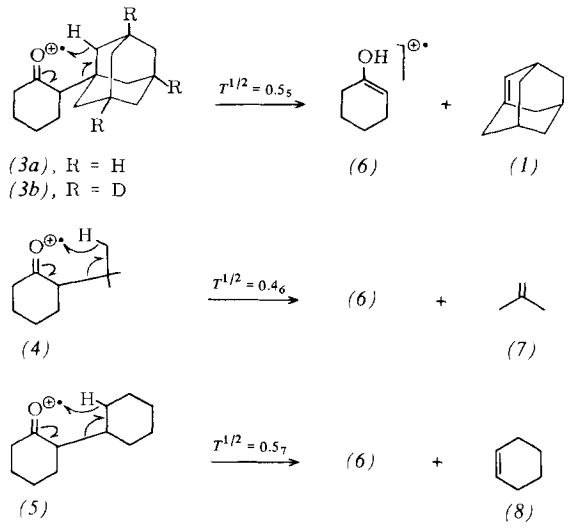

(1)


(2)

carried out in the condensed phase, contradictory results are is obtained with regard to the existence and properties of *(1)*[2].

We now wish to report a simple experiment in which adamantene *(1)* is generated directly as the neutral molecule under high vacuum conditions ($p \approx 10^{-6}$ torr) by an unequivocal decomposition of radical cations.

On ionization of 2-(1-adamantyl)cyclohexanone *(3)*[3] or the ketones *(4)* and *(5)* by electron impact (15 eV, 70 eV) the radical cations decompose *inter alia via* a McLafferty rearrangement[4] (Scheme 1). Peak shape analysis of the fragmentations of metastable ions (lifetime $t \approx 10^{-5}$ s; minimum excess energy in $M^{+\cdot}$) shows that (i) the peak profiles for the three fragmentation processes are identical (Gaussian form) and (ii) the translational energy T liberated on unimolecular decomposition is practically equal to within the limits of experimental error ($T^{1/2}$ values in Scheme 1).



Scheme 1. Olefin elimination from *(3)*—*(5)* ($T^{1/2}$ values in kcal mol^{-1}).

In view of the fact that (i) the T data are a very sensitive probe for the analysis of reaction mechanisms and can vary by up to four powers of ten depending upon the particular reaction type[5] and (ii) the reaction profile can also be influenced by the reaction type[5,6], it must be concluded from the experimental results that the fragmentations of *(3)*—*(5)* proceed *via* a single mechanism. According to the collision activation spectra[7] only the enol form *(6)* need be considered for the ionized fragment[8]. Since the neutral molecules C_4H_8 and C_6H_{10} [from *(4)* and *(5)*], respectively are undoubtedly olefins[4] and no deuterium is transferred from *(3b)* it must be concluded that the $C_{10}H_{14}$ fragment from *(3a)* or $C_{10}H_{11}D_3$ from *(3b)* has the structure of adamantene *(1)*. A hypothetical exothermic isomerization of the incipient neutral molecule should lead to peak broadening and hence to greater T values on decomposition of *(3)*. However, there is no experimental evidence for such a reaction. Two further points warrant mention: (i) formation of adamantene is not limited to cyclohexanone derivatives. T data and peak profile analysis suggest that *(1)* is also formed by unimolecular decomposition of the 2-(1-adamantyl)-derivatives of cyclopentanone and cyclooctanone. (ii) The generation of adamantene expectedly requires considerable energy. Whereas the intensities for *(6)* (15 eV) are 76 and 87%, respectively, for *(4)* and *(5)*, much lower values are found with the adamantyl derivatives ($\approx 2.5\%$)[9].

Received: May 31, 1979 [Z 352c IE]
German version: Angew. Chem. *91*, 1019 (1979)
Publication delayed at authors' request

[1] Review: *J. Bredt*, Justus Liebigs Ann. Chem. *437*, 1 (1924); *G. Köbrich*, Angew. Chem. *85*, 494 (1973); Angew. Chem. Int. Ed. Engl. *12*, 404 (1973); *R. Keese, ibid. 87*, 568 (1975) and *14*, 528 (1975), respectively; *H.-U. Wagner, G. Szeimies, J. Chandrasekhar, P. v. R. Schleyer, J. A. Pople, J. S. Binkley*, J. Am. Chem. Soc. *100*, 1210 (1978).

[2] Extensive literature and identification of *(1)* [as *(2)*]: *D. J. Martella, M. Jones, Jr., P. v. R. Schleyer*, J. Am. Chem. Soc. *100*, 2896 (1978); see also *J. I. G. Cadogan, R. Leardii*, J. Chem. Soc. Chem. Commun. *1979*, 783.

[3] Efficient synthesis of "adamantyl" derivatives [*e.g. (3)*] see: *M. T. Reetz, W. F. Maier, K. Schwellnus, I. Chatziiosifidis*, Angew. Chem. *91*, 78 (1979); Angew. Chem. Int. Ed. Engl. *18*, 72 (1979).

[4] *D. G. I. Kingston, J. T. Bursey, M. M. Bursey*, Chem. Rev. *74*, 215 (1974).

[5] *R. G. Cooks, J. H. Beynon, R. M. Caprioli, G. R. Lester:* Metastable Ions. Elsevier, Amsterdam 1973.

[6] *D. H. Williams*, Acc. Chem. Res. *10*, 280 (1977); *R. D. Bowen, D. H. Williams, H. Schwarz*, Angew. Chem. *91*, 484 (1979); Angew. Chem. Int. Ed. Engl. *18*, 451 (1979).

[7] *K. Levsen, H. Schwarz*, Angew. Chem. *88*, 589 (1976); Angew. Chem. Int. Ed. Engl. *15*, 509 (1976); *K. Levsen:* Fundamental Aspects of Organic Mass Spectrometry. Verlag Chemie, Weinheim 1978.

[8] *H. Schwarz*, Org. Mass Spectrom. *12*, 470 (1977); Nachr. Chem. Tech. Lab. *26*, 792 (1978).

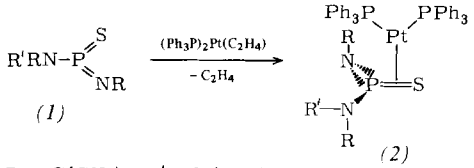
[9] The relationship between the strain energy of olefins and the tendency of the radical cations to decompose by a McLafferty rearrangement has already been pointed out: *R. R. Sauers, M. Grodetsky, J. A. Whittle, C. K. Hu*, J. Am. Chem. Soc. *93*, 5520 (1971). Preliminary ion cyclotron resonance studies show the strain energy of *(1)* to exceed 40 kcal mol^{-1} (*R. Houriet, H. Schwarz*, unpublished).

Synthesis of a Platinum Complex with a Derivative of Monomeric Metathiophosphoric Acid as η^2-Ligand[**]

By *Otto J. Scherer* and *Herbert Jungmann*[*]

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

Metathiophosphoric acid derivatives of type *(1)* can be isolated as monomeric double ylides[1] which prove to be extremely reactive[2]. Thus they should also be capable of σ- and/or π-coordination to transition metals. On reaction of $(Ph_3P)_2Pt(C_2H_4)$ with the amino(imino)thiophosphorane *(1)* we have now succeeded for the first time in preparing a complex containing such a species as π-bonded (side-on) ligand.



R = $C(CH_3)_3$, R' = $Si(CH_3)_3$

Compound *(2)* forms yellow crystals[3] which are moderately soluble in benzene, toluene, and ether, and readily soluble in CH_2Cl_2 and $CHCl_3$[4].

Unlike the free ligand[1] (sp^2 hybridization at the P atom) the complexed ligand *(1)* (sp^3 hybridization at the P atom)

[*] Prof. Dr. O. J. Scherer, Dipl.-Chem. H. Jungmann
Fachbereich Chemie der Universität
Postfach 3049, D-6750 Kaiserslautern (Germany)

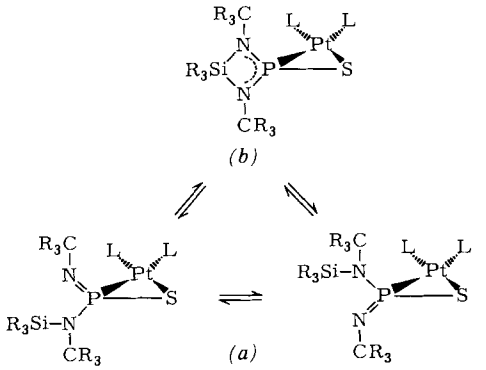
[**] This work was supported by the Fonds der Chemischen Industrie and by Degussa, Hanau.

Table 1. NMR data of compound *(2)*.

P(3) P(2) / Pt / P(1) S	$\delta(^1H)$, J [Hz] [a]		$\delta(^{13}C\{^1H\})$, J [Hz] [b]			$\delta(^{31}P\{^1H\})$, J [Hz] [c]		
	CH_3C	CH_3Si	NC	NCC	NSiC	P(1)	P(2)	P(3)
	1.22 (d)	0.39 (s)	53.8 (s)	34.8 (d)	10.4 (s)	51.0 (dd)	20.4 (d)	24.3 (d)
	$^4J_{PH}$			J_{PNCC}		J_{PtP}	J_{PtP}	J_{PtP}
	0.9			11.0		2257.2	2013.0	4749.6
						$J_{P(1)P(2)}$	$J_{P(2)P(3)}$	$J_{P(1)P(3)}$
						297.4	<2.0	20.0
						and $J_{P(1)P(3)}$	and $J_{P(1)P(2)}$	

[a] 20 °C (CD_2Cl_2), TMS int.; −120 °C: δCH_3C 1 br. signal, δCH_3Si 3 br. signals. [b] 20 °C (C_7D_8), TMS int.; −120 °C (CD_2Cl_2): δNCC 2 br. signals (separated by *ca.* 34 Hz), δNSiC 3 br. signals, δNC partly coincides with signals of CD_2Cl_2. [c] 20 °C (CD_2Cl_2), 85% H_3PO_4 ext.

exhibits dynamic behavior. Temperature-dependent ^1H- and ^{13}C-NMR spectra (Table 1) suggest the presence of form *(b)* having a pentacoordinated Si atom in solution at low temperature[5].



The equivalence of the two $(CH_3)_3C$ groups observed at room temperature (Table 1) is due to an intramolecular 1,3-shift of the $(CH_3)_3Si$ group. The ^{31}P-NMR data (Table 1)—they reflect the expected differences in the PP coupling constants for the *cis* and the *trans* arrangement of the P atoms[6]—show that the amino(imino)thiophosphorane ligand in *(2)* fails to undergo NMR-spectroscopically measurable rotation about an imaginary Pt/P=S bond axis at 20 °C. Crystal structure analysis[7] confirms structure *(a)*.

Procedure

A solution of $(Ph_3P)_2Pt(C_2H_4)$ (960 mg, 1.28 mmol) in anhydrous benzene (7 ml) is added dropwise within 5 min to a stirred, ice-cooled solution of *(1)*[1] (360 mg, 1.29 mmol) in anhydrous benzene (3 ml). After *ca.* 15 min at room temperature, the solution is concentrated in an oil-pump vacuum and the product allowed to crystallize in a refrigerator. The crystals are washed twice with a little cold benzene and dried in an oil-pump vacuum for 30 min at room temperature: yield 1.04 g (70%) *(2)*·$2C_6H_6$. Recrystallization once again from benzene and drying for 16 h in an oil-pump vacuum affords 650 mg (47%) of *(2)*·$1C_6H_6$. On washing these crystals twice in pentane and drying for several hours, benzene-free *(2)*, m.p. 147—149 °C (dec.), is obtained.

Received: July 5, 1979;
supplemented: October 16, 1979 [Z 353 IE]
German version: Angew. Chem. *91*, 1020 (1979)

[1] *O. J. Scherer, N. Kuhn*, Angew. Chem. *86*, 899 (1974); Angew. Chem. Int. Ed. Engl. *13*, 811 (1974).
[2] *O. J. Scherer, N. T. Kulbach, W. Glässel*, Z. Naturforsch. *B 33*, 652 (1978).
[3] Composition established by C,H,N analysis, mass spectrum, and cryoscopic molecular weight determination in dioxane.—Mild hydrolysis of *(2)* afforded the corresponding silicon-free Pt-π compound with the monomeric metathiophosphoric acid derivative *t*BuNH P(S)=N*t*Bu which is unknown as the uncoordinated compound.
[4] With slow partial decomposition.
[5] Hindrance of rotation about the Si N or/and P N bond in *(a)* would give the observed low-temperature coupling pattern only in certain conformations. On attempting to record the $^{29}Si\{^1H\}$-NMR spectrum of *(2)* we have so far been unable to observe any signal between δ = −150 and δ = +150 at 20 and −110 °C. *(1)* (20 °C, CD_2Cl_2, TMS int.): δ = 8.87 (d), $^2J_{SiP}$ = 1.8 Hz.
[6] This supports the assignment proposed for the η^2-CS_2 complex $(Ph_3P)_2Pt(CS_2)$ (greater PtP coupling constant of the P atom *trans* to the S atom): cf. *R. Meij, D. J. Stufkens, K. Vrieze*, J. Organomet. Chem. *144*, 239 (1978).
[7] Preliminary data: space group $P\bar{1}$, a = 10.99, b = 13.72, c = 22.38 Å, α = 72.5, β = 78.1, γ = 69.7°, Z = 2; R = 0.04. Selected bond lengths [pm] and bond angles [°]: P(1) S 207, P(1) Pt 229, Pt S 238, P(2) Pt 239, P(3) Pt 225, P(1)=N 157, P(1) N 168; Pt P(1) S 65.9, P(1) S Pt 61.3, P(1) Pt S 52.8, P(1) Pt P(3) 108.4, P(2) Pt P(3) 103.5, P(2) Pt S 95.8, sum of bond angles around Pt = 360.5, N P(1) N 99.7; P(2) *trans* to P(1), P(3) *trans* to S (cf. Table 1). We thank Dr. *C. Krüger*, Dr. *Y.-H. Tsay*, Dr. *G. Wolmershäuser*, Mülheim, for determining the crystal structure.

Preparation of Stable Vinylketenes by Metal Complex-Induced Olefination and Carbonylation of Alkynes[**]

By *Karl Heinz Dötz*[*]

Vinylketenes have been postulated as intermediates in the electrocyclic ring cleavage of cyclobutenones[1]. However, they have so far resisted all attempts at isolation and detailed characterization[2]. Our studies on the reactions of carbonyl-carbene complexes with alkynes[3] have now opened a new entry to vinylketenes which are stable and can be handled under normal conditions.

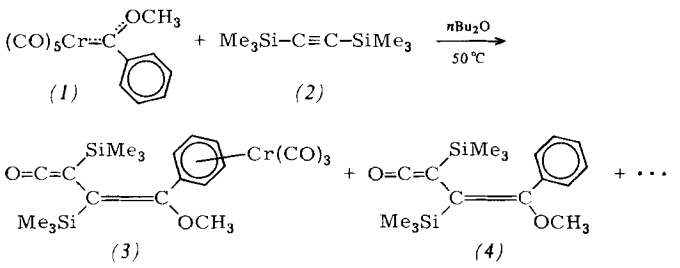
Pentacarbonyl[methoxy(phenyl)carbene]chromium *(1)* reacts with bis(trimethylsilyl)acetylene *(2)* on warming in dibutyl ether to give tricarbonyl[4-methoxy-4-phenyl-2,3-bis(trimethylsilyl)-1,3-butadienone]chromium *(3)*; in addition the metal-free vinylketene derivative *(4)* can also be isolated.

In their IR spectra[4a] the products show ν(C=O) absorptions at 2089 [alongside ν(Cr—C=O): 1980, 1917] for *(3)*

[*] Dr. K. H. Dötz
Anorganisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

[**] Vinylketenes, Part 1. This work was supported by the Deutsche Forschungsgemeinschaft.

and 2090 cm^{-1} for *(4)* while the ^{13}C-NMR spectrum[4b] exhibits signals at $\delta = 180.4$ and 18.3 for *(3)* and at 183.1 and 18.0



(1) *(2)*

(3) *(4)*

for *(4)*, which are to be assigned to the ketene carbon atoms C^1 and C^2[5]. As shown by the X-ray analysis[6] of a single crystal of *(3)* grown from a solution in ether/pentane (1:10) the vinylketene has a *s-trans* conformation and (with respect to the olefinic C=C bond) a *Z* configuration. Furthermore, as is already apparent from the IR and the ^{13}C-NMR spectrum for the dissolved state, a significant conjugation can be ruled out also in the crystal on the basis of the interatomic distances within the diene structural unit and the almost orthogonal arrangement of the olefin and the ketene function.

Hitherto, vinylketenes could only be stabilized by coordination of the diene moiety to transition metals, which considerably modifies their properties[7]. The characteristic steps leading to the formation of the novel compounds *(3)* and *(4)* may be insertion of the alkyne into the metal-carbene bond, giving a *Z*-styryl-carbene complex[8], and carbonylation of the new carbene atom. This vinylketene synthesis formally amounts to head-to-tail addition of a carbene and a carbonyl ligand to the alkyne.

Procedure

A solution of *(1)* (2.53 g, 8.12 mmol) in di-*n*-butyl ether (20 ml) is warmed to 50 °C in an N_2 atmosphere with compound *(2)* (1.90 ml, 8.95 mmol) for 2 h. After removal of the solvent the residue is taken up in dichloromethane/pentane (1:1, 6 ml) and chromatographed on silica gel (Merck, act. 2—3). Non-coordinated vinylketene *(4)* can be eluted in front of the main red zone and isolated as an orange oil which solidifies at −30 °C. There follows the complex *(3)* which precipitates as red crystals from ether/pentane (1:10). Yields: 1.92 g (52%) of *(3)*, m.p. 85 °C; 0.51 g (20%) of *(4)*.

Received: July 13, 1979 [Z 333 IE]
German version: Angew. Chem. *91*, 1021 (1979)

[1] *H. Mayr, R. Huisgen*, J. Chem. Soc. Chem. Commun. *1976*, 57.
[2] Detection of vinylketenes by low-temperature IR spectroscopy: *D. L. Chapman, J. D. Lassila*, J. Am. Chem. Soc. *90*, 2449 (1968); *D. Lemmer, H. Perst*, Tetrahedron Lett. *1972*, 2735; *P. Schiess, P. Radimerski*, Angew. Chem. *84*, 345 (1972); Angew. Chem. Int. Ed. Engl. *11*, 288 (1972); Helv. Chim. Acta *57*, 2583 (1974).
[3] *K. H. Dötz, R. Dietz*, Chem. Ber. *111*, 2517 (1978); and references cited therein.
[4] a) In *n*-octane; b) [D_6]acetone, TMS int. std.
[5] Cf. *J. Firl, W. Runge*, Z. Naturforsch. *B 29*, 393 (1973).
[6] *U. Schubert, K. H. Dötz*, Cryst. Struct. Commun., in press.
[7] *R. B. King*, Inorg. Chem. *2*, 642 (1963); *M. G. Newton, N. S. Pantaleo, R. B. King, C.-K. Chu*, J. Chem. Soc. Chem. Commun. *1979*, 10; *A. E. Hill, H. M. R. Hoffmann, ibid. 1972*, 574; *T.-A. Mitsudo, T. Sasaki, Y. Watanabe, Y. Takegami, S. Nishigaki, K. Nakatsu, ibid. 1978*, 252; *P. Binger, B. Cetinkaya, C. Krüger*, J. Organomet. Chem. *159*, 63 (1978).
[8] *K. H. Dötz*, Chem. Ber. *110*, 78 (1977); *H. Fischer, K. H. Dötz, ibid.*, in press.

The Homologous Series of Cyclic Polysilanes from $(Me_2Si)_5$ to $(Me_2Si)_{35}$[**]

By *Lawrence F. Brough, Koichi Matsumura*, and *Robert West*[*]

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

Because they show unusual properties resulting from electron delocalization[1], the cyclopolysilanes are of interest as model compounds for electronic effects in elemental silicon[6]. Variously substituted four-, five-, six-, and seven-membered silane rings are known[7], and $(Me_2Si)_8$ and $(Me_2Si)_9$ were recently isolated from the reaction of Me_2SiCl_2 with lithium metal[8]. We now report a modification of the synthesis of cyclopolysilanes from Me_2SiCl_2 and Na/K alloy, which apparently produces *all of the permethylcyclosilanes* $(Me_2Si)_n$ *from* $n = 5$ *through* $n = 35$.

The usual synthesis of $(Me_2Si)_n$ from Me_2SiCl_2 and Na/K in tetrahydrofuran (THF) yields mostly $(Me_2Si)_6$, along with about 10% $(Me_2Si)_5$ and 2% $(Me_2Si)_7$[9]. Medium and large-ring cyclosilanes are obtained only if the Me_2SiCl_2 is added *slowly* to Na/K in refluxing THF. In a typical experiment 1200 ml of dry THF and 185 ml (4.7 mol) of Na/K alloy were stirred at reflux in a 5-l flask equipped with a high capacity condenser and 244 ml (2.0 mol) of $(CH_3)_2SiCl_2$ was added dropwise over a period of 10 h. The mixture was cooled slightly, 1200 ml of hexane was added, and the excess alloy was gradually destroyed by the cautious dropwise addition of approximately 100 ml of water. Another 1000 ml of water was then added, after which the organic phase was separated, filtered to remove polymer, and washed with aqueous NaCl. The solvent was removed by distillation giving a crystalline precipitate. A combination of recrystallization from ethanol/THF (7:1) and fractional sublimation served to remove most of the $(Me_2Si)_5$ and $(Me_2Si)_6$ from the product mixture. The residual solids, now enriched in medium and large rings, could be separated by high pressure liquid chromatography (HPLC) as shown in Figure 1.

The compounds were identified as $(Me_2Si)_n$ oligomers by mass spectrometry. Peak matches were obtained at high resolution for $n = 8$ through 19 and for $n = 24$, all with deviations less than 3.5 ppm. The compounds appear to be pure as obtained by HPLC, in that only sharp singlets are observed in the ^1H-NMR spectra (Table 1). The cyclosilane structure is assigned to the higher fractions through $n = 35$ on the basis of the HPLC results.

Table 1. Yields and ^1H-NMR absorptions for permethylcyclosilanes, $(Me_2Si)_n$.

n	Yield [%] [a]	δ	*n*	Yield [%] [a]	δ
5	17.0	0.135	13	0.19	0.192
6	52.1	0.132	14	0.21	0.200
7	2.6	0.128	15	0.22	0.197
8	1.3	0.144	16	0.19	0.196
9	0.76	0.163	17	0.14	0.196
10	0.16	0.188	18	0.09	0.197
11	0.18	0.186	19	0.05	0.197
12	0.16	0.190	20—35	~0.15	—

[a] ±5% for $n = 5$, 6 and 7, ±20% for $n = 8$ to 19. Yields for $n > 8$ were estimated from HPLC peak areas using UV detection at 254 nm, corrected for molecular weight and molar absorbance for each compound.

[*] Prof. Dr. R. West, L. F. Brough, Dr. K. Matsumura
Department of Chemistry, University of Wisconsin
Madison, WI 53706 (USA)

[**] Cyclic Polysilanes, Part 14. This work was supported by the U. S. Air Force of Scientific Research, Grant AF-AFOSR-78-3570.—Part 13: [3].

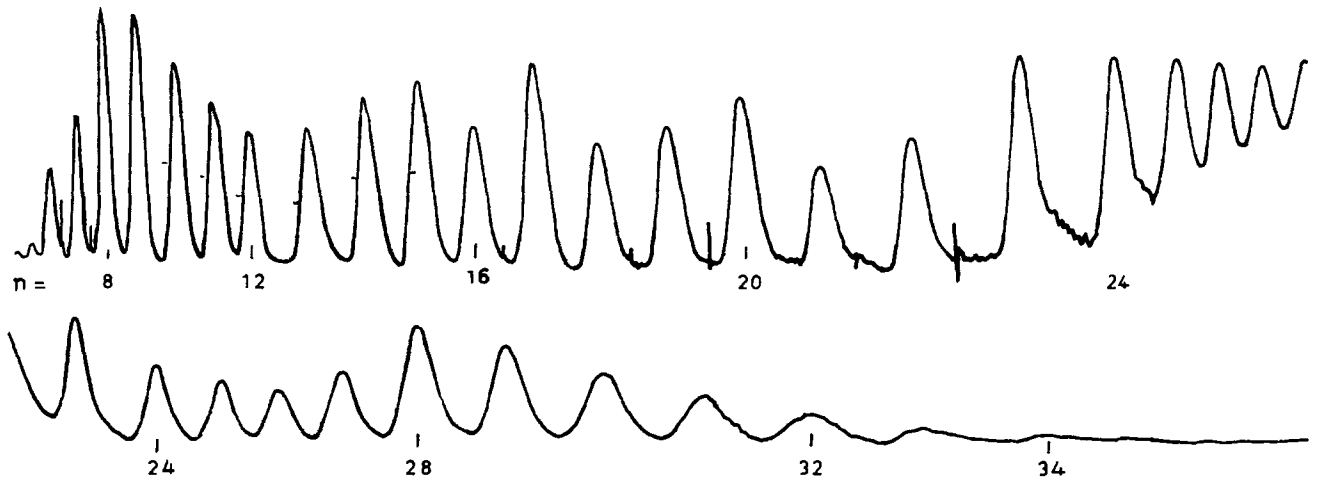


Fig. 1. High pressure liquid chromatogram of permethylcyclosilanes, $(Me_2Si)_n$ (methanol/THF on a Whatman M9 column containing Partisil-10 ODS).

Estimated yields are given in Table 1. As expected on statistical grounds, yields decrease with increasing ring size from $n=6$ to 10 and above $n=16$. However from $n=10$ to $n=16$ the yield of each compound is approximately equal. Apparently these cyclosilanes exhibit a medium-ring effect of the type known in cycloalkane chemistry, in which the increased entropy requirement for closure as ring size increases is balanced by decreased steric repulsion. Except for the cycloalkanes the 31 permethylcyclosilanes may form the longest homologous series of cyclic compounds known to chemistry.

Received: August 13, 1979 [Z 340 IE]
German version: Angew. Chem. *91*, 1022 (1979)

[1] For example they form delocalized anion [2] and cation [3] radicals, yield charge-transfer complexes with π-acceptors [4], and show strong directing effects of substituents on further substitution [5].
[2] *E. Carberry, R. West, G. E. Glass*, J. Am. Chem. Soc. *91*, 5446 (1969).
[3] *H. Bock, W. Kaim, M. Kira, R. West*, J. Am. Chem. Soc., in press.
[4] *V. F. Traven, R. West*, J. Am. Chem. Soc. *95*, 6824 (1973); *H. Sakurai, M. Kira, T. Uchida, ibid. 95*, 6826 (1973).
[5] *T. Drahnak, R. West*, Abstr. of Papers, Fourth International Symposium on Organosilicon Chemistry, Karlsruhe 1978, p. 132.
[6] *L. C. Snyder:* A Quantum Chemist's View of Silicon Chemistry Related to Silicon Surface Reconstruction. Paper presented at International Symposium on Atomic, Molecular and Solid State Theory, Flagler Beach, Florida, March 1978.
[7] *R. West, E. Carberry*, Science *189*, 179 (1975); *E. Hengge* in *A. Rheingold:* Homoatomic Rings, Chains and Macromolecules of Main-Group Elements. Elsevier, Amsterdam 1977, Chap. 9, p. 235; *E. Carberry, R. West*, J. Am. Chem. Soc. *91*, 5440 (1969).
[8] *K. Matsumura, L. F. Brough, R. West*, J. Chem. Soc. Chem. Commun. *1978*, 1092.
[9] *R. West, L. F. Brough, W. Wojnowski*, Inorg. Synth. *19*, 265 (1979).

One-Pot Syntheses of α-Ferrocenylalkylamines[**]

By *Rudolf Herrmann* and *Ivar Ugi*[*]

The use of 1-ferrocenyl-2-methylpropylamine *(4b)* permits asymmetric peptide syntheses with high overall yields and unlimited stereoselectivity[1]; however, this reagent was previously accessible only with difficulty[2].

[*] Prof. Dr. I. Ugi, Dipl.-Chem. R. Herrmann
Organisch-chemisches Institut der Technischen Universität München
Lichtenbergstrasse 4, D-8046 Garching (Germany)

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

$$\underset{(1)}{FcH} + \underset{(2)}{R^1R^2C{=}O} + \underset{(3)}{HNR^3R^4} \rightarrow \underset{(4)}{Fc{-}CR^1R^2{-}NR^3R^4} + H_2O \qquad (a)$$

Fc = Ferrocenyl; *(a)*, $R^1=R^2=H$, $R^3=R^4=Me$; *(b)*, $R^1=H$, $R^2=i$Pr, $R^3=R^4=H$; *(c)*, $R^1=H$, $R^2=i$Pr, $R^3=R^4=Me$

The synthesis of α-ferrocenylalkylamines *(4)* by α-aminoalkylation according to eq. (a) would seem an obvious course of action since *(4a)* can be obtained from ferrocene *(1)* and iminium ions [formally from *(2)* + *(3)*][3]. However, we were unable to obtain *(4b)* and *(4c)* by reaction of *(1)* with the iminium ions formed from isobutyraldehyde and ammonia or dimethylamine.

Since α-ferrocenylalkylcarbenium salts *(5)* are stabilized by the ferrocene substituent[4] we examined whether eq. (b) might be a practical proposition.

$$(1) + (2) \xrightarrow{HX} \underset{\underset{(5)}{\oplus}}{Fc{=}CR^1R^2}\ X^{\ominus} \xrightarrow[-HX]{HNR^3R^4\ (3)} (4) \qquad (b)$$

Condensations of ferrocene *(1)* with carbonyl compounds *(2)* to give macromolecular and "oligomeric", and in some cases also "monomeric", compounds have already been described[5]. These reactions probably proceed *via* carbenium ions as in *(5)*. We recently reported the reaction of ferrocene and isobutyraldehyde in trifluoroacetic acid to form the α-ferrocenylisobutylcarbenium ion[6].

We have now discovered that one-pot syntheses of compounds of type *(4)* according to eq. (b) proceed particularly favorably on working in the trichloroacetic acid/fluorosulfuric acid system and when the reaction mixture is introduced into a solution of the amine *(3)*. Some examples are shown in Table 1.

Procedure

Synthesis of *(4)*: Compounds *(1)* (1.86 g, 10 mmol) and *(2)* (20 mmol) are dissolved with stirring in a mixture of trichloroacetic acid (10.0 g) and acetic acid (1.5 ml) at −10 °C under N_2. After addition of fluorosulfuric acid (1.5 ml) the mixture is allowed to react for 20 to 40 min at −10 to 0 °C. The reaction mixture is diluted with dichloromethane (10 ml) and added with vigorous stirring at −78 °C to a mixture

Table 1. One-pot syntheses of α-ferrocenylalkylamines *(4)* by eq. (b).

(2) R^1	(2) R^2	(3) R^3	(3) R^4	Amount [g] [a]	(4) No.	Yield [%]	M.p. [°C]	Ref.
H	Me [b]	H	H	25	*(4d)*	23	—	[7]
H	Me [b]	Me	Me	13	*(4e)*	53	—	[8]
H	Me [c]	Me	Me	13	*(4e)*	62	—	[8]
H	Me [c]	H	Me	15	*(4f)*	31	—	[9]
H	Me [c]	H	*i*Pr	30	*(4g)*	42	—	—
H	*i*Pr	H	H	25	*(4b)*	32	—	[2]
H	*i*Pr	H	Me	15	*(4h)*	37	51.5—52	—
H	*i*Pr	Me	Me	13	*(4c)*	50	—	[2]
H	*i*Pr	H	*i*Pr	30	*(4i)*	40	79—80	—
H	*i*Pr	$-(CH_2)_2-O-(CH_2)_2-$		30	*(4j)*	49	75.5—76.5	—
H	*t*Bu	H	H	25	*(4k)*	57	66.5—67.5	[10]
H	*t*Bu	H	Me	15	*(4l)*	60	113.5—114	—
H	*t*Bu	Me	Me	13	*(4m)*	80	41—42	—
H	*t*Bu	H	Ph	40	*(4n)*	36	74.5—75.5	—
H	*t*Bu	H	*t*Bu	35	*(4o)*	36	53—54	—
H	*t*Bu	$-(CH_2)_5-$		30	*(4p)*	68	103—104	—
H	*t*Bu	$-(CH_2)_2-O-(CH_2)_2-$		30	*(4q)*	59	79.5—80	—
H	cHex	H	H	25	*(4r)*	40	88.5—89	[10]
H	cHex	H	Me	15	*(4s)*	37	98.5—99	—
H	cHex	H	CH_2Ph	30	*(4t)*	38	94—95	—
H	3-Oxo 2-bornyl	Me	Me	13	*(4u)*	12 [d]	—	—
Me	Me	H	H	25	*(4v)*	27	50—51	—
Me	Ph	H	H	25	*(4w)*	28	104.5—105.5	—
$-(CH_2)_5-$		Me	Me	13	*(4x)*	63 [e]	97.5—98.5	—

[a] This applies to syntheses according to the procedure given. [b] From acetaldehyde. [c] From paraldehyde. [d] In addition to 45% 3-(ferrocenylmethylene)camphor, m.p. 110—110.5 °C. [e] In addition to 17% 1-ferrocenylcyclohexene.

of isopropyl alcohol (20 ml) and the amine *(3)* (quantities given in Table 1). After slow warming to 20 °C, dichloromethane (100 ml) is added and the mixture is washed with water (3 × 100 ml), extracted with 8% phosphoric acid (2 × 100 ml), and the acid extracts are washed with dichloromethane (50 ml) and neutralized with conc. NaOH. Extraction is then performed twice with dichloromethane, the extracts are dried with Na_2SO_4, and the solvent is stripped off. The residue is recrystallized from hexane, distilled in vacuum or purified by chromatography.

Received: July 24, 1979 [Z 345 IE]
German version: Angew. Chem. *91*, 1023 (1979)

[1] *R. Urban, I. Ugi,* Angew. Chem. *87*, 67 (1975); Angew. Chem. Int. Ed. Engl. *14*, 61 (1975); *R. Urban, D. Marquarding, I. Ugi,* Hoppe-Seylers Z. Physiol. Chem. *359*, 1541 (1978); *I. Ugi* in *E. Gross, J. Maienhofer:* The Peptides. Vol. II. Academic Press, New York, in press; *J. Dugundji, R. Kopp, D. Marquarding, I. Ugi,* Top. Curr. Chem. *75*, 165 (1978); *J. Brandt, C. Jochum, I. Ugi, P. Jochum,* Tetrahedron *33*, 1353 (1977).

[2] *G. Eberle, I. Lagerlund, I. Ugi, R. Urban,* Tetrahedron *34*, 977 (1978); *D. Marquarding, H. Burghard, I. Ugi, R. Urban, H. Klusacek,* J. Chem. Res. *1977* (S) 82, (M) 915.

[3] *J. K. Lindsay, C. R. Hauser,* J. Org. Chem. *22*, 355 (1957).

[4] *T. D. Turbitt, W. E. Watts,* J. Chem. Soc. Perkin Trans. II *1974*, 177, 185, and references cited therein.

[5] *E. G. Perevalova, T. V. Nikitina,* Organomet. React. *4*, 267, 393 (1972); *E. W. Neuse, K. Koda,* J. Polym. Sci. A1, *4*, 2145 (1966); *W. Reeve, E. F. Group,* J. Org. Chem. *32*, 122 (1967); *M. Shiga, I. Motoyama, K. Hata,* Bull. Chem. Soc. Jpn. *41*, 1891 (1968); *A. N. Nesmeyanov, L. P. Yur'eva, O. T. Nikitin,* Izv. Akad. Nauk SSSR, Ser. Khim. *1969*, 1096; *P. Dudnik, J. M. Tancrede, M. Rosenblum,* J. Organomet. Chem. *18*, 365 (1969); *H. Valot,* Bull. Soc. Chim. Fr. *36*, 564 (1969); *M. I. Bruce, F. G. A. Stone, B. J. Thomson,* J. Organomet. Chem. *77*, 77 (1974).

[6] *R. Herrmann, I. Ugi,* Angew. Chem. *90*, 734 (1978); Angew. Chem. Int. Ed. Engl. *17*, 689 (1978).

[7] *K. Schlögl, M. Fried,* Monatsh. Chem. *95*, 558 (1964).

[8] *G. Gokel, P. Hoffmann, H. Klusacek, D. Marquarding, E. Ruch, I. Ugi,* Angew. Chem. *82*, 77 (1970); Angew. Chem. Int. Ed. Engl. *9*, 64 (1970).

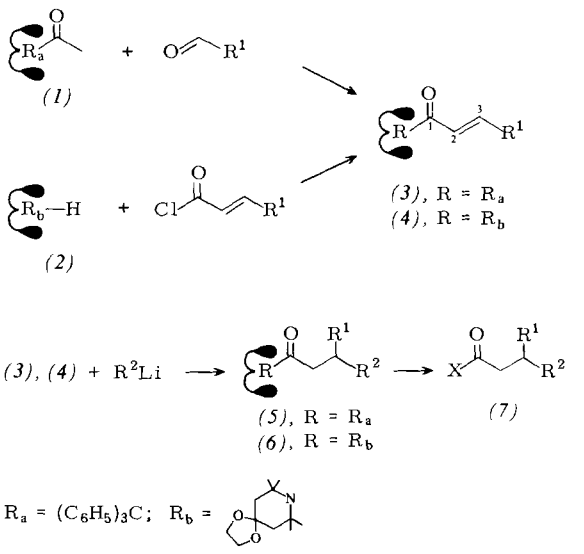
[9] *P. Dixneuf, R. Dabard,* Bull. Soc. Chim. Fr. *1972*, 2847.

[10] *G. Eberle,* Dissertation, Technische Universität München 1977.

α,β-Unsaturated Carbonyl Compounds with Sterically Protected Carbonyl Groups—Enforced a³ *versus* a¹ Reactivity

By *Dieter Seebach* and *Rita Locher*[*]

The ambident character of enones and of acrylic, crotonic, and cinnamic acid derivatives is an age-old synthetic problem; generally, organolithium compounds prefer the 1,2-addition[1a] and Gilman reagents the Michael addition[1b]. Grignard compounds are not selective. Steric hindrance of the carbonyl group shifts the reactivity into the β-position[1c].



[*] Prof. Dr. D. Seebach, Dipl.-Chem. R. Locher
Laboratorium für Organische Chemie der
Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

Compounds of type *(3)* and *(4)* with readily cleavable steric protecting groups[2] which do not cancel the effect of the CO group should only undergo addition at the C=C double bond.

Aldol condensation of 1,1,1-triphenylacetone *(1)*[3a], which—as expected—is smoothly deprotonated by butyllithium in tetrahydrofuran (THF), with acetaldehyde and benzaldehyde afforded the enones *(3a)* and *(3b)*, respectively. The amides *(4a)* to *(4c)* were obtained by acylation of the base *(2)*[2c] with acid chlorides (see Table 1).

Indeed, the enones *(3)* and amides *(4)* are extraordinarily reactive a^3 reagents: between -80 and $-40\,^{\circ}C$ (in THF) methyl-, *n*-butyl-, phenyl- and 1,3-dithian-2-yllithium add in high yields to give, respectively, the saturated carbonyl compounds *(5)* and *(6)*. Even with *tert*-butyllithium an adduct [*(5c)*] could be isolated (see Table 1). No alcohols resulting from carbonyl addition (a^1 reactivity) could be detected; surprisingly, deprotonation of *(3a)* in the γ-position, which would lead to a dienolate, takes place at most as a side reaction.

Table 1. Yields and physical data of the products of type *(3)*—*(6)* after purification by chromatography on silica gel and/or recrystallization. Reactions: *(1)*→*(3)*; *(2)*→*(4)*; *(3)*→*(5)*; *(4)*→*(6)* (if not otherwise indicated).

Product	R^1	R^2	Yield [%]	M.p. [°C] B.p. [°C/torr]
(3a)	CH_3		82	177
(3b)	C_6H_5		54	153—154
(4a)	H		47 [a]	69
(4b)	CH_3		83 [a]	76—77
(4c)	C_6H_5		45 [a]	118
(5aa)	CH_3	CH_3	89	81
(5ab)	CH_3	*n*-C_4H_9	90	oil [b]
(5ac)	CH_3	*t*-C_4H_9	22	102—103
(5ad) ≡ *(5ba)*	CH_3	C_6H_5	78	120—121
(5ae)	CH_3	1,3-dithian-2-yl	59	112—113
(5ba) ≡ *(5ad)*	C_6H_5	CH_3	62	120—121
(5bb)	C_6H_5	*n*-C_4H_9	78	102—103
(5bc)	C_6H_5	1,3-dithian-2-yl	77	161
(5c) [c]	H	C_6H_{13}	57	91
(6aa)	H	CH_3	36 [d]	$55/10^{-3}$
(6ab)	H	*n*-C_4H_9	80	oil [b]
(6ba)	CH_3	*n*-C_4H_9	67	oil [b]
(6ca)	C_6H_5	CH_3	87	oil [b]
(6cb)	C_6H_5	*n*-C_4H_9	81	oil [b]
(6d) [e]	H	C_6H_{13}	98	$80/10^{-2}$
R_b $COCH_3$ [f]			82 [a]	49

[a] Based on the acid chloride on reaction with *(2)* in the molar ratio 1:2 [2c]. [b] After chromatography on silica gel with hexane/ethyl acetate [in the case of amides *(6)*] or dichloromethane/hexane [in the case of ketone *(5ab)*]. [c] From *(1)* and 1-iodoheptane. [d] Together with 52% of the "dimeric methylation product" *(6)*, R^1 = H, R^2 = $CH(COR_b)(C_2H_5)$ in the α-position, m.p. 120—121 °C. [e] From R_b $COCH_3$ and 1-iodoheptane. [f] From *(2)* and acetyl chloride.

For cleavage of *(5)* we exploited the suitability of the trityl anion as a leaving group[4], and for the cleavage of *(6)* the retro-*Mannich* reaction of the group R_b[2c]. Thus, cleavage of the trityl ketones *(5c)*[3b] and *(5bb)* using a procedure recommended for carboxylic acid derivatives, which are difficult to hydrolyze[3c], afforded triphenylmethane (>96%) and the acids *(7)*, X = OH [nonanoic (82%) and 3-phenylheptanoic acid (81%), respectively]. On reaction with ethanolic hydrochloric acid, the amide *(6d)*[3d] is cleaved to give a mixture of nonanoic acid (10%) and its ethyl ester (62%)[3e]. All new compounds were identified spectroscopically and by elemental analyses; their melting points and yields are listed in Table 1.

The experiments described here show that Michael acceptors of the type *(3)* and *(4)* can be useful reagents for the synthesis of acid derivatives *(7)*: the adducts *(5)*, which can also be obtained with Grignard reagents, are beautifully crystalline and can be readily isolated. The carbonyl group is protected against nucleophilic attack, but can, if necessary, be converted into carboxylic acid functions.

Received: July 17, 1979 [Z 351a IE]
German version: Angew. Chem. *91*, 1024 (1979)

[1] a) Novel exceptions are the reactions of unsaturated thioamides [*Y. Tamaru, T. Harada, Z. Yoshida*, J. Am. Chem. Soc. *101*, 1316 (1979)] and of α,α′-dicarbonylphosphorus ylides [*M. P. Cooke, Jr., R. Goswami, ibid. 99*, 642 (1977)]; b) *G. Posner*, Org. React. *19*, 1 (1972); c) mesityl vinyl ketone is *e.g.* a pure Michael-acceptor toward Grignard reagents [*W. A. De Meester, R. C. Fuson*, J. Org. Chem. *30*, 4332 (1965)].

[2] a) (Trityl = R_a) *R. Schlecker, D. Seebach, W. Lubosch*, Helv. Chim. Acta *61*, 512 (1978); b) (2,4,6-tri-*tert*-butylphenoxy = TBPO) *D. Seebach, T. Hassel*, Angew. Chem. *90*, 296 (1978); Angew. Chem. Int. Ed. Engl. *17*, 274 (1978); c) (acetal of 2,2,6,6-tetramethyl-4-oxo-piperidyl = R_b) *T. Hassel, D. Seebach*, Helv. Chim. Acta *61*, 2237 (1978); Angew. Chem. *91*, 427 (1979); Angew. Chem. Int. Ed. Engl. *18*, 399 (1979), and references cited therein.

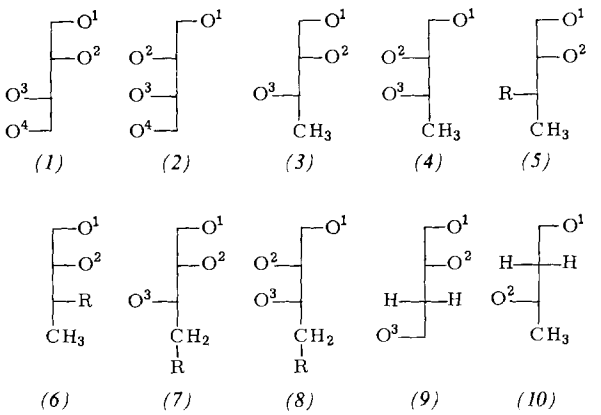
[3] a) *J. Cason, F. J. Schmitz*, J. Org. Chem. *25*, 1293 (1960); b) from *(1)*/BuLi and 1-iodoheptane in THF, see Table 1; c) *t*-BuOK/H_2O/24 h/20 °C, and 72 h/50 °C, respectively, cf. *P. G. Gassman, P. K. G. Hodgson, R. J. Balchunis*, J. Am. Chem. Soc. *98*, 1275 (1976); d) from R_b, $COCH_3$/BuLi and 1-iodoheptane in THF/hexamethylphosphoric triamide, see Table 1; e) 5N ethanolic HCl, 4 d, 60 °C.

[4] *D. J. Cram*: Fundamentals of Carbanion Chemistry. Academic Press, New York 1965, Chap. 4 and references cited therein.—*Haller-Bauer* cleavage see the review: *K. E. Hamlin, A. W. Weston*, Org. React. *9*, 1 (1957).

Chiral Reagents from Tartaric Acid—1-Benzyloxy-3,4-epoxy-2-butanol, a Versatile Intermediate for the Synthesis of Enantiomers

By *Ernst Hungerbühler, Dieter Seebach,* and *Daniel Wasmuth*[*]

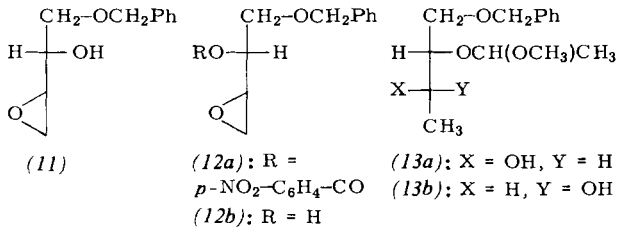
Tartaric acid, *both enantiomeric forms* of which are readily accessible, has already proven its value as precursor for chiral reagents in natural product synthesis. The number of possible target molecules would increase enormously if the structural changes indicated in *(1)*—*(10)* for natural (*R,R*)-tartaric acid could be effected. All the transformations



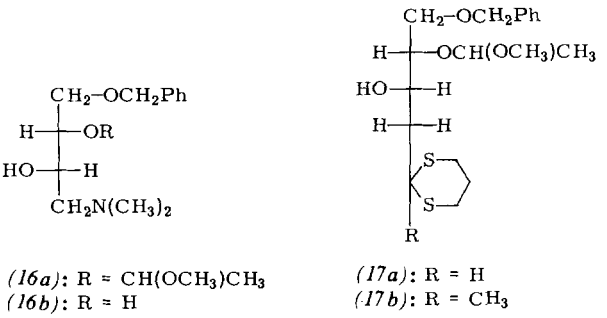
should be capable of being carried out in high yields and with large quantities. *All the structures (1)—(10) with reversed chirality* would then also be preparable from unnatural tartaric acid.

[*] Prof. Dr. D. Seebach, Dipl.-Chem. E. Hungerbühler, Dipl. sc. nat. D. Wasmuth
Laboratorium für Organische Chemie der
Eidgenössischen Technischen Hochschule
ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich (Switzerland)

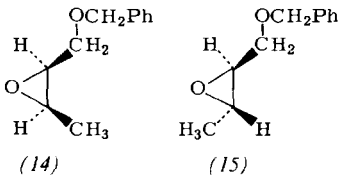
We describe here the synthesis of the key compound *(11)*, *via* which structures of the type *(1)*—*(8)* are accessible, as well as a productive route from natural tartaric acid to unnatural malic acid [cf. *(9)*] and from this to a 1,3-butanediol derivative [see *(10)*]. The individual steps with conditions and yields are given in Table 1. The *epoxyalcohol (11)* [cf. *(1)*] is a distillable liquid (b.p. 130 °C/0.01 torr) and can be stored in the refrigerator; the total yield from tartrate is 45%, while the intermediate products (Table 1) are either distillable or can—like the tosylates—be used further without purification. Inversion at C-2 of *(11)* [cf. *(2)*] can be achieved by the method of *Mitsunobu* [azocarboxylate/triphenylphosphane/RCOOH[1], →*(12a)*], whereby the *erythro*-isomer *(12b)* is accessible. Protection of the OH group of *(11)* by reaction with methyl vinyl ether and opening of the epoxide ring with $LiHB(C_2H_5)_3$ [tetrahydrofuran (THF), −40 to 20 °C, 3 h, then H_2O_2/NaOH] leads to the *triol derivative (13a)* [79% from *(11)*] whose epimer *(13b)* is prepared *via* the benzoate according to the method of *Mitsunobu* [46% from *(11)*]. Tosylation of the free hydroxy group in the two diastereomers *(13a)* and *(13b)*, cleavage of the methoxyethyl protecting group and γ-elimination with KOH/CH_3OH affords the *cis/trans* isomeric *epoxides (14)* and *(15)* [yield from *(13)* 69 and 76%, respectively]. In *(13)*—*(15)* the structural changes to *(3)* and *(4)* are effected. The oxiranes *(14)* and *(15)* are precursors for *branching* [see *(5)* and *(6)*]; they are attacked regioselectively at the methylated C atom by nucleophiles[2].—Opening of the methoxyethyl derivative of *(11)* with dimethylamine or 2-lithio-1,3-dithianes affords the benzyloxyaminodiol *(16b)* [62% from *(11)*][3] and the *chain-lengthened* [cf. *(7)*, *(8)*] compounds *(17)*, respectively. *(17b)* [78% from *(11)*] is a ketotriol containing three different types of protecting groups and a free functional group; it derives from a 4,6-dideoxyhexose, whose derivatives occur as glycons of macrolide antibiotics[4]. *(17a)* [82% from *(11)*] is a derivative of 2-deoxy-L-lyxose; correspondingly, from the mirror image of *(12b)* a thioacetal of 2-deoxy-L-ribose would be formed.



(11) *(12a)*: R = *p*-NO_2–C_6H_4–CO *(12b)*: R = H *(13a)*: X = OH, Y = H *(13b)*: X = H, Y = OH

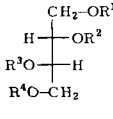
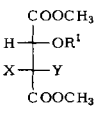
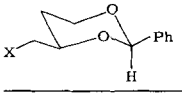


(16a): R = $CH(OCH_3)CH_3$ *(16b)*: R = H *(17a)*: R = H *(17b)*: R = CH_3



(14) *(15)*

Table 1. Synthesis of the epoxide *(11)*, of (*R*)-malic acid methyl ester [cf. *(9)*] and of (*S*)-4-methyl-2-phenyl-1,3-dioxane (1,3-butanediol acetal) [cf. *(10)*] from (*R,R*)-tartaric acid esters.

	Compound	Reagent for conversion to the subsequent compound	
	(*R,R*)-tartaric acid methyl or -ethyl ester	CH_2=CH $OCH_3/H^{\oplus}$	(98%)
	2,3-Di-*O*-(1-methoxyethyl)tartaric acid ethyl ester	$LiAlH_4/Et_2O$	(92%)
	$R^1=R^4=H$, $R^2=R^3=CH(OCH_3)CH_3$	NaH/$PhCH_2Br$ [a]	(84%)
	$R^1=CH_2Ph$, $R^2=R^3=CH(OCH_3)CH_3$, $R^4=H$	$TosCl/Pyridine/CH_2Cl_2$ [b]	↓
	$R^1=CH_2Ph$, $R^2=R^3=CH(OCH_3)CH_3$, $R^4=Tos$	$H_2O/H^{\oplus}$/Acetone [c]	↓
	$R^1=CH_2Ph$, $R^2=R^3=H$, $R^4=Tos$	KOH/CH_3OH/H_2O [d]	(59%)
	(11)		
	$R^1=H$, X=OH, Y=H [(*R,R*)-tartaric acid methyl ester]	CH_3COCl	(61%)
	$R^1=OCOCH_3$, X=OH, Y=H	$SOCl_2$/pyridine	(79%)
	$R^1=OCOCH_3$, X=H, Y=Cl	$HSnBu_3/C_6H_5CH_3$	(94%)
	$R^1=OCOCH_3$, X=Y=H	$CH_3OH/H^{\oplus}$	(97%)
	$R^1=X=Y=H$ [(*R*)-malic acid methyl ester] [e]	CH_2=CH $OC_2H_5/H^{\oplus}$	(99%)
	$R^1=CH(OC_2H_5)CH_3$, X=Y=H	$LiAlH_4/Et_2O$	(96%)
	CH_2OH instead of $COOCH_3$, $R^1=CH(OC_2H_5)CH_3$, X=Y=H	$H^{\oplus}/CH_3OH/H_2O$	(70%)
	CH_2OH instead of $COOCH_3$, $R^1=X=Y=H$	PhCHO/$H^{\oplus}$	(91%)
	X=OH	TosCl/pyridine	(56%)
	X=OTos	$LiHBEt_3$/THF	(95%)
	X=H [f]		

[a] Separation of the dibenzylated product by bulb-to-bulb distillation (b.p. 145 °C/0.005 torr). [b] Before workup, excess TosCl must be hydrolyzed by dropwise addition of water. [c] The hydrolysis must be carried out in homogeneous solution, otherwise it forms very difficultly hydrolyzable cyclic acetaldehyde acetals. [d] Distillation of *(11)* from the crude product without decomposition is possible only if it does not contain tosylates (^{1}H-NMR monitoring). If necessary, tosylates are removed chromatographically (silica gel, ether). [e] The correlation of tartaric acid with malic acid was first described by *Freudenberg* in 1922 [6]. For the conversion [7] of malic acid methyl ester into 1-bromo-3,4-epoxybutane and its use in the synthesis of vermiculin, see [8]. [f] For the use of the respective diols in the synthesis of pyrenophorin see [8, 9].

A few characteristic data of the compounds *(11)*, *(12)*, and *(14)—(17)* are collected in Table 2. Apart from the diastereomerism caused by the methoxyethyl protecting group in *(13)*, *(16a)*, and *(17)*, the compounds are, according to the ^{1}H- and ^{13}C-NMR spectra, diastereomerically pure and thus in the present case also enantiomerically pure; we have prepared *(11)* and *(14)* in both enantiomeric forms.

Table 2. Characteristic physical data of the compounds *(11)*, *(12)*, *(14)—(17)* obtained from (*R,R*)-tartaric acids. ^{1}H-NMR, ^{13}C-NMR, IR, and MS data are consistent with the given structures.

Cpd.	B.p., M.p., Spec. Rotation ($c \approx 1$, $CHCl_3$)	^{1}H-NMR ($CDCl_3$), δ-values, coupling constants [Hz]
(11)	130 °C/0.01 torr $[\alpha]_D^{25} = +13.5°$ $[\alpha]_D^{25} = -12.5°$ [from (*S,S*)-tartaric acid]	4.55 (s, CH_2Ph), 3.08 (q, $J=4$, 3-H), 2.4 (d, $J=6$, OH [a])
(12a)	72—73 °C $[\alpha]_D^{25} = +2.8°$	5.16 (q, $J=5$, 2-H), 2.82 (m, 2 4-H)
(12b)	$[\alpha]_D^{25} = -10.5°$	4.55 (s, CH_2Ph), 2.9—3.15 (m, 3-H), 2.34 (d, $J=4$, OH [a])
(14)	75 °C/0.05 torr $[\alpha]_D^{25} = +17.7°$	4.4 and 4.3 (AB, $J=12$, CH_2Ph), 2.66 (q × d, $J_q=5.5$, $J_d=4$, 3-H) [b]
(15)	75 °C/0.05 torr $[\alpha]_D^{25} = -14.0°$	4.4 and 4.33 (AB, $J=11$, CH_2Ph), 2.54 (q × d, $J_q=5.5$, $J_d=2$, 3-H) [b]
(16b)	53—54 °C $[\alpha]_D^{25} = -18.4°$	4.54 (s, CH_2Ph), 3.1—3.4 (m, 2 OH [a]), 1.25 (s, $N(CH_3)_2$)
(17a)		4.51 (s, CH_2Ph), 2.6 (d, $J=7$, OH [a])
(17b)		4.52 (s, CH_2Ph), 3.3 and 3.28 (each 1 s, OCH_3 (diastereomeric ratio 1:1)), 3.15 (d, $J=4$) and 3.06 (d, $J=5$, OH [a]), 1.65 (s, 3 6-H)

[a] Exchangeable with D_2O. [b] 360-MHz ^{1}H-NMR spectra in $CDCl_3$ and in C_6D_6 were also recorded.

Through the reagents described here the *enantiomeric* tartaric acids[5] have become a versatile source of chirality. In contrast to the carbohydrates generally employed so far (see references cited in [8]) inexpensive tartaric acid has only two types (C_2 axis!) of functional groups, whose number can be readily doubled [see *(1)*, *(2)*]; moreover, a C_4 unit can be incorporated with less effort into a greater number of target molecules than a C_6 building block.

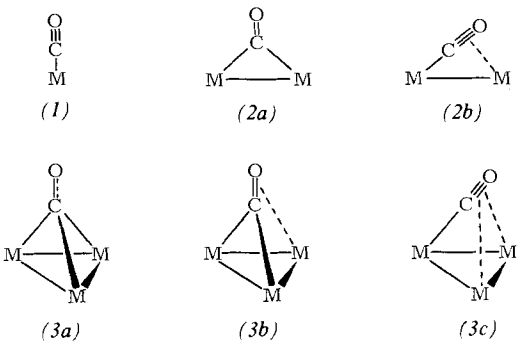
Received: August 21, 1979 [Z 351 b IE]
German version: Angew. Chem. *91*, 1025 (1979)

[1] *O. Mitsunobu et al.*, Tetrahedron Lett. *1976*, 2455; *H. Leibner, E. Zbiral*, Helv. Chim. Acta *59*, 2100 (1976); *60*, 417 (1977).
[2] *E. J. Corey et al.*, J. Am. Chem. Soc. *100*, 4618 (1978); *G. Shtacher, R. Rubinstein*, J. Med. Chem. *21*, 678 (1978).
[3] Cf. *J. A. Musich, H. Rappoport*, J. Am. Chem. Soc. *100*, 4865 (1978).
[4] *W. Keller-Schierlein*, Fortschr. Chem. Org. Naturst. *30*, 313 (1973).
[5] On purchasing 100 kg quantities, the natural (*R,R*)-tartaric acid is available at SFr 5 per kg, the unnatural (*S,S*)-tartaric acid at SFr 170 per kg. We thank the Chemische Fabrik Uetikon (CH-8707 Uetikon) for the generous supply of tartaric acid dimethyl esters. The sugars are only attainable in one enantiomeric form and are—with few exceptions—very expensive.
[6] *K. Freudenberg, F. Brauns*, Ber. Dtsch. Chem. Ges. *55*, 1339 (1922).
[7] *B. Seuring, D. Seebach*, Helv. Chim. Acta *60*, 1175 (1977); *D. Seebach, H.-O. Kalinowski*, Nachr. Chem. Tech. *24*, 415 (1976).
[8] *B. Seuring, D. Seebach*, Justus Liebigs Ann. Chem. *1978*, 2044; *D. Seebach, B. Seuring, H.-O. Kalinowski, W. Lubosch, B. Renger*, Angew. Chem. *89*, 270 (1977); Angew. Chem. Int. Ed. Engl. *16*, 264 (1977).
[9] *H. Gerlach, K. Oertle, A. Thalmann*, Helv. Chim. Acta *60*, 2860 (1977); *59*, 755 (1976).

The μ_3-($\eta^3C\eta^2O$) Bridge—A Novel Mode of Coordination in the Structural Chemistry of Carbonylmetal Compounds[1]

By *Wolfgang A. Herrmann, Manfred L. Ziegler, Klaus Weidenhammer*, and *Helmut Biersack*[*]

Hock and *Mills'* first encounter with the phenomenon of "semibridging" carbonyl ligands in 1961, which was later interpreted by *Cotton*[2,3], provided yet another challenge to carbonylmetal chemistry. Apart from the "classical" coordination modes *(1)*, *(2a)*, *(3a)* previously reported exclusively, it has recently also proved possible to detect the quasi-bridging CO ligands *(2b)*[3,4] and *(3b)*[5] in which the π-system of the carbonyl unit engages in bonding interaction with a further metal center. Precisely these chemically reversible complexation types [*e.g. (2b)→(1)*] are nowadays assigned a key function in carbonylation processes proceeding on surfaces and possibly also in homogeneously catalyzed systems[6]. The mode of coordination also has a decisive influence on the kinetics of CO substitution[7] and the molecular dynamics of carbonyl clusters[3].



During our experiments on the photochemistry of tetracarbonyl(η^5-cyclopentadienyl)niobium *(4)*, now accessible on a large scale by a new synthesis[1], we not only produced the first carbonylniobium cluster compound *(5)* but also detected the hitherto unknown structural type *(3c)*, in which the terminal CO ligand is coordinated *via* both its orthogonal π systems to two further metal centers and thus constitutes a novel variant of the classical bonding type *(1)*.

In contrast to the photolysis of the half-sandwich (η^5-C_5H_5)$V(CO)_4$, which affords the dinuclear species (η^5-$C_5H_5)_2V_2(CO)_5$[8], the action of sunlight on *n*-hexane solutions of the homologous niobium compound *(4)* leads directly (with CO elimination) to a crystalline, nonsublimable product *(5)*, which is air-stable for a short period of time and does not decompose thermally below 100 °C. Compound *(5)* was identified as a trinuclear cluster (η^5-$C_5H_5)_3Nb_3(CO)_7$ by complete elemental analysis and its FD mass spectrum ($m/e = 670$; from acetone).

$$3(\eta^5\text{-}C_5H_5)Nb(CO)_4 \xrightarrow{h\nu} (\eta^5\text{-}C_5H_5)_3Nb_3(CO)_7 + 5\,CO\uparrow$$
(4) *(5)*

Since the ^{1}H- and the ^{13}C-NMR as well as the IR data[9] did not permit unequivocal structural assignment, we have car-

[*] Prof. Dr. W. A. Herrmann, H. Biersack
Chemisches Institut der Universität
Universitätsstrasse 31, D-8400 Regensburg 1 (Germany)
Prof. Dr. M. L. Ziegler, Dr. K. Weidenhammer
Anorganisch-chemisches Institut der Universität
Im Neuenheimer Feld 270, D-6900 Heidelberg 1 (Germany)

ried out an X-ray structure analysis (Fig. 1)[10], which shows the geometry of *(5)* to have the following characteristics (cf. Table 1):

1) The principal structural feature is an almost equilateral Nb_3 triangle which arises by aggregation of the photochemically generated $(\eta^5\text{-}C_5H_5)Nb(CO)_x$ fragments ($x=2$, 3). The symmetrically π-bonded cyclopentadienyl rings are tipped towards the quasi-bridging group C(33)—O(33) relative to the triangular cluster plane. The six exclusively terminal CO ligands are expectedly coordinated in linear fashion.

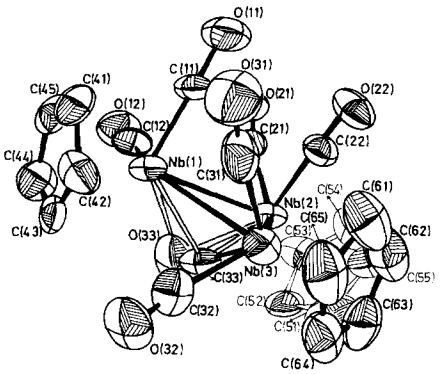


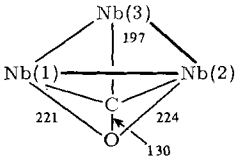
Fig. 1. ORTEP drawing of $(\eta^5\text{-}C_5H_5)_3Nb_3(CO)_7$ *(5)*. The ellipsoids of thermal vibration correspond to 50% probability.

2) The structural outfit of the seventh CO group is surprising: although terminally bonded to the metal center Nb(3), thus representing an almost linear carbonyl-metal function [Nb(3)—C(33)—O(33): 170°], its contact with the two metal atoms Nb(1) and Nb(2) is so close that a true bonding interaction is present beyond any doubt! The corresponding distances Nb(1)—O(33), Nb(2)—O(33), Nb(1)—C(33), and Nb(2)—C(33) are admittedly 24—30 pm greater than the Nb(3)—C(33) contact of 197 pm, responsible for terminal coordination, but only slightly greater than the sum of the covalent *Pauling* radii. Hitherto, M···CO distances of 230—250 pm have been found in "semi-bridging" systems of type *(2b)* and *(3b)* (M = V, Mo, Rh, *etc.*), whereas the M—CO distances range in the order of 190 pm[3-5, 7].

Table 1. Selected structural parameters of *(5)*.

Bond lengths [pm]			Angles [°]			
Nb(1)	Nb(2)	304.4(2)	Nb(1)	Nb(2)	Nb(3)	64.43(5)
Nb(1)	Nb(3)	332.0(2)	Nb(2)	Nb(1)	Nb(3)	59.79(5)
Nb(2)	Nb(3)	318.1(2)	Nb(1)	Nb(3)	Nb(2)	55.79(4)
Nb(1)	C(11)	203.6(19)	Nb(1)	C(33)	Nb(2)	85.04(48)
Nb(2)	C(22)	205.6(15)	Nb(1)	O(33)	Nb(2)	86.32(31)
Nb(3)	C(32)	211.7(23)	Nb(3)	C(33)	O(33)	169.6(1.1)
Nb(3)	C(33)	196.6(12)				
Nb(1)	C(33)	227.8(14)				
Nb(2)	C(33)	222.6(18)				
Nb(1)	O(33)	221.2(10)				
Nb(2)	O(33)	223.8(10)				
C(11)	O(11)	116.9(23)				
C(22)	O(22)	114.2(20)				
C(32)	O(32)	108.2(29)				
C(33)	O(33)	130.3(14)				

3) As a consequence of this additional twofold bridging function, the C(33)—O(33) distance (130 pm) exceeds the distances in the other CO groups by 13—22 pm. This is associated with a drastic lowering of the carbonyl bond order: in the solid-state IR spectrum a sharp, extremely long-wave shifted band at 1330 cm^{-1} is demonstrated by ^{13}CO and $C^{18}O$ labeling (30 and 10% enrichment, respectively) to belong to the corresponding CO frequency. In keeping with the requirements of the synergic mechanism of bonding of CO ligands, the Nb(3)—C(33) bond length is significantly shorter than the "normal" niobium-carbonyl distances.



This unusual molecular structure becomes understandable on considering the electronic requirements of the $(\eta^5\text{-}C_5H_5)Nb(CO)_x$ units ($x=2$, 3) including the metal-metal bonds: while Nb(3) has an 18-electron configuration and therefore has no need of any further coordination, the two $(\eta^5\text{-}C_5H_5)Nb(CO)_2$ fragments [Nb(1) and Nb(2)] are coordinatively unsaturated. This situation can be alleviated by the sterically available Nb(3)—CO group which, as a twofold donating bridge, helps to saturate these electron-deficient centers. In this function we see the molecular origin of ligand bridging in *(5)*. The finding that the angles Nb(1)—C(33)—Nb(2) and Nb(1)—O(33)—Nb(2) are close to 90° is no accident, and suggests that the CO ligand interacts to equal extents with Nb(1) and Nb(2) *via* its two orthogonal systems, thus formally acting as 6-electron donor.

Procedure[11]:

A solution of *(4)*[1] (2.70 g, 10 mmol) in *n*-hexane (250 ml) is exposed to sunlight (coolants CH_3OH; HAAKE KT 33) for 15 to 80 h, depending upon the light intensity, in a thermostatable Schlenk tube (DURAN; Hg relief valve). Slow evolution of CO is accompanied by precipitation of dark black lustrous needles, which occasionally have to be removed from the wall of the vessel. (Photolysis in conventional immersion well apparatus with a Hg lamp—*e.g.* Original Hanau TQ 150—failed to give crystalline products.) The crystals are washed several times with *n*-hexane and dried *in vacuo*. Yield 1.45—1.83 g (65—82%). Dec. $>$*ca.* 100 °C with partial formation of *(4)*. Moderately soluble in diethyl ether, readily soluble in dichloromethane and tetrahydrofuran (brown, air-sensitive solutions).

Received: July 19, 1979;
revised: August 1, 1979 [Z 354 IE]
German version: Angew. Chem. *91*, 1026 (1979)

[1] Metalcarbonyl Syntheses, Part 4. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.—Part 3: *W. A. Herrmann, H. Biersack*, Chem. Ber. *112*, 3942 (1979).
[2] *A. A. Hock, O. S. Mills*, Acta Crystallogr. *14*, 139 (1961).
[3] *F. A. Cotton*, Progr. Inorg. Chem. *21*, 1 (1976) and references cited therein; *F. A. Cotton, B. A. Frenz, L. Kruczynski*, J. Am. Chem. Soc. *95*, 951 (1973); *F. A. Cotton, J. M. Troup, ibid. 96*, 1233 (1974); *F. A. Cotton, L. Kruczynski, B. A. Frenz*, J. Organometal. Chem. *160*, 93 (1978).
[4] *R. J. Klingler, W. M. Butler, M. D. Curtis*, J. Am. Chem. Soc. *100*, 5034 (1978) and references cited therein; *K. S. Wong, W. R. Scheidt, J. A. Labinger*, Inorg. Chem. *18*, 1709 (1979); *M. P. Brown, A. N. Keith, Lj. Manojlović-Muir, K. W. Muir, R. J. Puddephatt, K. R. Seddon*, Inorg. Chim. Acta *34*, L 223 (1979).
[5] *W. D. Jones, M. A. White, R. G. Bergman*, J. Am. Chem. Soc. *100*, 6770 (1978).
[6] *E. L. Muetterties*, Science *196*, 839 (1977); Pure Appl. Chem. *50*, 941 (1978).
[7] *L. N. Lewis, K. G. Caulton*, Inorg. Chem., in press; *J. C. Huffman, L. N. Lewis, K. G. Caulton, ibid.*, in press.
[8] *W. A. Herrmann, J. Plank*, Chem. Ber. *112*, 392 (1979).
[9] ^{1}H-NMR ([D$_6$]-acetone, +33 °C, TMS int.): $\tau C_5H_5 = {}^1$4.34, ^{1}4.48, int. 1:2.—^{13}C-NMR (CD_2Cl_2, +32 °C, int. TMS, 20% ^{13}CO enrichment): $\delta C_5H_5 = 95.26$, 94.40; $\delta CO \approx 247$ (broad).—IR: 1993 w, 1973 vs, 1952 w, 1934 m, 1907 s [νCO; cyclohexane]; 1982 s—vs, 1961 vs, 1947 vs, 1915 vs, 1885 s, 1850 s—vs, 1838 s, 1330 w—m [νCO; KBr].

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0961 $ 02.50/0*

[10] Compound *(5)* crystallizes from *n*-hexane in the space group C_{2h}^5-$P2_1/c$ with $a = 1717.0(8)$, $b = 775.2(4)$, $c = 1876.0(8)$ pm, $\beta = 117.57(3)°$, $Z = 4$. 3253 independent non-zero reflections were recorded with an automatic single crystal diffractometer (Siemens) with $Mo_{K\alpha}$ radiation ($4.36 \leq 2\Theta \leq 57.94$°) and corrected in the usual way. $R_f = 8.4\%$.—For preparative, spectroscopic, and X-ray analytical details, see: *M. L. Ziegler, K. Weidenhammer, W. A. Herrmann, H. Biersack*, J. Am. Chem. Soc., in press.

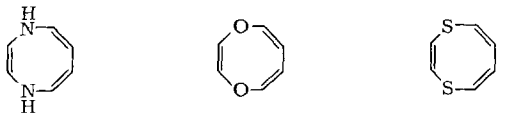
[11] Rigorous exclusion of O_2 and H_2O required (N_2 atmosphere, anhydrous solvents).

1,4-Dihydro-1,4-diazocine and *N,N'*-Disubstitution Products—A Rational Synthesis

By *Hans-Josef Altenbach, Hartmut Stegelmeier, Monika Wilhelm, Burkhard Voss, Johann Lex,* and *Emanuel Vogel*[*]

1,4-Dihydro-1,4-diazocine *(1)* and the 1,4-diheterocins *(2)* and *(3)*—eight-membered heterocycles isoelectronic with the cyclooctatetraene dianion—have recently attracted both theoretical[1] and practical interest as potential 10π-aromatic species. A straightforward entry to *(1)*—*(3)* and derivatives consists in the intramolecular retro-Diels-Alder reaction of *syn*-benzene diimines[2], *syn*-benzene dioxides[3], and *syn*-benzene bisepisulfides[4]. Indeed, it proved possible in this way to prepare the 1,4-dioxocin *(2)* (an olefinic compound[3a,b]) and some *N,N'*-derivatives of *(1)*, including the dimethylated compound *(12)* formulated as an aromatic molecule[2].

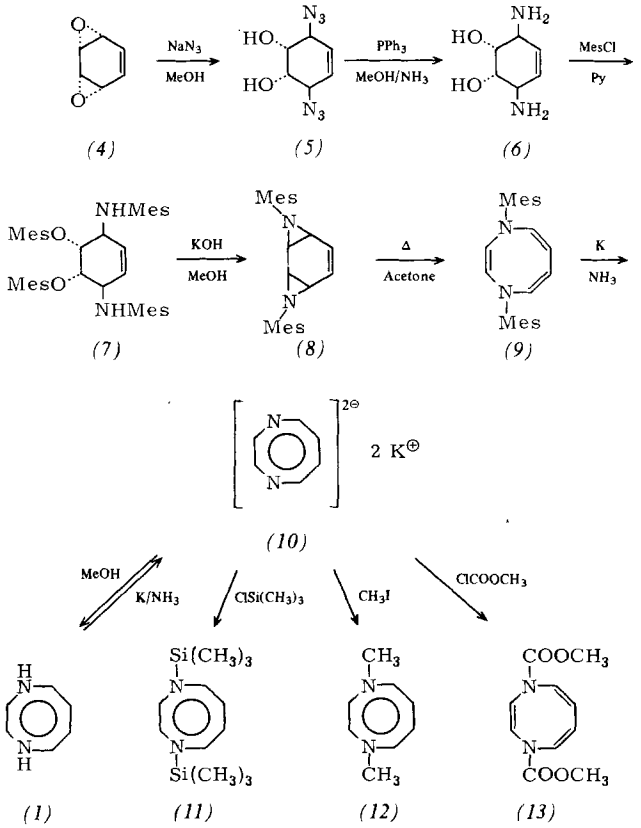
This communication describes a rational synthesis of the parent compound *(1)*, its dipotassium salt *(10)*, and some of



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

its *N,N'*-derivatives with the bismethanesulfonate *(8)* of *syn*-benzene diimine serving as intermediate[5].

On reaction with sodium azide in methanol in the presence of magnesium chloride, *syn*-benzene dioxide *(4)*[3b,c] undergoes the expected regioselective opening of the two oxirane rings to form the diazide *(5)* [m.p. 59—60 °C (ether/pentane), yield 79%][6]. Transformation of *(5)* into *(6)*, which was unsuccessful when attempted with the usual reducing agents, was effected by triphenylphosphane in ammoniacal methanol/pyridine[7]. Compound *(6)* which was only sparingly soluble in organic solvents was converted as the crude product into tetrakismethanesulfonate *(7)* by treatment with methanesulfonyl chloride in pyridine. After isolation of *(7)* by chromatography on silica gel (acetone) [m.p. 218—219 °C, dec. (methanol), yield 40% referred to *(5)*] it reacts with 5% methanolic potassium hydroxide *via* twofold aziridine ring closure to give *(8)* [m.p. 157 °C (dichloromethane/ether), yield 83%] which rearranges completely to the valence isomeric bismethanesulfonate *(9)* [m.p. 157 °C (dichloromethane), yield 94%] on heating in acetone (2 h). Reaction of *(9)* with potassium in liquid ammonia proceeds *via* reductive elimination of the mesyl groups to give a poorly soluble salt-like product, shown by its NMR spectra to be the dipotassium salt *(10)* of *(1)*[8]. Treatment of *(10)* with methanol gives a 74% yield [based on *(9)*] of the parent compound *(1)* [which regenerates *(10)* with potassium in liquid ammonia], while its reaction with electrophiles such as chlorotrimethylsilane, methyl iodide, and methyl chloroformate also smoothly affords the corresponding *N,N'*-disubstituted 1,4-dihydro-1,4-diazocines [*(11)*, m.p. 113 °C (pentane), yield 70%; *(12)*[2], colorless liquid, molecular distillation at 60 °C/1 torr, yield 75%; *(13)*[2], m.p. 80 °C (ethanol), yield 73%].



Compound *(1)* is very sensitive to oxygen in solution and is best purified by sublimation (60 °C/1 torr); colorless crystals, m.p. 196—198 °C (in evacuated capillary; heating in the presence of air leads to decomposition over a wide temperature range). Interestingly, *(1)* undergoes neither acid- nor alkali-catalyzed prototropic shift, although transformation of an enamine into an imine structure is normally accompanied by a gain in energy (10—14 kcal/mol); this finding, which is suggestive of a relationship between *(1)* and pyrrole and azonine[9], can be regarded as chemical evidence for a 10π aromatic compound.

The ^{1}H- and ^{13}C-NMR spectra of *(1)* and its derivatives (cf. Table 1) reveal the following points of value for elucidation of the problem of aromaticity: Compounds *(1)*, *(11)*, *(12)*, in which the lone pairs of the N atoms can delocalize into the ring, exhibit ^{13}C resonances at relatively high field strength for all ring carbon atoms, in keeping with such a charge transfer. In parallel herewith, comparatively large and nearly equal vicinal coupling constants J_{56} and J_{67} are observed for *(1)*, *(11)*, and *(12)*, indicating that not only the β-effect of the heteroatoms is operative[3a,b] but that there is also some equalization of the bond orders in the diene moiety. Moreover, the resonance signals of the ring protons are to be regarded as diamagnetically shifted, as already established by *Prinzbach et al.*[2] in the case of *(12)* [comparison with 1,4,7-trimethyl-1*H*-4,7-dihydro-1,4,7-triazonine and the [*b*]benzo derivative of *(12)*].

These results can readily be reconciled with each other by assuming cyclic 10π-electron delocalization in *(1)*, *(11)*, and

[*] Prof. Dr. E. Vogel, Dr. H.-J. Altenbach, Dipl.-Chem. H. Stegelmeier, Dipl.-Chem. M. Wilhelm, B. Voss, Dr. J. Lex
Institut für Organische Chemie der Universität
Greinstrasse 4, D-5000 Köln 41 (Germany)

 © Verlag Chemie, GmbH, 6940 Weinheim, 1979 0570-0833/79/1212-0962 $ 02.50/0

Table 1. ^{1}H- and ^{13}C-NMR data of 1,4-dihydro-1,4-diazocines.

Cpd.	^{1}H-NMR ([D$_6$]-Acetone, TMS int., δ)			Coupling constants [Hz] [a]				^{13}C-NMR ([D$_6$]-Acetone, TMS int., δ) [b]		
	H-2, 3	H-5, 8	H-6, 7	J_{56}	J_{67}	J_{57}	J_{58}	C-2, 3	C-5, 8	C-6, 7
(1)	6.15	6.71	5.68	10.38	10.85	0.25	0.41	97.5	112.1	91.7 [c]
(11)	6.19	6.70	5.67	10.49	10.89	0.07	0.25	102.3	115.9	95.6
(12)	5.85	6.45	5.52	10.62	11.19	0.13	0.43	103.1	117.5	93.0
(9)	6.44	6.76	5.90	9.82	7.06	−0.75	0.47	107.3	121.1	111.2
(13)	6.12	6.34	5.96	8.96	4.75	−1.26	0.34	113.1	127.1	117.5

[a] We are indebted to Dr. *H. Schmickler* for the exact spectral analysis. [b] Assignment from the non-^{1}H-decoupled spectra. [c] No evidence has so far been obtained for the existence of *syn*-benzene diimine in equilibrium with *(1)*.

(12)—but not in the electron-acceptor substituted derivatives *(9)* and *(13)*. By analogy with the situation in the azonines[9], it appears justifiable to classify the 1,4-dihydro-1,4-diazocines as aromatic or olefinic species, depending upon the nature of the substituents on nitrogen.

Such a distinction is also suggested by the observation that the UV spectra of *(1)* [(acetonitrile) $\lambda_{max}=262$ nm ($\varepsilon=9000$)], *(11)*, and *(12)* resemble that of the cyclooctatetraene dianion, whereas those of *(9)* and *(13)* are more like that of 1,3,6-cyclooctatriene.

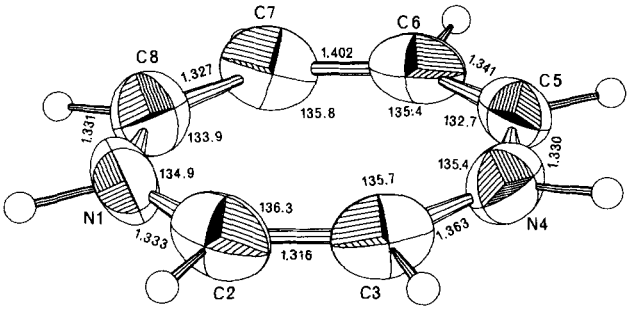


Fig. 1. Structure of 1,4-dihydro-1,4-diazocine *(1)* in the crystal. The bond lengths [Å] and angles [°] refer to one of the four independent molecules in the asymmetric unit. The corresponding values for the other three molecules do not deviate significantly.

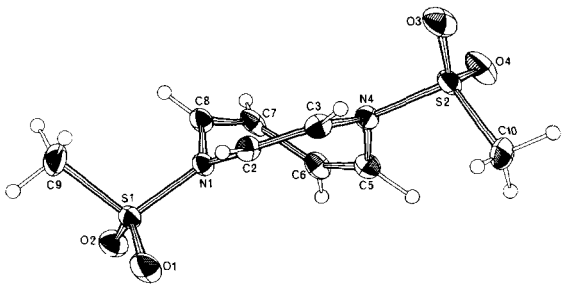


Fig. 2. Structure of *N,N'*-bis(methanesulfonyl)-1,4-dihydro-1,4-diazocine *(9)* in the crystal. Bond lengths and angles: N1 C2 1.426, C2 C3 1.323, C3 N4 1.418, N4 C5 1.429, C5 C6 1.327, C6 C7 1.436, C7 C8 1.316, C8 N1 1.453 Å; N1 C2 C3 128.4, C2 C3 N4 128.4, C3 N4 C5 123.2, N4 C5 C6 123.3, C5 C6 C7 124.8, C6 C7 C8 127.4, C7 C8 N1 123.2, C8 N1 C2 123.3°.

The conclusions drawn from chemical and spectroscopic properties concerning the π-electron configuration of the 1,4-dihydro-1,4-diazocines receive support from X-ray structure analyses performed by *J. Lex* on *(1)* (Fig. 1), *(9)* (Fig. 2), and *(11)*[10]. In agreement with their postulated aromatic character, compounds *(1)* and *(11)*[11] possess a planar ring skeleton—maximum deviation of atoms from the mean ring plane 0.02 Å—while compound *(9)*, being regarded as an olefin, has a twisted conformation [mean value of the ring bond angles is 135° for *(1)* and *(11)* and 125° for *(9)*]. On going from *(9)* to *(1)* and *(11)* there is a noticeable tendency for equalization of the bond lengths in the 1,4-dihydro-1,4-diazocine system[12]; however, this trend is not so pronounced as expected from the flattening of the ring.

Received: March 12, 1979;
revised: July 5, 1979 [Z 335a IE]
German version: Angew. Chem. *91*, 1028 (1979)
Publication delayed at authors' request

CAS Registry numbers:
(1), 56039-49-7; *(4)*, 39078-08-5; *(5)*, 72160-92-0; *(6)*, 72160-93-1; *(7)*, 72160-94-2; *(8)*, 72160-95-3; *(9)*, 72160-96-4; *(10)*, 72160-97-5; *(11)*, 72160-98-6; *(12)*, 72160-99-7; *(13)*, 58672-89-2; sodium azide, 26628-22-8; methanesulfonyl chloride, 124-63-0; chlorotrimethylsilane, 75-77-4; methyl chloroformate, 79-11-8

[1] *B. A. Hess, L. J. Schaad*, J. Am. Chem. Soc. *95*, 3907 (1973); *S. Inagaki, Y. Hirabayashi, ibid. 99*, 7418 (1977).

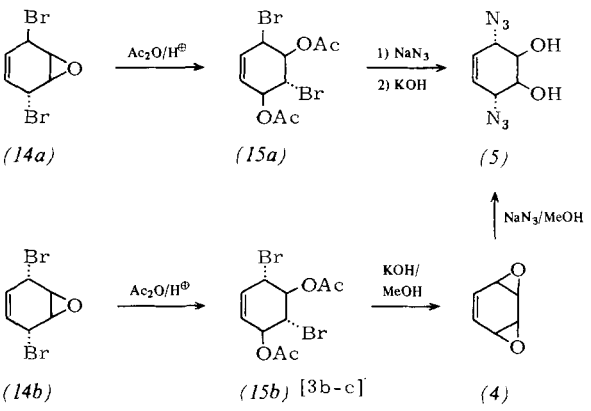
[2] *H. Prinzbach, M. Breuninger, B. Gallenkamp, R. Schwesinger, D. Hunkler*, Angew. Chem. *87*, 350 (1975); Angew. Chem. Int. Ed. Engl. *14*, 348 (1975).

[3] a) *E. Vogel, H.-J. Altenbach, D. Cremer*, Angew. Chem. *84*, 983 (1972); Angew. Chem. Int. Ed. Engl. *11*, 935 (1972); b) *H.-J. Altenbach, E. Vogel, ibid. 84*, 985 (1972) and *11*, 937 (1972), respectively; c) *E. Vogel, H.-J. Altenbach, E. Schmidbauer, ibid. 85*, 862 (1973) and *12*, 838 (1973), respectively; d) concerning a naturally occurring *syn*-benzene dioxide/1,4-dioxocin system, see *D. B. Borders, J. E. Lancaster*, J. Org. Chem. *39*, 435 (1974).

[4] *E. Vogel, E. Schmidbauer, H.-J. Altenbach*, Angew. Chem. *86*, 818 (1974); Angew. Chem. Int. Ed. Engl. *13*, 736 (1974).—The first synthesis of a simple 1,4-dithiocin, the 6-acetoxy derivative, proceeded *via* an eight-membered ring precursor. The compound is not planar and does not possess aromatic character: *H. J. Eggelte, F. Bickelhaupt*, Tetrahedron *33*, 2151 (1977); *H. J. Eggelte, F. Bickelhaupt, B. O. Loopstra, ibid. 34*, 3631 (1978).

[5] An independent synthesis of *(1)* has been developed by *M. Breuninger, B. Gallenkamp, K.-H. Müller, H. Fritz, H. Prinzbach, J. J. Daly, P. Schönholzer*, Angew. Chem. *91*, 1030 (1979); Angew. Chem. Int. Ed. Engl. *18*, 970 (1979).

[6] *(5)* is also accessible from *(15a)* [3b, c] by reaction with sodium azide in 2-methoxyethanol at 100 °C and saponification of the resulting acetate with methanolic potassium hydroxide (yield 79%). This additional route to *(5)* considerably enhances the value of the synthesis of *(1)* and its *N,N'*-disubstitution products because both the stereoisomers *(14a)* and *(14b)* arising on NBS-bromination of 1,2-epoxy-4-cyclohexene can now be utilized:



Transformation of *(5)* into *(1)* (*via syn*-benzene diimine) by reaction with phosphanes [*Y. Ittah, Y. Sasson, I. Shahak, S. Tsaroom, J. Blum*, J. Org. Chem. *43*, 4271 (1978)] is possible, but we found it to be an unpractical method.

[7] *L. Horner, A. Gross*, Justus Liebigs Ann. Chem. *591*, 117 (1955); *W. S. Mungall, G. L. Greene, G. A. Heavner, R. L. Letsinger*, J. Org. Chem. *40*, 1659 (1975).

[8] ^{1}H-NMR [$(CD_3)_2SO$]: $\delta = 6.16$ (s, H-2,3), 6.70 and 5.34 (AA'XX'-system with $J_{56} = 9.29$, $J_{67} = 10.70$, $J_{57} = 0.47$, $J_{58} = 0.29$ Hz, H-5,8 and H-6,7); ^{13}C-NMR [$(CD_3)_2SO$]: $\delta = 99.8$ (C-2,3), 112.0 (C-5,8) and 90.3 (C-6,7). The relatively slight differences between these data and those of the parent compound *(1)* suggest that most of the negative charge is located on the two nitrogen atoms in *(10)*.

[9] *A. G. Anastassiou*, Top. Nonbenzenoid Aromat. Chem. *1*, 1 (1973); *A. V. Kemp-Jones, S. Masamune, ibid. 1*, 121 (1973).

[10] Crystal data of *(1)*: triclinic, space group $P\bar{1}$, $a = 6.965(2)$, $b = 12.124(2)$, $c = 15.076(6)$ Å, $\alpha = 85.77(2)$, $\beta = 103.33(3)$, $\gamma = 106.65(2)°$, $Z = 8$, $\rho_{exp} = 1.19$, $\rho_{calc} = 1.21$ g/cm^3; Nonius CAD4, 2133 reflections with $I > 2\sigma(I)$, $R = 0.047$.—*(11)*: monoclinic, space group $P2_1/n$, $a = 6.711(2)$, $b = 23.565(5)$, $c = 9.888(1)$ Å, $\beta = 100.92(3)°$, $Z = 4$, $\rho_{exp} = 1.07$, $\rho_{calc} = 1.092$ g/cm^3; Nonius CAD4, 2086 reflections with $I > 2\sigma(I)$, $R = 0.053$.—*(9)*: monoclinic, space group $P2_1/c$, $a = 9.449(2)$, $b = 5.618(1)$, $c = 21.562(3)$ Å, $\beta = 98.25(1)°$, $Z = 4$, $\rho_{exp} = 1.55$, $\rho_{calc} = 1.55$ g/cm^3; Nonius CAD4, 1772 reflections with $I > 2\sigma(I)$, $R = 0.050$.

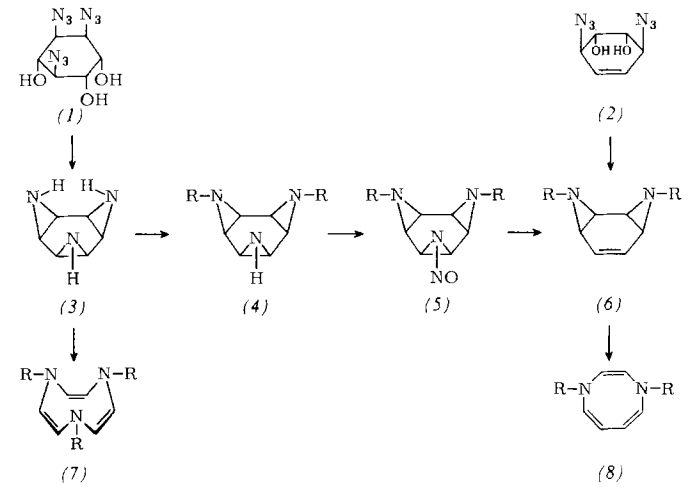
[11] It follows from the presence of a delocalized 10π electron system in *(11)* that the SiN bond has only weak $d_\pi p_\pi$ character, by analogy with the situation in trimethylsilylpyrrole [*J. Nagy, P. Hencsei, E. Gergö*, Z. Anorg. Allg. Chem. *367*, 293 (1969)].

[12] Cf. the largely equalized CC bond lengths in pyrrole [*A. Gossauer*: Die Chemie der Pyrrole. Springer-Verlag, Berlin 1974, p. 7].

1,4-Dihydro-1,4-diazocine; *N*-Substitution and Structure ("Aromaticity")[**]

By *Manfred Breuninger, Bernd Gallenkamp, Klaus-Helmut Müller, Hans Fritz, Horst Prinzbach, John J. Daly*, and *Peter Schönholzer*[*]

We have already reported on the synthesis of the *cis*-"benzene triimine" *(3)* from the *chiro*-triazidocyclohexanetriol *(1)*[1a] and the synthesis of *N,N'*-disubstituted *cis*-"benzene diimines" *(6)* from *(3)* as well as on the cycloreversion reactions to the 1*H*-4,7-dihydro-1,4,7-triazonines *(7)* and 1,4-dihydro-1,4-diazocines *(8)*[1b], respectively. It was established that the nature of the *N*-substituents (R) determines the geometry and electron density distribution ("aromaticity") in the ring skeleton of *(8)*: the dimethyl compound *(8f)* is planar/diatropic, the amides *(8b)* and *(8c)* are twisted/non-diatropic. As mentioned in a previous communication[1b] this relationship between substitution and molecular structure, which for larger azaannulenes is typical[1b,2] yet seldom so pronounced, was corroborated by synthesis of the parent compound *(8a)*, its dianion *(9)* and other derivatives[3].

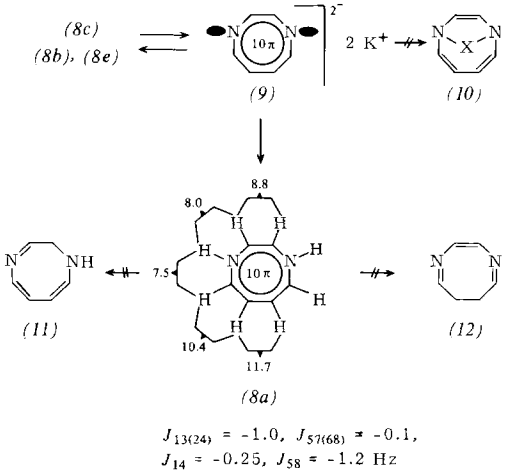


Unsubstituted *(6a)* and *(8a)* were not accessible *via* the route primarily intended for the isolation of the labile diimines *(6)* (E_a for the most stable derivative *(6b)* 23.2 ± 0.5 kcal/mol) and outlined in the formula scheme. On attempting a selective mononitrosation of the triimine *(3)*—stabilized by H-bridges[4]—(to *(5a)*) we obtained practically only benzene (*e.g.* from *(5g)*).

(8a) was therefore prepared by alcoholysis of the bisurethane *(6c)* (methanol/sodium methoxide) or preferably *via* the dianion *(9)* (potassium *tert*-butylate, $-60\,°C$)[5]. The dipotassium salt *(9)*, which is obtained in almost quantitative yield, rapidly decomposes on exposure to air but can be stored in an inert atmosphere and is soluble *e.g.* in anhydrous [D_6]-dimethyl sulfoxide, giving a deep-brown solution. The ^{1}H-NMR spectrum resembles that of the derivatives *(8b)—(8f)* except that the two multiplets for 5(8)- and 6(7)-H ($\delta = 6.72$, 5.33) show no fine splitting; the coupling constants ($J_{56(78)} \simeq 14$, $J_{57(68)} \simeq 0.1$, $J_{58} \simeq 1.5$, $J_{67} \simeq 9$ Hz) are therefore only approximated values. Treatment of a solution of *(9)* in tetrahydrofuran at $-60\,°C$ with an excess of water, toluenesulfonic anhydride or dimethylcarbamoyl chloride leads quantitatively to *(8a)*, *(8b)* and *(8e)*, respectively. On the other hand, attempted *N,N'*-bridging (phosgene, thiophosgene, sulfinyl chloride, sulfonyl chloride) to *(10)* or oxidation (I_2) of *(9)* to 1,4-diazocine has so far failed.

(8a), which is isolable as colorless crystals, is very sensitive to air only in solution; when heated above $150\,°C$ it decomposes without melting and turns brown, but it can be sublimed at *ca.* $60\,°C/2$ torr. As in the case of *(8f)* the molecular ion [$m/e = 108$ (44%)] is rather stable and preferentially fragments to the pyridinium ion [$m/e = 80$ (100%)].

The electronic spectrum [λ_{max} (CH_3CN) = 282 (sh, $\varepsilon = 24560$), 263 (6550), 254 (sh, 5920)] is similar to that of the cyclooctatetraene dianion[6] as regards the position, intensity and structure of the longest wavelength absorption bands.



$J_{13(24)} = -1.0$, $J_{57(68)} = -0.1$, $J_{14} = -0.25$, $J_{58} = -1.2$ Hz

(8a) is stable towards base (*e.g.* aqueous NaOH, sodium methoxide/methanol) and acid (dil. formic acid, silica gel). After treatment with acid or base, there are besides *(8a)* no (TLC, ^{1}H-NMR; <3%) tautomeric imines *(11)* or "diimines"

[*] Prof. Dr. H. Prinzbach, Dr. M. Breuninger, Dr. B. Gallenkamp, Dipl.-Chem. K.-H. Müller, Prof. Dr. H. Fritz
Lehrstuhl für Organische Chemie der Universität
Albertstrasse 21, D-7800 Freiburg (Germany)
Dr. J. J. Daly, P. Schönholzer
Hoffmann-La Roche & Co. AG
CH-4002 Basel (Switzerland)

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

(12) present; as shown by MS and ^{1}H-NMR analysis two hydrogen atoms (N–H) in *(8a)* are exchanged in deuterated solvents (D_2O, CH_3OD).

The additional data obtained from *(8a)*, *(8d)*, *(8e)* and *(9)* are consistent with those found for *(8b)*, *(8c)* and *(8f)*[1b]. In particular, the trend in the quotients $J_{67}/J_{56(78)}$ and $J_{57(68)}/J_{56(78)}$ and the $\delta(^1H)$ and $\delta(^{13}C)$ values—compared with those of the analogously substituted pyrroles or 1*H*-4,7-dihydrotriazonines *(7)*—emphasize the difference between planar/diatropic [*(8a)*, *(8e)*, *(8f)*] and twisted/non-diatropic [*(8b)*—*(8d)*][7]. How subtle the balance between these alternatives is, follows from the fact that the attenuation of the $N^1(N^4)CO$ resonance in *(8e)* by the $N(CH_3)_2$ groups—in concert with the steric hindrance of coplanarity—facilitates the inner-cyclic availability of the N-electron pairs to such an extent that even this "amide" is planar and diatropic. An estimation of the "aromaticity" is facilitated, *inter alia*, by the finding that no tautomers are detectable in equilibrium with *(8a)*; thus a stabilization energy of *ca.* 20 kcal/mol is plausible. The first results on the stability of charge-transfer complexes (1,3,5-trinitrobenzene/*(8f)* isolated) or diene reactivity ([4+2]-adducts of *(8c)* and *(8d)* with *N*-phenyltriazoline-dione isolated) as characteristic chemical criteria are available.

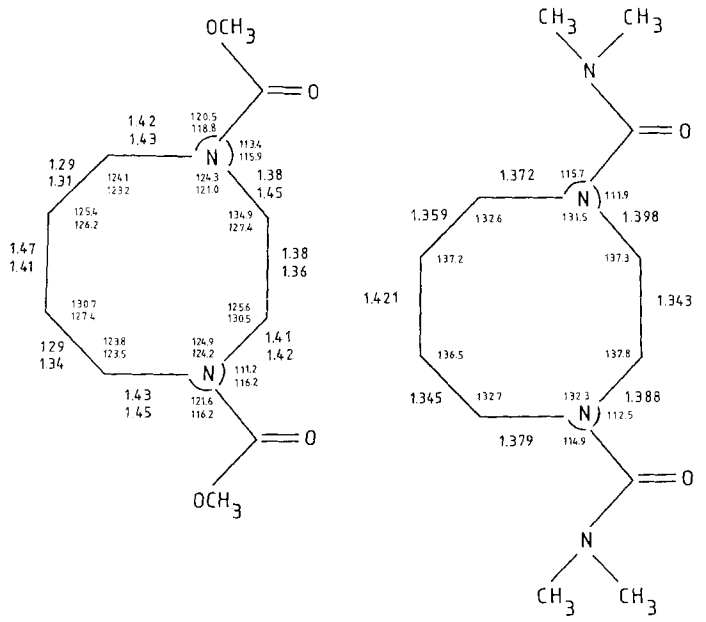


Fig. 1. X-ray structure data (bond lengths and angles) of (8c) and (8e).

X-ray structure analyses (Fig. 1)[8] confirm the spectroscopic investigations: In the crystal *(8c)* has a twisted conformation (approaching C_2) with distinct alternance of bond lengths (cf. azepines[9a]) and an average bond angle of 125.4° (128.0°) in the eight-membered ring. On the other hand, *(8a)* and *(8c)* are practically planar (mean deviation from the ideal plane 0.014(2) and 0.052 Å, resp.); the bond lengths are more equalized (cf. pyrrole[9b]), the mean bond angle is 135.0 and 134.9°, respectively. Thus, the theoretical prediction[10] that a 10π-electron delocalization is most unlikely in *(8a)* is not consistent with experimental findings. Compared to the analogous dithia skeleton[11], *(8a)* might have the advantage that planarization requires less energy.

Received: June 8, 1979 [Z 335b IE]
Revised: July 5, 1979
Publication delayed at authors' request
German version: Angew. Chem. *91*, 1030 (1979)

[1] a) *R. Schwesinger, H. Prinzbach,* Angew. Chem. *85*, 1107 (1973); Angew. Chem. Int. Ed. Engl. *12*, 989 (1973); b) *H. Prinzbach, M. Breuninger, B. Gallenkamp, R. Schwesinger, D. Hunkler, ibid. 87*, 350 (1975) and references cited therein. In the meantime the precursors have been considerably optimized: *R. Schwesinger, H. Fritz, H. Prinzbach,* Chem. Ber. *112*, 3318 (1979).

[2] *A. G. Anastassiou, E. Reichmanis,* J. Am. Chem. Soc. *98*, 8266 (1976); *H. Röttele, G. Heil, G. Schröder,* Chem. Ber. *111*, 84 (1978); *A. G. Anastassiou, H. S. Kasmai,* Adv. Heterocycl. Chem. *23*, 55 (1978).

[3] These studies were completed in 1977 and form part of the dissertations by *M. Breuninger* and *B. Gallenkamp*, Universität Freiburg 1977. Their publication in Chem. Ber. was planned on completion of a series of X-ray structure analyses. The present publication stems from a friendly arrangement (May 28, 1979) with Prof. *E. Vogel*, who had prepared a manuscript containing pertinent results: *H.-J. Altenbach, H. Stegelmeier, M. Wilhelm, B. Voss, J. Lex, E. Vogel*, Angew. Chem. *91*, 1028 (1979); Angew. Chem. Int. Ed. Engl. *18*, 968 (1979).

[4] *U. Drück, W. Littke,* Acta Crystallogr. B *35*, 1905 (1979).

[5] The alternative approach to the synthesis of *(3)* from *(1)* via the diazidocyclohexenediol *(2)* according to the method of *Blum et al.* [J. Org. Chem. *43*, 4771 (1978)] offered no advantages: *K.-H. Müller*, part of dissertation, Universität Freiburg.

[6] *P. G. Farrell, S. F. Mason,* Z. Naturforsch. *B 16*, 848 (1961).

[7] *R. Schwesinger,* Dissertation, Universität Freiburg 1978.

[8] *(8a):* triclinic, $P\bar{1}$, $Z=8$, $\alpha=76.53(3)$, $\beta=73.31(3)$, $\gamma=86.75(3)°$, $a=12.138(4)$, $b=15.080(6)$, $c=6.982(2)$ Å; *(8c):* orthorhombic, $Pna2_1$, $Z=8$, $a=15.905$, $b=8.902$, $c=15.388$ Å; *(8e):* orthorhombic, Fdd2, $Z=16$, $a=49.449$, $b=15.732$, $c=6.803$ Å.

[9] a) *I. C. Paul, S. M. Johnson, L. A. Paquette, J. H. Barrett, R. J. Haluska,* J. Am. Chem. Soc. *90*, 5023 (1968); *H. J. Lindner, B. v. Gross,* Chem. Ber. *105*, 434 (1972); b) *A. Gossauer:* Die Chemie der Pyrrole. Springer, Berlin 1974, p. 7.

[10] *E. A. Jauregui, F. H. Ferretti, C. A. Ponce,* Rev. Latinoam. Quim. *6*, 13 (1975); *S. Inagaki, Y. Hirabayashi,* J. Am. Chem. Soc. *99*, 7418 (1977).

[11] Cf. the X-ray structure analysis of 6-acetoxy-1,4-dithiocin: *H. J. Eggelte, F. Bickelhaupt, B. O. Loopstra,* Tetrahedron *34*, 3631 (1978).

 © *Verlag Chemie, GmbH, 6940 Weinheim, 1979* *0570-0833/79/1212-0965 $ 02.50/0*

AUTHOR INDEX

G.E. = Reference to Volume 91 (1979) of the German Edition of Angewandte Chemie. References are given for Review Articles and Short Communications only. – No "GE" reference is given for a Book Review.

ACHENBACH, CH. 882 [G.E. 944]
Acher, R. 846 [G.E. 905]
Adam, W. 468, 788 [G.E. 512, 855]
Adamsky, F. 674 [G.E. 738]
Akiba, K. 166 [G.E. 176]
Akse, J. R. 738 [G.E. 765]
Allison, N. T. 545 [G.E. 579]
Alper, H. 792 [G.E. 858]
Altenbach, H.-J. 940, 962 [G.E. 1005, 1028]
Altnau, G. 60 [G.E. 62]
Amin, N. 223 [G.E. 243]
Angerbauer, R. 304 [G.E. 325]
Anzinger, H. 686 [G.E. 747]
Apel, J. 165 [G.E. 179]
Appel, R. 169, 469, 872, 873 [G.E. 177, 497, 935, 936]
Arai, S. 166 [G.E. 176]
Arnold, B. 320 [G.E. 337]
Arvanaghi, M. 614 [G.E. 649]

BAILEY, P. S. 492
Bahr, U. 882 [G.E. 944]
Baranne-Lafont, J. 413 [G.E. 443]
Barker, B. J. 503 [G.E. 560]
Bars, O. 797 [G.E. 859]
Barth, V. 469, 872, 873 [G.E. 497, 935, 936]
Bartholomé, E. 88, 491
Basedow, A. M. 321 [G.E. 341]
Basile, L. J. 418
Bäther, W. 530 [G.E. 565]
Bats, J. W. 538 [G.E. 573]
Battersby, A. R. 675 [G.E. 752]
Bau, R. 80 [G.E. 86]
Baudler, M. 877 [G.E. 939]
Bauer, J. 111 [G.E. 99]
Bayer, E. 533, 686 [G.E. 568, 747]
Beck, W. 463 [G.E. 499]
Becker, K. B. 685 [G.E. 746]
Beltrami, H. 792 [G.E. 856]
Bensmann, W. 677 [G.E. 754]
Benson, W. 862 [G.E. 921]
Bernal, I. 861 [G.E. 920]
Berti, C. 864 [G.E. 923]
Bestmann, H. J. 687, 876, 947 [G.E. 748, 945, 1012]
Beurich, H. 690 [G.E. 751]
Bezrukov, M. G. 599 [G.E. 634]
Bianchi, G. 721 [G.E. 781]
Bianchini, C. 673 [G.E. 739]
Bichlmayer, K. 156 [G.E. 170]
Bickelhaupt, F. 395 [G.E. 423]
Biekert, E. 88, 491
Biersack, H. 960 [G.E. 1026]
Bihlmaier, W. 331 [G.E. 347]
Binnewies, M. 679 [G.E. 755]
Bino, A. 332, 462 [G.E. 356, 496]
Birr, Ch. 147, 394, 536 [G.E. 156, 422, 571]
Blecher, A. 677 [G.E. 740]
Bliefert, C. 703
Boche, G. 218 [G.E. 228]
Bock, H. 944 [G.E. 1008]
Bogdanović, B. 681, 683, 684 [G.E. 742, 744, 745]
Bögge, H. 628 [I.E. 656]
Boggs, J. E. 944 [G.E. 1008]
Böhle, Ch. 949 [G.E. 1014]
Böhme, R. 876 [G.E. 945]
Bonetti, M. 634 [G.E. 670]
Bott, K. 259 [G.E. 279]
Bowen, R. D. 451 [G.E. 484]
Bracher, G. 155 [G.E. 169]
Brame, E. G. 237
Brandt, J. 111 [G.E. 99]
Brauer, D. J. 949 [G.E. 1014]
Braunstein, P. 797 [G.E. 859]
Bremser, W. 320 [G.E. 341]
Breuninger, M. 964 [G.E. 1030]
Briehl, H. 467 [G.E. 503]
Brille, F. 400 [G.E. 428]
Brinker, U. H. 396 [G.E. 424]
Brintzinger, H. H. 777 [G.E. 837]
Brion, F. 688 [G.E. 736]
Brooks, D. W. 72 [G.E. 76]
Brough, L. F. 955 [G.E. 1022]
Browne, A. R. 546 [G.E. 581]
Brückner, H. 476 [G.E. 508]
Brüggemann, K. 540 [G.E. 575]
Brunner, H. 620, 861 [G.E. 655, 920]
Brüntrup, G. 622, 793 [G.E. 654, 840]
Burow, W. 61, 542 [G.E. 71, 577]
Bürvenich, C. 225 [G.E. 225]
Burzlaff, H. 876 [G.E. 945]
Buss, B. 231 [G.E. 253]
Busse, B. 629 [G.E. 664]

CALAS, R. 402 [G.E. 430]
Campanella, S. 80 [G.E. 86]
Caruana, A. 328 [G.E. 335]
Caruso, J. A. 503 [G.E. 560]
Cech, F. 557 [G.E. 585]
Cesarotti, E. 779 [G.E. 842]
Chamot, E. 546 [G.E. 581]
Chapman, N. B. 703
Chatziiosifidis, I. 72, 952 [G.E. 78, 1019]
Cheuk Man Lee, 792 [G.E. 856]
Chini, P. 80 [G.E. 86]
Chucholowski, A. 622 [G.E. 654]
Cooks, R. G. 171
Cotton, F. A. 332, 462, 874 [G.E. 356, 496, 937]
Creswick, M. 861 [G.E. 920]
Crooks, J. E. 560

DALE, J. 419
Daly, J. J. 964 [G.E. 1030]
Dapporto, P. 469 [G.E. 510]
Dederer, B. 223 [G.E. 243]
Defoin, A. 413 [G.E. 443]
Degel, F. 75 [G.E. 80]
Dehmlow, E. V. 170 [G.E. 163]
Dehnicke, K. 507 [G.E. 527]
De Lucchi, O. 468, 788 [G.E. 512, 855]
De Meijere, A. 809 [G.E. 867]
De Micheli, C. 721 [G.E. 781]
Deschler, U. 408 [G.E. 437]
Dever, D. F. 639
Devreese, J. T. 884
Diederich, F. 699 [G.E. 733]
Dislich, H. 49 [G.E. 52]
Doelle, H.-J. 266 [G.E. 309]
Dörr, F. 323 [G.E. 348]
Dose, K. 478 [G.E. 510]
Dötz, K. H. 954 [G.E. 1021]
Dräger, M. 677 [G.E. 740]
Drauz, K. 474 [G.E. 504]
Drück, U. 406 [G.E. 434]
Dunoguès, J. 402 [G.E. 430]
Dürner, G. 556 [G.E. 584]
Dürr, H. 945 [G.E. 1010]
Dye, J. L. 587 [G.E. 613]
Dyong, I. 933 [G.E. 997]

EBERT, K. H. 321 [G.E. 341]
Eckert, H. 794 [G.E. 841]
Ederer, H. J. 321 [G.E. 341]
Effenberger, F. 474 [G.E. 504]
Ege, G. 67 [G.E. 62]
Eichenauer, H. 397 [G.E. 425]
Eigen, M. 20 [G.E. 20]
Ellington, R. T. 87
Eltzner, W. 168 [G.E. 158]
Enders, D. 397 [G.E. 425]
Engbert, Th. 228 [G.E. 240]
Engel, P. 685 [G.E. 746]
Engels, H.-W. 229 [G.E. 251]
Engels, J. 148, 942 [G.E. 155, 1007]
Englhardt, A. 86
Erden, I. 468 [G.E. 512]
Erdtmann, G. 703
Ermer, O. 685 [G.E. 746]
Ertl, G. 313 [G.E. 333]
Eschenmoser, A. 634, 636, 637, 675 [G.E. 670, 672, 673, 752]
Ettlinger, M. 687 [G.E. 748]
Etzbach, K.-H. 470 [G.E. 500]
Evrard, R. P. 884

FACHINETTI, G. 619 [G.E. 657]
Fehlhammer, W. P. 75, 626 [G.E. 80, 661]
Felix, G. 402 [G.E. 430]
Fenske, D. 677, 679 [G.E. 754, 755]
Ferraro, J. R. 418
Feser, R. 157 [G.E. 171]
Feuerherd, K.-H. 319 [G.E. 334]
Fischer, E. O. 327, 871 [G.E. 345, 929]
Fischer, H. 871 [G.E. 929]
Fischer, J. 167 [G.E. 168]
Fitjer, L. 868 [G.E. 927]
Fitzer, E. 295 [G.E. 316]
Fleischhauer, I. 396 [G.E. 424]
Fleischhauer, J. 652 [G.E. 696]
Flockerzi, D. 62, 63 [G.E. 64, 65]
Franck, B. 429 [G.E. 453]
Francke, W. 796 [G.E. 843]
Franck-Neumann, M. 688 [G.E. 736]
Frank, A. 408 [G.E. 437]
Fray, G. I. 236
Friedrich, A. 538 [G.E. 573]
Friedrich, J. 111 [G.E. 99]
Friedrich, P. 327 [G.E. 345]
Fritch, J. R. 409 [G.E. 439]
Fritz, H. 611, 964 [G.E. 646, 1030]
Fuess, H. 538 [G.E. 573]
Funk, G. 535 [G.E. 569]

GALLAGHER, P. T. 900 [G.E. 965]
Gallenkamp, B. 964 [G.E. 1030]
Gandolfi, R. 721 [G.E. 781]
Gasparis, T. 326 [G.E. 357]
Gasteiger, J. 111 [G.E. 99]
Geckeler, K. 533 [G.E. 568]
Gerecht, B. 467 [G.E. 503]
Gieren, A. 223 [G.E. 243]
Giese, B. 154 [G.E. 167]
Gilb, W. 312 [G.E. 332]
Gilbert, K. 67 [G.E. 62]
Gokel, G. W. 559
Gompper, R. 156, 470 [G.E. 170, 500]
Goodson, A. L. 887 [G.E. 951]
Gosselck, J. 165 [G.E. 179]
Gotthardt, H. 868 [G.E. 926]
Götzfried, F. 463 [G.E. 499]
Graf, C. 780 [G.E. 846]
Grandjean, D. 797 [G.E. 859]
Grandjean, J. 153 [G.E. 166]
Grasselli, J. 237
Grätzel, M. 624, 630, 701 [G.E. 659, 669, 759]
Greiner, M. 476 [G.E. 508]
Griffiths, P. R. 420
Grimme, W. 224 [G.E. 254]
Groth, U. 863 [G.E. 922]
Grove, D. M. 155 [G.E. 169]
Grubmüller, P. 939 [G.E. 1004]
Grugel, Ch. 543 [G.E. 577]
Grund, H. 78 [G.E. 91]
Grunwald, E. 639
Grüter, H.-W. 881 [G.E. 943]
Gundermann, K.-D. 872 [G.E. 930]
Gupta, B. G. B. 612 [G.E. 648]
Gustafson, F. J. 738 [G.E. 765]
Gutmann, V. 560

HABERMANN, G. 877 [G.E. 939]
Hafner, K. 161, 162, 641 [G.E. 173, 175, 685]
Hagenmuller, P. 884
Halstenberg, M. 872 [G.E. 935]
Hammen, G. 614 [G.E. 649]
Hammes, G. G. 559

Hanack, M. 322, 614, 870 [G.E. 343, 649, 928]
Hanke, M. 214 [G.E. 227]
Hanzawa, Y. 544 [G.E. 578]
Hart, D. W. 80 [G.E. 86]
Hartwig, W. 310, 863 [G.E. 329, 922]
Haspra, P. 617 [G.E. 652]
Hassel, T. 399 [G.E. 427]
Hasslberger, 408 [G.E. 437]
Hauck, G. 945 [G.E. 1010]
Haupt, E. 556 [G.E. 584]
Hecht, H. J. 698 [G.E. 751]
Heermann, D. 308 [G.E. 330]
Hegen, D. 295 [G.E. 316]
Heidenhain, F. 218 [G.E. 228]
Heimbach, P. 400 [G.E. 428]
Heinz, B. 478 [G.E. 510]
Hellmann, H. 88
Helmchen, G. 62, 63, 65 [G.E. 64, 65, 66]
Henglein, A. 418 [G.E. 449]
Henkel, G. 325, 780 [G.E. 343, 846]
Henrici-Olivé, G. 77 [G.E. 83]
Herberhold, M. 220, 631 [G.E. 241, 662]
Herrmann, R. 956 [G.E. 1023]
Herrmann, W. A. 960 [G.E. 1026]
Hertel, M. 473 [G.E. 506]
Heumann, A. 866, 867 [G.E. 924, 925]
Heydt, A. 531 [G.E. 566]
Heyns, K. 878 [G.E. 940]
Hiemenz, P. C. 86
Hiltbrunner, K. 784, 785 [G.E. 844, 845]
Himbert, G. 405 [G.E. 432]
Himmele, W. 320 [G.E. 341]
Hnida, P.-J. 872 [G.E. 930]
Hoehne, S. 534, 535 [G.E. 568, 569]
Hoffmann, E. W. 415 [G.E. 448]
Hoffmann, R. W. 306, 563 [G.E. 329, 625]
Hofmann, P. 554 [G.E. 591]
Hofmann, W. 158 [G.E. 172]
Hofmeister, P. 789 [G.E. 863]
Holzbach, W. 548, 549 [G.E. 582, 583]
Hönle, W. 679 [G.E. 755]
Hopf, H. 215, 329, 483 [G.E. 232, 336, 517]
Hoppe, R. 61, 542 [G.E. 71, 577]
Hosomi, A. 163 [G.E. 178]
Houriet, R. 951 [G.E. 1018]
Hub, W. 323 [G.E. 348]
Huisgen, R. 330, 331 [G.E. 346, 347]
Hummel, D. O. 702
Humphrey-Baker, R. 630 [G.E. 669]
Hungerbühler, E. 958 [G.E. 1025]
Huttner, G. 76, 233, 872 [G.E. 82, 244, 935]
Huynh Ba Tuong, 633 [G.E. 675]
Huys, F. 615, 616 [G.E. 650, 651]

IDDON, B. 900 [G.E. 965]
Ilsley, W. H. 874 [G.E. 937]
Irngartinger, H. 694 [G.E. 750]
Ishii, H. 547 [G.E. 582]
Itoh, Y. 82 [G.E. 84]
Iwasaki, F. 166 [G.E. 176]

JÄGER, H. 786 [G.E. 852]
Jäger, V. 78 [G.E. 91]
Jaisli, F. 634, 636, 637 [G.E. 670, 672, 673]
Janousek, Z. 333, 615, 616, 917 [G.E. 355, 650, 651, 982]
Jansen, M. 464, 698 [G.E. 500, 762]
Jarglis, P. 936 [G.E. 1001]
Jen, T.-L. 796 [G.E. 843]
Jennings, W. 237
Jochum, C. 111 [G.E. 99]
Johnston, M. V. 738 [G.E. 765]
Jonas, K. 487, 488, 549, 550 [G.E. 520, 521, 590, 590]
Jończyk, A. 217 [G.E. 228]
Jones, K. 675 [G.E. 752]
Jones, P. G. 231 [G.E. 253]
Jordan, P. C. 885
Joyeux, M. 83, 85 [G.E. 72, 73]
Jung, G. 476 [G.E. 508]
Jung, W. 310 [G.E. 329]
Jungmann, H. 953 [G.E. 1020]
Jutz, Ch. 214 [G.E. 227]
Jutzi, P. 59 [G.E. 81]

KAGAN, H. B. 485, 779 [G.E. 511, 842]
Kaim, W. 874 [G.E. 937]
Kalyanasundaram, K. 701 [G.E. 759]
Kambe, N. 547 [G.E. 582]
Kammerer, P. 778 [G.E. 838]
Kämper, M. 486 [G.E. 517]
Kappenstein, Ch. 408 [G.E. 437]
Karsch, H. H. 484, 484 [G.E. 518, 519]
Kasai, N. 83 [G.E. 85]
Katada, M. 946 [G.E. 1011]
Kato, S. 82, 83 [G.E. 84, 85]
Kato, T. 393 [G.E. 421]
Katritzky, A. R. 792 [G.E. 856]
Kauffmann, Th. 1 [G.E. 1]
Kaupp, G. 215, 881 [G.E. 232, 943]
Kawamoto, K. 393 [G.E. 421]
Keay, J. G. 792 [G.E. 856]
Keehn, P. M. 639
Keese, R. 685 [G.E. 746]
Keller, H.-L. 464 [G.E. 500]
Kerimis, D. 545 [G.E. 579]
Kessler, H. 538 [G.E. 573]
Kiener, V. 313 [G.E. 333]
Kinast, G. 541 [G.E. 576]
Kinzel, A. 324 [G.E. 344]
Kirmse, W. 228 [G.E. 240]
Kisch, H. 328 [G.E. 335]
Kiwi, J. 624 [G.E. 659]
Klaar, M. 698 [G.E. 751]
Klärner, F.-G. 674 [G.E. 738]
Klebach, T. C. 395 [G.E. 423]
Kleemann, A. 797 [G.E. 858]
Kleemann, G. 944 [G.E. 1008]
Klein, C. M. 800 [G.E. 861]
Klein, R. 220 [G.E. 241]
Kleiner, E. 556, 557 [G.E. 584, 585]
Kleinschroth, J. 329 [G.E. 336]
Klessinger, M. 826 [G.E. 885]
Kluth, J. 400 [G.E. 428]
Knoche, W. 171
Knoll, F. 873 [G.E. 936]
Kochi, J. K. 804
Koehler, F. 882 [G.E. 944]
Koetzle, T. F. 80 [G.E. 86]
Kohl, F. 59 [G.E. 81]
Köhler, F. 308 [G.E. 327]
Kolb, O. 865 [G.E. 930]
Köll, P. 70, 71 [G.E. 74, 75]
Kondo, K. 547, 691, 692 [G.E. 582, 760, 761]
König, K.-H. 319 [G.E. 334]
König, W. A. 476 [G.E. 508]
Koo Tze Mew, P. 159 [G.E. 163]
Köpf, H. 477 [G.E. 509]
Köpf-Maier, P. 477 [G.E. 509]
Korte, H. J. 415 [G.E. 444]
Kragten, J. 236
Krahmer, U. 942 [G.E. 1007]
Kraus, H.-J. 948 [G.E. 1013]
Krebs, B. 235, 325, 415, 780 [G.E. 231, 343, 444, 846]
Kricheldorf, H. R. 689 [G.E. 749]
Krieger, C. 699 [G.E. 733]
Krivan, V. 123 [G.E. 132]
Krohn, K. 621 [G.E. 658]
Kroner, J. 934 [G.E. 998]
Krüger, C. 59, 487, 550, 683, 684, 949 [G.E. 81, 520, 590, 744, 745, 1014]
Kuchen, W. 415 [G.E. 448]
Kühn, A. 416 [G.E. 447]
Kuzmin, O. 683 [G.E. 744]

LASZLO, P. 153 [G.E. 166]
Laub, R. T. 966
Laumanns, R. 325 [G.E. 343]
Lechtken, P. 572 [G.E. 597]
Lehmann, B. 797 [G.E. 858]
Leibfritz, D. 556 [G.E. 584]
Leismann, H. 652 [G.E. 696]
Lentz, D. 66, 944 [G.E. 68, 1008]
Lenz, W. 868 [G.E. 926]
Leonhard, K. 627 [G.E. 663]
Lerf, A. 463 [G.E. 499]
Leung, C. W. F. 792 [G.E. 856]
Levinson, A. R. 796 [G.E. 843]
Levinson, H. Z. 796 [G.E. 843]
Lex, J. 962 [G.E. 1028]
Ley, H. 88, 491
Leznoff, C. C. 221 [G.E. 255]
Lichtenthaler, F.W. 936 [G.E. 1001]
Lindner, E. 534, 535 [G.E. 568, 569]
Lindner, H. J. 161, 162 [G.E. 173, 175]
Lister, D. G. 419
Littke, W. 406 [G.E. 434]
Locatelli, P. 684 [G.E. 745]
Locher, R. 957 [G.E. 1024]
Lommel, H. 86
Longoni, G. 80 [G.E. 86]
Lorenz, I. 693 [G.E. 735]
Lozac'h, N. 887 [G.E. 951]
Lu, L. D.-L. 72 [G.E. 76]
Lübbe, F. 149 [G.E. 157]
Luber, J. 412 [G.E. 442]
Luck, W. A. P. 350 [G.E. 408]
Lukas, K. L. 694 [G.E. 750]
Lütolf, J. 786 [G.E. 852]

MACDONALD, D. D. 334
Macdonald, J. N. 419
Madach, T. 690 [G.E. 751]
Maier, G. 308 [G.E. 327]
Maier, W. F. 72, 939, 952 [G.E. 78, 1004, 1019]
Malhotra, R. 612 [G.E. 648]
Mangold, D. 319 [G.E. 334]
Mangold, H. K. 493 [G.E. 550]
Manske, R. 165 [G.E. 179]
Mark, C. 485 [G.E. 511]
Mark, H. F. 237, 491, 704
Märkl, G. 789 [G.E. 863]
Martens, J. 797 [G.E. 858]
Masamune, S. 72 [G.E. 76]
Masquelier, M. 616 [G.E. 651]
Mästle, W. 538 [G.E. 573]
Matsumura, K. 955 [G.E. 1022]
Matt, D. 797 [G.E. 859]
Mauer, W. 224 [G.E. 254]
Mäusle, H.-J. 152 [G.E. 165]
Mayr, A. 626 [G.E. 661]
McArthur, C. R. 221 [G.E. 255]
McKervey, A. 939 [G.E. 1004]
McVey, J. 572 [G.E. 597]
Mealli, C. 673 [G.E. 739]
Meixner, J. 154 [G.E. 167]
Meli, A. 673 [G.E. 739]
Menke, K. 483 [G.E. 517]
Merényi, R. 333, 615, 616, 917 [G.E. 355, 650, 651, 982]
Merz, A. 938 [G.E. 1002]
Meth-Cohn, O. 900 [G.E. 951]
Methong, U. 619 [G.E. 657]
Metiu, H. 377 [G.E. 363]
Metzger, J. 70, 71 [G.E. 74, 75]
Metzler, D. E. 335
Mews, R. 231, 235 [G.E. 253, 231]
Meyer, B. 878 [G.E. 940]
Meyer, H. 551 [G.E. 587]
Meyer, M. W. 786 [G.E. 852]
Michel, U. 870 [G.E. 928]
Midollini, S. 81, 469 [G.E. 93, 510]
Milat, M.-L. 464 [G.E. 501]
Miller, M. P. 738 [G.E. 765]
Mimoun, H. 485 [G.E. 511]
Mitulla, K. 322 [G.E. 343]
Miyoshi, N. 691, 692 [G.E. 760, 761]
Mizuta, M. 82, 83 [G.E. 84, 85]
Mohan, N. 168 [G.E. 158]
Mohr, G. 76 [G.E. 82]
Montforts, F.-P. 632, 675 [G.E. 656, 752]
Moore, D. S. 738 [G.E. 765]
Mühlhausen, D. 74 [G.E. 79]
Mukaiyama, T. 707 [G.E. 798]
Müllen, K. 229, 784 [G.E. 251, 844]
Müller, A. 168, 530, 628 [G.E. 158, 565, 656]
Müller, C. 778 [G.E. 838]
Müller, H.-D. 76 [G.E. 82]
Müller, K.-H. 964 [G.E. 1030]
Müller, U. 693 [G.E. 735]
Müller, W. 407 [G.E. 438]
Müller, W. M. 623 [G.E. 676]
Mulzer, J. 622, 793 [G.E. 654, 840]
Murai, S. 393, 547, 691, 692, 837 [G.E. 421, 582, 760, 761, 896]
Murata, I. 946 [G.E. 1011]
Mutter, M. 686 [G.E. 747]

NAGORSEN, G. 551 [G.E. 587]
Nahrstedt, A. 234 [G.E. 238]
Naimann, A. 411 [G.E. 440]
Nakagawa, M. 202 [G.E. 215]
Nakamoto, K. 639
Nakasuji, K. 946 [G.E. 1011]
Narang, S. C. 612 [G.E. 648]

Neugebauer, D. 484, 484 [G.E. 518, 519]
Neumann, A. 530 [G.E. 565]
Neumann, W. P. 543 [G.E. 577]
Nikaido, H. 337 [G.E. 394]
Nill, G. 62, 63, 65 [G.E. 64, 65, 66]
Nishiyama, S. 936 [G.E. 1001]
Noda, I. 82, 83 [G.E. 84, 85]
Noltemeyer, M. 231 [G.E. 253]
Nöth, H. 326 [G.E. 357]
Nuber, B. 548 [G.E. 582]

OBERHAMMER, H. 944 [G.E. 1008]
Oeser, H.-G. 319 [G.E. 334]
Ofner, S. 632, 675 [G.E. 656, 752]
Olah, G. A. 612, 614 [G.E. 648, 649]
Olivé, S. 77 [G.E. 83]
Orlandini, A. 81, 673 [G.E. 93, 739]
Ossowski, P. 222 [G.E. 242]
Ostertag, W. 313 [G.E. 333]
Oth, J. F. M. 229 [G.E. 251]
Othmer, D. F. 237, 491, 704
Overberger, C. G. 237, 491, 704
Owen, N. L. 419

PAO, J.-H. 86
Paquette, L. A. 544, 546 [G.E. 578, 581]
Pardy, R. B. A. 871 [G.E. 929]
Patai, S. 639, 804
Pattenden, G. 884
Pawlowski, G. 322 [G.E. 343]
Pecsok, R. L. 966
Pelizzetti, E. 630 [G.E. 669]
Perkins, M. J. 864 [G.E. 923]
Peters, E. M. 944 [G.E. 1008]
Peters, K. 679 [G.E. 755]
Pfordt, J. 305 [G.E. 328]
Pieronczyk, W. 620 [G.E. 655]
Piers, E. 791 [G.E. 857]
Pipkorn, R. 536 [G.E. 571]
Poate, J. M. 560
Pohl, S. 412 [G.E. 442]
Poll, W. 415 [G.E. 448]
Pörschke, K. R. 488 [G.E. 521]
Porter, L. C. 738 [G.E. 765]
Powell, W. H. 887 [G.E. 951]
Pracejus, H. 171
Preetz, W. 150, 151 [G.E. 159, 160]
Pregosin, P. S. 155 [G.E. 169]
Priesner, C. 472 [G.E. 505]
Prikner, B. 548 [G.E. 582]
Prinzbach, H. 611, 964 [G.E. 646, 1030]
Pucci, S. 619 [G.E. 657]
Pullman, B. 418
Püttmann, M. 679 [G.E. 741]

QUAN LAM-CHI 933 [G.E. 997]
Quast, H. 788 [G.E. 855]
Quellmalz, E. 236
Quinkert, G. 556, 557 [G.E. 584, 585]

RABEK, J. F. 335
Rademacher, P. 826 [G.E. 885]
Ramamurthy, V. 572 [G.E. 597]
Ranby, B. 335
Rao, M. N. S. 780 [G.E. 846]
Rasetti, V. 675 [G.E. 752]
Rau, Angelika 231, [G.E. 239]
Rau, Axel 534 [G.E. 568]
Rautenstrauch, V. 83, 85 [G.E. 72, 73]
Ray, N. H. 559
Recktenwald, R. 788 [G.E. 855]
Reetz, M. T. 72, 173, 952 [G.E. 78, 185, 1018]
Regen, S. L. 421 [G.E. 464]
Regitz, M. 320, 531 [G.E. 337, 566]
Reglier, M. 866, 867 [G.E. 924, 925]
Rehm, D. 557 [G.E. 585]
Reichardt, Ch. 98, 803 [G.E. 119, 864]
Reichrath, M. 466 [G.E. 497]
Reinhardt, G. 224 [G.E. 254]
Reissig, H.-U. 330, 331, 791 [G.E. 346, 347, 857]
Reitel, Ch. 319 [G.E. 334]
Remmers, G. 223 [G.E. 243]
René, L. 616 [G.E. 651]
Ressler, I. 652 [G.E. 696]
Richter, F. 531, 690 [G.E. 566, 751]
Ried, W. 478 [G.E. 510]
Riekert, L. 266 [G.E. 309]
Riemann, U. 223 [G.E. 243]
Rigaudy, J. 413 [G.E. 443]
Rittner, W. 530 [G.E. 565]
Roesky, H. W. 91, 223, 415, 780 [G.E. 112, 243, 444, 846]
Rogers, D. N. 792 [G.E. 856]
Röper, H. 878 [G.E. 940]
Röper, S. 878 [G.E. 940]
Rösch. L. 60 [G.E. 62]
Rosen, M. J. 419
Rosenfarb, J. 503 [G.E. 560]
Ross, J. 377 [G.E. 363]
Rossa, L. 514 [G.E. 534]
Roth, K. 687, 876 [G.E. 748, 945]
Rothe, M. 74, 538 [G.E. 79, 573]
Rothermel, W. 949 [G.E. 1014]
Rücker, C. 611 [G.E. 646]
Rudzik, L. 150 [G.E. 159]
Ruppert, I. 873, 880 [G.E. 936, 941]

SACCONI, L. 81, 469, 673 [G.E. 93, 510, 739]
Saenger, W. 226, 227 [G.E. 234, 237]
Sakurai, H. 163 [G.E. 178]
Sališová, M. 792 [G.E. 858]
Sammes, M. P. 792 [G.E. 856]
Saxton, R. G. 236
Schäfer, H. 325 [G.E. 343]
Schäfer, H. J. 68, 69, 787 [G.E. 77, 78, 852]
Scharf, H.-D. 652 [G.E. 696]
Scheffler, K. 943 [G.E. 1007]
Scheidt, W. 401 [G.E. 429]
Schenkluhn, H. 400, 401 [G.E. 428, 429]
Scherer, O. J. 234, 679, 953 [G.E. 238, 741, 1020]
Schieferstein, L. 549, 550 [G.E. 590, 590]
Schier, A. 794 [G.E. 841]
Schilling, M. 950, 952 [G.E. 1017, 1019]
Schleker, W. 652 [G.E. 696]
Schleyer, P. von R. 553, 939 [G.E. 588, 1004]
Schlosser, M. 489, 633, 875 [G.E. 515, 675, 938]
Schmidbaur, H. 408, 781, 782 [G.E. 437, 847, 848]
Schmidpeter, A. 411, 412, 934, 935 [G.E. 441, 442, 998, 1000]
Schmidt, H.-J. 68, 69, 787 [G.E. 77, 78, 852]
Schmidt, R. R. 304, 466 [G.E. 325, 497]
Schmidt, U. 308 [G.E. 330]
Schmidt, Werner 801, 802 [G.E. 850, 851]
Schmidt, Wolfram 309 [G.E. 337]
Schmitt, B. J. 273 [G.E. 286]
Schmock, F. 693 [G.E. 735]
Schnabel, M. 943 [G.E. 1007]
Schneider, H.-J. 407 [G.E. 438]
Schneider, J. 76 [G.E. 82]
Schneider, M. 231 [G.E. 239]
Schneider, P. 489 [G.E. 515]
Schneider, S. 323 [G.E. 348]
Schnorrenberg, G. 307 [G.E. 326]
Schnutenhaus, H. 777 [G.E. 837]
Schöllkopf, U. 310, 863 [G.E. 329, 922]
Schönholzer, P. 964 [G.E. 1030]
Schriewer, M. 543 [G.E. 577]
Schröder, G. 311, 312 [G.E. 331, 332]
Schröder, U. 309 [G.E. 337]
Schubert, U. 408, 484, 484, 696, 871 [G.E. 437, 518, 519, 757, 929]
Schubert, W. 111 [G.E. 99]
Schühle, W. 62 [G.E. 64]
Schulten, H.-R. 882 [G.E. 944]
Schultz, O. E. 334
Schulz, R. 692 [G.E. 737]
Schulze, W. 404 [G.E. 432]
Schurig, V. 485 [G.E. 511]
Schwab, W. 78 [G.E. 91]
Schwarz, H. 451, 950, 951, 952 [G.E. 484, 1017, 1018, 1019]
Schwedt, G. 180 [G.E. 192]
Schweig, A. 692 [G.E. 737]
Schweitzer, D. 699 [G.E. 733]
Schwellnus, K. 72 [G.E. 78]
Schwentner, J. 222 [G.E. 242]
Scriven, F. V. 900 [G.E. 965]
Seaborg, G. T. 237, 491, 704
Sebald, A. 463 [G.E. 499]
Seebach, D. 239, 399, 784, 785, 957, 958 [G.E. 259, 427, 844, 845, 1024, 1025]
Seela, F. 536 [G.E. 570]
Seki, Y. 393 [G.E. 421]
Sekutowski, J. C. 487 [G.E. 520]
Senning, A. 941 [G.E. 1006]
Seppelt, K. 66, 186, 944 [G.E. 68, 199, 1008]
Sharma, R. C. 530 [G.E. 565]
Sheldrick, G. M. 231, 934, 935 [G.E. 253, 998, 1000]
Shibuya, M. 634, 636, 637 [G.E. 670, 672, 673]
Shirahata, A. 163 [G.E. 178]
Shorter, J. 703
Shukla, A. K. 151 [G.E. 160]
Siebert, W. 949 [G.E. 1014]
Siegel, Hardo 320 [G.E. 341]
Siegel, Herbert 784, 785 [G.E. 844, 845]
Sieger, H. 226 [G.E. 234]
Simon, A. 944 [G.E. 1008]
Sinaÿ, P. 464 [G.E. 501]
Slopianka, M. 170 [G.E. 163]
Smith, P. D. 220, 631 [G.E. 241, 622]
Snatzke, G. 363 [G.E. 380]
Soliman, F. M. 947 [G.E. 1012]
Solouki, B. 944 [G.E. 1008]
Sommer, J. 614 [G.E. 649]
Sommer, S. 695, 696 [G.E. 756, 757]
Sonoda, N. 393, 547, 691, 692, 837 [G.E. 421, 582, 760, 761, 896]
Soyka, W. 703
Spiteller, G. 305 [G.E. 328]
Sprotte, U. 310 [G.E. 329]
Staab, H. A. 699 [G.E. 733]
Stahl, I. 165 [G.E. 179]
Stähle, M. 875 [G.E. 938]
Stamm, E. 685 [G.E. 746]
Staudigl, B. 218 [G.E. 228]
Steckhan, E. 801, 802 [G.E. 850, 851]
Stegelmeier, H. 962 [G.E. 1028]
Steglich, W. 167, 307, 698 [G.E. 168, 326, 751]
Stegmann, H. B. 943 [G.E. 1007]
Stein, P. M. 939 [G.E. 1004]
Stella, L. 615, 616, 917 [G.E. 650, 651, 982]
Sternbach, D. 634, 637 [G.E. 670, 673]
Steudel, R. 152 [G.E. 165]
Stezowski, J. J. 225 [G.E. 243]
Stollenwerk, U. 394 [G.E. 422]
Stolzenberg, H. 626 [G.E. 661]
Storch, W. 326 [G.E. 357]
Strehlow, H. 171
Subramanian, L. R. 322 [G.E. 343]
Sucrow, W. 149 [G.E. 157]
Suschitzky, H. 900 [G.E. 965]
Sutter, A. 617 [G.E. 652]
Suzuki, N. 787 [G.E. 852]

TALLANT, D. R. 738 [G.E. 765]
Teller, G. G. 80 [G.E. 86]
Tesky, F.-M. 235 [G.E. 231]
Teufel, E. 215 [G.E. 232]
Theng Khin Hwang, 628 [G.E. 656]
Thiem, J. 222 [G.E. 242]
Thies, I. 939 [G.E. 1004]
Tietze, L.-F. 539, 540, 541[G.E. 574, 575, 576]
Tomahogh, R. 938 [G.E. 1002]
tom Dieck, H. 324 [G.E. 344]
Tröger, W. 798 [G.E. 860]
Trotter, J. 87
Tsay, Y.-H. 550 [G.E. 590]
Tsuchiya, T. 166 [G.E. 176]
Tundo, P. 630 [G.E. 669]
Turro, N. J. 572 [G.E. 597]

UDE, W. 161, 162 [G.E. 173, 175]
Ugi, I. 111, 956 [G.E. 99, 1023]
Ugo, R. 779 [G.E. 842]
Uzar, H. C. 539, 541 [G.E. 574, 576]

VAHRENKAMP, H. 531, 690 [G.E. 566, 751]
Van Broeck, D. 333 [G.E. 355]
Van Dongen, H. 395 [G.E. 423]
Van Doren, V. E. 884
Van Gool, W. 884
Vankar, Y. D. 614 [G.E. 649]
Venanzi, L. M. 155 [G.E. 169]
Viehe, H. G. 333, 615, 616, 917 [G.E. 355, 650, 651, 982]
Vilsmaier, E. 798, 800 [G.E. 860, 861]

Voelter, W. 225 [G.E. 243]
Vogel, E. 229, 545, 962 [G.E. 251, 579, 1028]
Vögtle, F. 159, 226, 514, 623, 753 [G.E. 163, 234, 534, 676, 813]
Vollhardt, K. P. C. 409, 411 [G.E. 439, 440]
von Seyerl, J. 76, 233, 872 [G.E. 82, 244, 935]
von Schnering, H. G. 679 [G.E. 755]
Voss, B. 962 [G.E. 1028]

WACHTER, J. 861 [G.E. 920]
Waegell, B. 866, 867 [G.E. 924, 925]
Wagner, H. Gg. 663 [G.E. 707]
Wagner, M. 486 [G.E. 517]
Waid, K. 169 [G.E. 177]
Wasmuth, D. 958 [G.E. 1025]
Wassen, J. 545 [G.E. 579]
Weber, B. 531 [G.E. 566]
Weber, E. 219, 753 [G.E. 230, 813]
Weber, Gabriela 226, 227 [G.E. 234, 237]
Weber, Gisela 483 [G.E. 517]
Weber, W. P. 559
Wehle, D. 868 [G.E. 927]
Wei, C.-Y. 80 [G.E. 86]
Weidenhammer, K. 404, 960 [G.E. 432, 1026]
Weigert, W. M. 88, 491
Weil, G. 629 [G.E. 664]
Weimann, B. 401 [G.E. 429]
Weinmaier, J. H. 412 [G.E. 442]
Weise, E. 491
Weiss, A. 486 [G.E. 517]
Weiss, E. 781, 782 [G.E. 847, 848]
Weiss, J. 548 [G.E. 582]
Weiss, R. 472, 473 [G.E. 505, 506]
Weitz, R. 652 [G.E. 696]
Wells, G. 544 [G.E. 578]
Wengert-Müller, M. 147 [G.E. 156]
Wentrup, C. 467 [G.E. 503]
Werner, H. 157, 158, 416, 627, 865, 948 [G.E. 171, 172, 447, 663, 930, 1013]
Wesdemiotis, Ch. 950, 952 [G.E. 1017, 1018]
West, R. 955 [G.E. 1022]
Whitesides, G. M. 377 [G.E. 363]
Whitten, D. G. 440 [G.E. 472]
Wieghardt, K. 548, 549 [G.E. 582, 583]
Wilhelm, E. 876 [G.E. 945]
Wilhelm, M. 962 [G.E. 1028]
Williams, D. H. 451 [G.E. 484]
Winkeler, D. 536 [G.E. 570]
Winkler-Oswatitsch, R. 20 [G.E. 20]
Winterfeldt, E. 862 [G.E. 921]
Wirz, J. 617 [G.E. 652]
Witt, M. 415 [G.E. 444]
Witt, W. 311 [G.E. 331]
Woggon, W.-D. 675 [G.E. 752]
Wohlfahrt, L. 76 [G.E. 82]
Wolf, H. 472, 473 [G.E. 505, 506]
Wörner, G. 778 [G.E. 838]
Worster, P. M. 221 [G.E. 255]
Wright, J. C. 738 [G.E. 765]
Wulff, G. 309 [G.E. 337]
Wunderlich, H. 415 [G.E. 448]
Wunsch, G. 313 [G.E. 333]
Würthwein, E.-U. 553 [G.E. 588]

YAMAMOTO, Y. 166 [G.E. 176]
Yani, F. 788 [G.E. 855]
Yasuoka, N. 83 [G.E. 85]
Yokoyama, S. 691, 692 [G.E. 760, 761]
Youssef, M. S. K. 62, 63 [G.E. 64, 65]
Yus, M. 681 [G.E. 742]

ZÄHRES, M. 401 [G.E. 429]
Zanazzi, P. F. 619 [G.E. 657]
Zechlin, L. 698 [G.E. 751]
Zeiss, H.-J. 306 [G.E. 329]
Zellerhof, R. 545 [G.E. 579]
Zellner, R. 663 [G.E. 663]
Ziegler, M. L. 404, 960 [G.E. 432, 1026]
Zimmer-Gasser, B. 484, 782 [G.E. 519, 848]
Ziskoven, R. 882 [G.E. 944]
Zwaschka, F. 411, 934, 935 [G.E. 441, 998, 1000]

SUBJECT INDEX

FP = Full paper (review article) SC = Short communication
G.E. = Reference to Volume *91* (1979) of the German Edition of Angewandte Chemie
References are given for Review Articles and Short Communications only.

ABIETOSPIRAN, the triterpene from the bark of the white fir (Abies alba) (SC) 698 [G.E. 751]
Absolute conformation, Circular dichroism and ~: application of qualitative MO theory to chiroptical phenomena (FP) 363 [G.E. 380]
Acetophenone enol, Acidity in aqueous solution (SC) 617 [G.E. 652]
Acetylene, Redox addition/elimination processes of cluster-bound ligands: oxidative elimination of CO from $Co_3(CO)_9C$—OH and reductive addition of ~ to $Co_3(CO)_9H$ (SC) 619 [G.E. 657]
Acetylene bond, Chemistry of functional groups. Chemistry of the carbon-carbon triple bond (Book Review) 639
Acetylenedicarboxylate, Di-tert-butyl ~ and its cyclotrimerization (SC) 149 [G.E. 157]
Acetylenes, Synthesis of allenes from electrophilic ~ via novel allenemanganese complexes (SC) 688 [G.E. 736]
Acidity of acetophenone enol in aqueous solution (SC) 617 [G.E. 652]
Activation analysis—its present state of development and its importance as an analytical tool (FP) 123 [G.E. 132]
C-Acylation under virtually neutral conditions (SC) 72 [G.E. 76]
Acyl halides, Flash vacuum thermolysis of doubly unsaturated ~ to give phenols (SC) 170 [G.E. 163]
Acyl ortho esters, Directed synthesis (SC) 309 [G.E. 337]
Adamantene in the gas phase (SC) 952 [G.E. 1019]
α-Adamantyl carbonyl compounds, General synthesis of potentially antiviral ~ (SC) 72 [G.E. 78]
2-Adamantyl cation, Stable ~ in the gas phase (SC) 950 [G.E. 1017]
Ion cyclotron resonance studies on tert-butyl, 2-norbornyl, and 1-adamantyl cation and ~ (SC) 951 [G.E. 1018]
Adenylates, Directed synthesis of the trimeric isoadenylate A2′p5′A2′p5′A (SC) 942 [G.E. 1007]
Adiabatic photoreactions of organic molecules (FP) 572 [G.E. 597]
β-Alanine, Cyclooligocondensation of amino acids: macrocyclic amides of ~ (SC) 74 [G.E. 79]
Aldehydes, Catalytic conversion of ~ into higher α-siloxy-~ by hydrosilane and carbon monoxide (SC) 393 [G.E. 421]
Fragmentation of γ-hydroxyammonium compounds to unsaturated ~ by flash thermolysis (SC) 541 [G.E. 576]
Stereoselective synthesis of Z-α,β-unsaturated ~ (SC) 687 [G.E. 748]
α-Amino-~ from enamines and chloramine-T (SC) 933 [G.E. 997]
Alkali metal anions, Compounds (FP) 587 [G.E. 613]
Alkali metals, Steric course of the reduction of ketoacetal esters with ~ in liquid ammonia (SC) 637 [G.E. 673]
Alkaloids, Thermodynamically controlled stereoselective synthesis of geissoschizine (SC) 862 [G.E. 921]
Alkanes, Thermal pericyclic reaction between alkynes and ~ (SC) 71 [G.E. 75]
Alkenediazonium salts, A new chapter of classical organic chemistry (FP) 259 [G.E. 279]
Alkenes, Reversal of the selectivity principle in free-radical additions to ~ (SC) 154 [G.E. 167]
Alkoxylipids, Synthesis and biosynthesis (FP) 493 [G.E. 550]
Alkylammonium ions, Long-chain ~ as phase transfer reagents for the synthesis of mixed-ligand complexes of the platinum metals (SC) 151 [G.E. 160]
Alkylation, Catalytic ~ of benzene with CO and H_2: a homogeneously catalyzed Fischer-Tropsch synthesis (SC) 77 [G.E. 83]
Asymmetric synthesis of ant alarm pheromones—α-~ of acyclic ketones with almost complete asymmetric induction (SC) 397 [G.E. 425]
Regioselective ~ of 1,4,5-trihydroxy-9,10-anthraquinone with formaldehyde and glyoxylic acid (SC) 621 [G.E. 658]
2-Alkylcyclohexanones, Asymmetric synthesis of ~ on solid phases (SC) 221 [G.E. 255]
Alkyne metathesis, Cyclobutadiene-metal complexes as potential intermediates in ~: flash vacuum pyrolysis of substituted η^4-cyclobutadiene-η^5-cyclopentadienylcobalt complexes (SC) 409 [G.E. 439]
Alkynes, Thermal pericyclic reaction between ~ and alkanes (SC) 71 [G.E. 75]
Preparation of stable vinylketenes by metal complex-induced olefination and carbonylation of ~ (SC) 954 [G.E. 1021]
Allenes, Synthesis from electrophilic acetylenes via novel allenemanganese complexes (SC) 688 [G.E. 736]
Allyl bromides, Ring-opening of 5-(bromomethyl)-2-isoxazolines to β,γ-enoximes—a new principle for the γ-substitution of ~ by α-functionalized alkyl groups (SC) 78 [G.E. 91]
Allylurea, A metalated ~ with sterically protected carbonyl group as novel d^3-reagent (SC) 399 [G.E. 427]
Amide chlorides, Synthesis and intramolecular 1,3 Cl,H disproportionation of ethyl 2,2-dichloro-2-(dimethylamino)acetate (SC) 615 [G.E. 650]
Amides, Extreme liquid chromatographic separation effects in the case of diastereomeric ~ containing polar substituents (SC) 62 [G.E. 64]
Preparative scale directed resolution of enantiomeric amines via liquid chromatography of diastereomeric 4-hydroxybutyr-~ (SC) 65 [G.E. 66]
Amines, Preparative scale directed resolution of enantiomeric ~ via liquid chromatography of diastereomeric 4-hydroxybutyramides (SC) 65 [G.E. 66]
^{23}Na-NMR study of the competition of biogenic ~ with sodium ion for binding to lasalocid (X-537 A) (SC) 153 [G.E. 166]
Tellurium catalyzed reactions of ~ with carbon monoxide (SC) 547 [G.E. 582]
Reactions of carbonyl selenide with ~ and amino alcohols to produce ureas and carbamates (SC) 692 [G.E. 760]
Amino acid esters, Economic synthesis of activated N-tert-butyloxycarbonyl-~ (Z) (SC) 307 [G.E. 326]
Amino acids, Cyclooligocondensation of ~: macrocyclic amides of β-alanine (SC) 74 [G.E. 79]
New synthesis from halogenated carboxylic esters (SC) 474 [G.E. 504]
Thermal generation of pteridines and flavines from amino acid mixtures (SC) 478 [G.E. 510]
Enantioselective synthesis of α-methyl-α-aminocarboxylic acids by alkylation of the lactim ether of cyclo-(L-Ala-L-Ala) (SC) 863 [G.E. 922]
N-Nitroso sugar ~ (SC) 878 [G.E. 940]
Amino alcohols, Reactions of carbonyl selenide with amines and ~ to produce ureas and carbamates (SC) 692 [G.E. 760]
α-Aminoaldehydes from enamines and chloramine-T (SC) 933 [G.E. 997]
Aminobicyclo[4.1.0]heptanes, The morpholino group as stereoindicator in ~ (SC) 798 [G.E. 860]
Aminoethynylation, β-Stannylated ynamines as ~ reagents (SC) 405 [G.E. 432]
Aminophosphanes, Synthesis, resolution, and characterization of an aminophosphane rotamer pair (SC) 679 [G.E. 741]
Aminyl oxides, Enantioselective oxidation by a chiral acylaminyl oxide (SC) 864 [G.E. 923]
Ammonium ions, Long-chain alkyl-~ as phase transfer reagents for the synthesis of mixed-ligand complexes of the platinum metals (SC) 151 [G.E. 160]
Analytical methods, Activation analysis—its present state of development and its importance as an analytical tool (FP) 123 [G.E. 132]
Liquid column chromatography with chemical derivatizations after separation (FP) 180 [G.E. 192]
Applications of SEPIL to the solid state defect chemistry of fluorites and ultra-trace inorganic analysis (FP) 738 [G.E. 765]
Anchimeric assistance, Anchimerically accelerated bond homolysis (FP) 173 [G.E. 185]
Anions, Compounds of alkali metal ~ (FP) 587 [G.E. 613]
Dianion and tetraanion of octalene (SC) 229 [G.E. 251]
Annulenes, Aza[18]-~ (SC) 312 [G.E. 332]
Annulenoannulenes (FP) 202 [G.E. 215]
Ant alarm pheromones, Asymmetric synthesis of ~—α-Alkylation of acyclic ketones with almost complete asymmetric induction (SC) 397 [G.E. 425]
syn-Anthracene 4a,10:9,9a-dioxide (SC) 413 [G.E. 443]
Anthraquinone, Mono- and bis(η^3-allylnickel) derivatives of 1,8-dihydroxy-~ and of some 1,3,5-triketones (SC) 681 [G.E. 742]
Antibiotic, Sequences of the membrane-modifying peptide ~ trichotoxin A-40 (SC) 476 [G.E. 508]
Antigenic determinant, Chemical synthesis of human blood group B ~: type 2 tetrasaccharide (SC) 464 [G.E. 501]
Antimonate, Tris(trichlorophosphoranediylamino)carbenium hexachloro-~, $[C(NPCl_3)_3]^+SbCl_6^-$ (SC) 693 [G.E. 735]
D-Arabinofuranosyl-7-deazapurine, Preferred β-glycoside formation by phase transfer catalysis in the synthesis of ~ nucleosides (SC) 536 [G.E. 570]
Areno-analogy, From the principle of ~ to heterocyclopolyaromatic compounds (FP) 1 [G.E. 1]
Arsanediylphosphorane, Stabilization (SC) 233 [G.E. 244]
Arsanes, Mesityl(diphenylmethylene)arsane (SC) 395 [G.E. 423]
Novel polycyclic phosphanes and ~: $P_{11}(SiMe_3)_3$ and $As_7(SiMe_3)_3$ (SC) 679 [G.E. 755]
Arsenic compounds, Phosphadiarsiranes (SC) 877 [G.E. 939]
Arylnitrene chemistry, Developments in ~ syntheses and mechanisms (FP) 900 [G.E. 965]

Asymmetric epoxidation of simple olefins with an optically active molybdenum(VI) peroxo complex (SC) 485 [G.E. 511]
Asymmetric induction, Unusually high ~ in the photochemical formation of oxetane (SC) 868 [G.E. 926]
Asymmetric synthesis, ~ of 2-alkylcyclohexanones on solid phases (SC) 221 [G.E. 255]
~ of ant alarm pheromones—α-Alkylation of acyclic ketones with almost complete asymmetric induction (SC) 397 [G.E. 425]
Atmosphere, Rates of reactive removal of anthropogenic emissions (FP) 663 [G.E. 707]
Aza[18]annulenes (SC) 312 [G.E. 332]
Aza-arenes, New synthetic reactions based on the onium salts of ~ (FP) 707 [G.E. 798]
Azacyclopentadienylium salts, Stable ~ and diazacyclopentadienylium salts (SC) 156 [G.E. 170]
Azoalkanes, Polycyclic ~ via dipolar cycloaddition of 4-phenyl-1,2,4-triazoline-3,5-dione with strained bicyclic olefins (SC) 468 [G.E. 512]
Azoalkenes, [3+2]-Cycloadditions of ~ to enamines—"criss-cross" cycloadditions to ~ (SC) 695 [G.E. 756]
[4+2]-Cycloadditions of ~ to azodicarbonyl compounds. A novel facile route to the 1,2,3,4-tetrazine system (SC) 696 [G.e. 757]
Azodicarbonyl compounds, [4+2]-Cycloadditions of azoalenes to ~. A novel facile route to the 1,2,3,4-tetrazine system (SC) 696 [G.E. 757]
Azo esters, Competition in the three-component system triphenylphosphane/azo ester/3-hydroxy-carboxylic acid: OH- versus COOH-activation (SC) 622 [G.E. 654]
Azulene, Surprising transformation of ~ by cycloaddition with 1-(diethylamino)propyne (SC) 161 [G.E. 173]
Synthesis of 5,5'-biazulenyl (SC) 214 [G.E. 227]

BACTERIA, Permeability of the outer membrane of ~ (FP) 337 [G.E. 394]
Bee venom, Synthesis of the mast cell degranulating (MCD) peptide from ~ (SC) 147 [G.E. 156]
Benzaldehyde, Synthesis and X-ray structure analysis of a Mo complex with η^2-coordinated ~; transformation of a CO ligand by double α-addition (SC) 861 [G.E. 920]
Benzene, Catalytic alkylation of ~ with CO and H_2: a homogenously catalyzed Fischer-Tropsch synthesis (SC) 77 [G.E. 83]
Tricyclo[4.2.2.$1^{2,5}$]undeca-3,7,9-triene, the [4+4]cycloadduct of ~ and cyclopentadiene. Reaction sequence of its retro-cleavage (SC) 224 [G.E. 254]
Benzene derivatives, Regiospecific synthesis of disubstituted ~ (SC) 402 [G.E. 430]
Benzenehexacarboxylate, Di-tert-butyl acetylenedicarboxylate and its cyclotrimerization (SC) 149 [G.E. 157]
Benzenetricarboxylate, Di-tert-butyl acetylenedicarboxylate and its cyclotrimerization (SC) 149 [G.E. 157]
1,2,3-Benzoxadiazole, Existence of ~ in the gas phase (SC) 692 [G.E. 737]
Benzyl ether, Oxidative removal of the ~ protecting group by homogeneous electron transfer (SC) 801 [G.E. 850]
Benzyl(triethyl)ammonium permanganate, Detonation (SC) 786 [G.E. 852]
Stability (SC) 787 [G.E. 852]
5,5'-Biazulenyl, Synthesis (SC) 214 [G.E. 227]
Bicyclo[n.1.0]alkanes, Morpholino group as stereoindicator in aminobicyclo[4.1.0]heptanes (SC) 798 [G.E. 860]
Morpholino(succinimido)-~ from enaminosulfonium salts (SC) 800 [G.E. 861]
Bicyclo[1.1.0]butane, Bonding in ~ derivatives (SC) 694 [G.E. 750]
Bicyclo[4.2.1]non-1(8)-ene, Metal complexes of Bredt olefins: synthesis and structure of ~-bis(triphenylphosphane)platinum(0) 685 [G.E. 746]
Bicyclo[2.2.2]octa-5,7-diene-2-carboxylic acid, and 7-methylenebicyclo[2.2.2]octa-2,5-diene (SC) 470 [G.E. 500]
Bicyclo[2.2.0]pent-2-ene, Thermal "walk" rearrangement in the ~ system (SC) 674 [G.E. 738]
Bilane, Enzymatic formation of uroporphyrinogen I and III from a substituted ~ (SC) 778 [G.E. 838]
Biochemistry—The chemical reactions of the living cell (Book Review) 335
Biogenic amines, ^{23}Na-NMR study of the competition of ~ with sodium ion for binding to lasalocid (X-537 A) (SC) 153 [G.E. 166]
Bis(bicyclo[1.1.0]butane), An expeditious synthesis of heptalene from naphthalene via a ~ intermediate (SC) 546 [G.E. 581]
Bis(chlorophenylphosphoranediyl)methane (SC) 169 [G.E. 177]
Blood group B, Chemical synthesis of human ~ antigenic determinant: type 2 tetrasaccharide (SC) 464 [G.E. 501]
Blood plasma, ω-Formyl- and 4-oxocarboxylic acids in ~ (SC) 305 [G.E. 328]
Boc-Amino acid esters, Economic synthesis of activated ~ (SC) 307 [G.E. 326]
Bond delocalization, 1H-1,2,3λ^2-diazaphospholes—~ in λ^2-phospholes (SC) 413 [G.E. 442]
Bond energy, Existence and ~ of the cesium auride molecule (SC) 629 [G.E. 664]
Bonding, Structure and ~ in cyclic sulfur-nitrogen compounds (FP) 91 [G.E. 112]
~ properties of cyclopropane and their chemical consequences (FP) 809 [G.E. 867]
Bond length, Discovery of an exceptionally long unbridged carbon-carbon bond (SC) 406 [G.E. 434]
Bond switch with participation of π-bonded S^{IV} in thiathiophthene-analogous systems (SC) 166 [G.E. 176]
Boron compounds, Chemistry of the $H_3B(CH_3)_2P$ group: unusual properties of some simple reference compounds (SC) 781 [G.E. 847]
Synthesis and crystal structure of a salt containing the anion $[H_3B(CH_3)_2P{-}CH{-}P(CH_3)_2BH_3]^-$; precursors and related compounds (SC) 782 [G.E. 848]
Borylamines, Bis(dichloroboryl)silylamines and tris(dichloroboryl)amine (SC) 326 [G.E. 357]
Breathing crown ethers, Crown ethers with fluctuating ring size ("~") (SC) 311 [G.E. 331]
Bredt olefins, Metal complexes of ~: synthesis and structure of bicyclo[4.2.1]non-1(8)-enebis(triphenylphosphane)platinum(0) (SC) 685 [G.E. 746]
μ_3-(η^3Cη^2O) bridge—a novel mode of coordination in the structure in the structural chemistry of carbonylmetal compounds (SC) 960 [G.E. 1026]
Bridging mode, New ~ of carbon disulfide in a dinuclear cobalt(I) complex (SC) 673 [G.E. 739]
(Bromoacetylmethylene)triphenylphosphorane—a novel cyclopentannelating agent (SC) 940 [G.E. 1005]
Bromolithiocarbenoids, Direct ^{13}C-NMR spectroscopic observation of cyclopropylidene ~ (SC) 784 [G.E. 844]
3-Bromo-3-methyl-2-trimethylsiloxy-1-butene—A new cycloaddition reagent (SC) 163 [G.E. 178]
Bromotrimethylsilane, Ring-opening of lactones and cyclic carbonates with ~ or iodotrimethylsilane (SC) 689 [G.E. 749]
Bullvalene, Crown ethers with fluctuating ring size ("breathing crown ethers") (SC) 311 [G.E. 331]
Butadiene, Ligand concentration-control in the system nickel(0)/triphenylphosphane/~ (SC) 400 [G.E. 428]
N-tert-Butyloxycarbonyl amino acid esters, Economic synthesis of activated ~ (SC) 307 [G.E. 326]
CADMIUM compounds, Bis(trimethylsilyl)-zinc and -cadmium (SC) 60 [G.E. 62]
Cancerostatic activity, Titanocene dichloride—the first metallocene with ~ (SC) 477 [G.E. 509]
Capto-dative substituent effects in syntheses with radicals and radicophiles (FP) 917 [G.E. 982]
Carbamates, Reactions of carbonyl selenide with amines and amino alcohols to produce ureas and ~ (SC) 692 [G.E. 760]
Carbamoyl chlorides, α,β-Unsaturated isocyanates by thermolysis of N-(1-alkenyl)-N-alkyl-~ (SC) 319 [G.E. 334]
Carbamoyllithium, Carbonylation of lithium dialkylamides to give ~-s (SC) 83 [G.E. 73]
Carbene-carbene rearrangements of cis- and trans-2-(1,3-butadienyl)cyclopropylidene (SC) 396 [G.E. 424]
Carbene complexes, Spontaneous rearrangement of a carbene- to a carbyne complex: C,Cr migration of a $Sn(C_6H_5)_3$ group (SC) 871 [G.E. 929]
Carbene reactions, (Diazomethyl)cyclopropenes—synthesis, isomerization, and ~ (SC) 531 [G.E. 566]
Carbenes, Iminocarbene/ketenimine rearrangement (SC) 320 [G.E. 337]
Carbenoids, Direct ^{13}C-NMR spectroscopic observation of cyclopropylidene bromolithio-~ (SC) 784 [G.E. 844]
Carbido carbon, A metalloporphyrin containing carbyne-like ~: 5,10,15,20-tetraphenylporphyrinato[bis(μ-carbidotricarbonylrhenium)]tin(IV) (SC) 83 [G.E. 85]
Carbocations, Ion cyclotron resonance studies on tert-butyl, 2-norbornyl, and 1- and 2-adamantyl cations (SC) 951 [G.E. 1018]
Carbodiphosphoranes, Problem of the structure of ~, R_3PCPR_3: new aspects (SC) 408 [G.E. 437]
Carbohydrates, Chemical synthesis of human blood group B antigenic determinant: type 2 tetrasaccharide (SC) 464 [G.E. 501]
Facile, highly selective synthesis of α- and β-disaccharides from 1-O-metalated D-ribofuranoses (SC) 466 [G.E. 497]
Carbonates, Ring-opening of lactones and cyclic ~ with bromo- or iodotrimethylsilane (SC) 689 [G.E. 749]
Carbon-carbon bond, Discovery of an exceptionally long unbridged ~ (SC) 406 [G.E. 434]
Carbon disulfide, New bridging mode of ~ in a dinuclear cobalt(I) complex (SC) 673 [G.E. 739]
Carbon-halogen bond, Model system for the electrochemical reduction of the ~ (SC) 938 [G.E. 1002]
Carbon monoxide, Catalytic reactions with hydrosilane and ~ (FP) 837 [G.E. 896]
Catalytic alkylation of benzene with ~ and H_2: a homogeneously catalyzed Fischer-Tropsch synthesis (SC) 77 [G.E. 83]
Catalytic conversion of aldehydes into higher α-siloxy aldehydes by hydrosilane and ~ (SC) 393 [G.E. 421]
Tellurium catalyzed reactions of amines with ~ (SC) 547 [G.E. 582]
Carbonylation, ~ of lithium dialkylamides to give carbamoyllithiums (SC) 83 [G.E. 73]
~ of lithium monoalkylamides to give N-lithio(alkyl)formamides (SC) 85 [G.E. 72]
Carbonyl compounds, Facile regeneration from 1,3-dithiane 1-oxides via 1-ethoxy-1,3-dithianium salts (SC) 165 [G.E. 179]
α,β-Unsaturated ~ with sterically protected carbonyl groups—enforced a^3 versus a^1 reactivity (SC) 957 [G.E. 1024]
Carbonyl group, Metalated allylurea with sterically protected ~ as novel d^3-reagent (SC) 399 [G.E. 427]
Carbonylmetal compounds, The μ_3-(η^3Cη^2O) bridge—a novel mode of coordination in the structural chemistry of ~ (SC) 960 [G.E. 1026]

Carbonyl selenide, New synthesis (SC) 691 [G.E. 760]
Reactions with amines and amino alcohols to produce ureas and carbamates (SC) 692 [G.E. 760]
Carboxylic acids, Preparative scale directed resolution of enantiomeric ~ and lactones via liquid chromatography and neighboring-group assisted hydrolysis of diastereomeric amides (SC) 63 [G.E. 65]
Carbyne complexes, Complex-stabilized hydroxy(p-tolyl)acetylene by reaction of trans-chlorotetracarbonyl(tolylcarbyne)-tungsten with acetylacetone (SC) 327 [G.E. 345]
Spontaneous rearrangement of a carbene- to a carbyne complex: C,Cr migration of a $Sn(C_6H_5)_3$ group (SC) 871 [G.E. 929]
Catalysis, Triphase ~ (FP) 421 [G.E. 464]
Catalytic reactions with hydrosilane and carbon monoxide (FP) 837 [G.E. 896]
Koordinationschemische Katalyse organischer Reaktionen (Book Review) 171
Organometallic mechanisms and catalysis (Book Review) 804
Catalysts, Complexes with chiral alkylcyclopentadienyl ligands for homogeneous catalytic asymmetric hydrogenation of 2-phenyl-1-butene (SC) 779 [G.E. 842]
Cations, Chemistry of isolated ~ (FP) 451 [G.E. 484]
Cesium auride, Existence and bond energy of the ~ molecule (SC) 629 [G.E. 664]
Chemical technology, Kirk-Othmer: Encyclopedia of ~ (Book Review) 237, 491, 704
Chirality, $(-)_{579}$-Bis[(S)-(+)-O,O'(1,1'-binaphthyl-2,2'-diyl)dithiophosphato]nickel-(II)—The first dithiophosphato complex to have axial ~ (SC) 415 [G.E. 448]
Chiral reagents from tartaric acid—1-benzyloxy-3,4-epoxy-2-butanol, a versatile intermediate for the synthesis of enantiomers (SC) 958 [G.E. 1025]
Chiroptical phenomena, Circular dichroism and absolute conformation: application of qualitative MO theory to ~ (FP) 363 [G.E. 380]
Chloramine-T, α-Aminoaldehydes from enamines and ~ (SC) 933 [G.E. 997]
Chlorine-hydrogen exchange, Synthesis and intramolecular 1,3 Cl,H disproportionation of ethyl 2,2-dichloro-2-(dimethylamino)acetate (SC) 615 [G.E. 650]
Intramolecular Cl,H disproportionation of an oxamide chloride. An entry to imidazole derivatives (SC) 616 [G.E. 651]
Chromatography, Liquid column ~ with chemical derivatizations after separation (FP) 180 [G.E. 192]
Extreme liquid chromatographic separation effects in the case of diastereomeric amides containing polar substituents (SC) 62 [G.E. 64]
Preparative scale directed resolution of enantiomeric carboxylic acids and lactones via liquid ~ and neighboring-group assisted hydrolysis of diastereomeric amides (SC) 63 [G.E. 65]
Preparative scale directed resolution of enantiomeric amines via liquid ~ of diastereomeric 4-hydroxybutyramides (SC) 65 [G.E. 66]
Chromium catalyst, Homogeneously catalyzed dimerization of isoprene to 2,7-dimethyl-2,trans-4,6-octatriene at chromium (SC) 324 [G.E. 344]
Chromium complexes, η^5-Cyclopentadienylchromium complexes with thiocarbonyl and nitrosyl ligands (SC) 631 [G.E. 662]
Chromium compounds, [(triphos)Co(μ-P_3)$Cr_2(CO)_{10}$]: A trinuclear heterometal complex containing cyclo-triphosphorus as μ_3-ligand (SC) 81 [G.E. 93]
Stabilization of an arsanediylphosphorane (SC) 233 [G.E. 244]
Spontaneous rearrangement of a carbene- to a carbyne complex: C,Cr migration of a $Sn(C_6H_5)_3$ group (SC) 871 [G.E. 929]
Tetracarbanilanilidodichromium(II): A clue to the understanding of the CrCr quadruple bond (SC) 874 [G.E. 937]
Cinnamic acid, Asymmetric hydrogenation of (Z)-α-(acetylamino)-~ by a Rh/norphos catalyst (SC) 620 [G.E. 655]
Circular dichroism and absolute conformation: application of qualitative MO theory to chiroptical phenomena (FP) 363 [G.E. 380]
Clusters, Synthesis and structure of the nido-cluster $(CH_3)_5C_5Sn^+$ (SC) 59 [G.E. 81]
Reversible opening of a trinuclear heterometal cluster (SC) 76 [G.E. 82]
$FeCoMoWS(AsMe_2)Cp_2(CO)_7$: The first cluster to contain four different metal atoms (SC) 531 [G.E. 566]
Coal, Liquid fuels from ~ (Book Review) 87
Cobalt complexes, Stepwise addition of a Lewis acid and a Lewis base to a metal-metal bond (SC) 158 [G.E. 172]
Cyclobutadiene-metal complexes as potential intermediates in alkyne metathesis: flash vacuum pyrolysis of substituted η^4-cyclobutadiene-η^5-cyclopentadienylcobalt complexes (SC) 409 [G.E. 439]
$(C_5H_5)_3Co_3(CS)(S)$; the first complex to have a μ_3-thiocarbonyl bridge (SC) 627 [G.E. 663]
New bridging mode of carbon disulfide in a dinuclear cobalt(I) complex (SC) 673 [G.E. 739]
Experiments on the HOMO-LUMO nature of metal-metal bonds (SC) 690 [G.E. 751]
New pathways to trinuclear complexes—structure of the tetradecker sandwich complex bis(η-thiadiborolencobalt-μ,η-thiadiborolene)iron (SC) 949 [G.E. 1014]
Cobalt compounds, Coordination number 3 in Co^{II}: $Na_{10}[Co_4O_9]$, an oligooxocobaltate(II) (SC) 61 [G.E. 71]
Six-coordinate hydrogen: structure of $[(Ph_3P)_2N]^+[HCo_6(CO)_{15}]^-$ by single-crystal neutron diffraction analysis (SC) 80 [G.E. 86]
[(triphos)Co(μ-P_3)$Cr_2(CO)_{10}$]: A trinuclear heterometal complex containing cyclo-triphosphorus as μ_3-ligand (SC) 81 [G.E. 93]
Stable coordination compounds of "thiazyl fluoride": structure of $[Co(NSF)_6]^{2+}$ in the crystal (SC) 231 [G.E. 253]
$FeCoMoWS(AsMe_2)Cp_2(CO)_7$: The first cluster to contain four different metal atoms (SC) 531 [G.E. 566]
Co^{II} with coordination number 3: $Na_4[CoO_3]$—the first oxocobaltate(II) with an island structure (SC) 542 [G.E. 577]
Cobalt(I)phthalocyanine vitamin B_{12s}-model: selectivity in reactions with electrophiles (SC) 794 [G.E. 841]
Collision spectroscopy (Book Review) 171
Colloid chemistry, Principles of colloid and surface chemistry (Book Review) 86
Column chromatography, Liquid ~ with chemical derivatizations after separation (FP) 180 [G.E. 192]
Complexation, Multidentate acyclic neutral ligands and their ~ (FP) 753 [G.E. 813]
Complexation equilibria, Atlas of metal-ligand equilibria in aqueous solutions (Book Review) 236
Computers in chemistry, New applications of ~ (FP) 111 [G.E. 99]
Conformation, Circular dichroism and absolute ~: application of qualitative MO theory to chiroptical phenomena (FP) 363 [G.E. 380]
Boat ~ of cyclo-[L-Pro_2-D-Pro] 538 [G.E. 573]
Conformational analysis, ~ by photoelectron spectroscopy (FP) 826 [G.E. 885]
Stereochemie und Konformationsanalyse (Book Review) 419
Coordination, The μ_3-(η^3Cη^2O) bridge—a novel mode of ~ in the structural chemistry of carbonylmetal compounds (SC) 960 [G.E. 1026]
Cope rearrangement, Synthesis of cis-2-vinylcyclopropyl ketones: a new synthesis of 4-cycloheptenones (SC) 791 [G.E. 857]
The first 1,3,4,6-tetraphospha-1,5-hexadiene, a molecule with fluxional bonds (identical tetraphospha ~) and configurational isomerism (SC) 873 [G.E. 936]
Copper complexes, [{Cu_3WS_3Cl}/$(PPh_3)_3O$], directed synthesis of a compound containing different metal atoms in a cubane-like skeleton (SC) 628 [G.E. 656]
Coronates, Complexes of γ-cyclodextrin with crown ethers, cryptands, ~, and cryptates (SC) 623 [G.E. 676]
Criss-cross cycloaddition, Formal ~ of sulfur trioxide to cyanogen (SC) 223 [G.E. 243]
[3+2]-Cycloadditions of azoalkenes to enamines—~ to azoalkenes (SC) 695 [G.E. 756]
Crown ethers, "Multi-loop ~" with multiple selectivity (SC) 219 [G.E. 230]
Spherical wrapping of a linear polyether around a cation—1,20-bis(8-quinolyloxy)-3,6,9,12,15,18-hexaoxaeicosane·RbI (SC) 226 [G.E. 234]
~ with fluctuating ring size ("breathing ~") (SC) 311 [G.E. 331]
Complex of γ-cyclodextrin with ~, cryptands, coronates, and cryptates (SC) 623 [G.E. 676]
Structure of the dicyanophosphide ion in a crown-ether sodium salt (SC) 934 [G.E. 998]
Crown ether surfactants, Complexes of nitrogen-containing ~ with stable silver atoms (SC) 630 [G.E. 669]
Cryptands, Spherical wrapping of a linear polyether around a cation—1,20-bis(8-quinolyloxy)-3,6,9,12,15,18-hexaoxaeicosane·RbI (SC) 226 [G.E. 234]
Complexes of γ-cyclodextrin with crown ethers, ~, coronates, and cryptates (SC) 623 [G.E. 676]
Cryptates, Complexes of γ-cyclodextrin with crown ethers, cryptands, coronates, and ~ (SC) 623 [G.E. 676]
Cubane, [{Cu_3WS_3Cl}/$(PPh_3)_3O$], directed synthesis of a compound containing different metal atoms in a ~-like skelton (SC) 628 [G.E. 656]
Cyanides, Krypton and xenon inclusion compounds of complex metal ~ (SC) 486 [G.E. 517]
Cyanogen, Formal criss-cross cycloaddition of sulfur trioxide to ~ (SC) 223 [G.E. 243]
Cyanohalophosphates(III)—Hypervalent anions containing λ^5-phosphorus(III) (SC) 411 [G.E. 441]
Cyclization, Mechanistic aspects of the palladium catalyzed ~ of 5-methylenecyclooctene (SC) 867 [G.E. 925]
Cycloaddition, Synchronous mechanism of the 1,1-~ of nitrile ylides to C=C double bonds (SC) 167 [G.E. 168]
Formal criss-cross ~ of sulfur trioxide to cyanogen (SC) 223 [G.E. 243]
~-s of α-diazo carbonyl compounds to enamines (SC) 330 [G.E. 346]
[2+4]-~-s with di-tert-butyl acetylenedicarboxylate (SC) 483 [G.E. 517]
[2+2]-~ of a vinyl cation (SC) 614 [G.E. 649]
[3+2]-~-s of azoalkenes to enamines—"criss-cross" ~-s to azoalkenes (SC) 695 [G.E. 756]
[4+2]-~-s of azoalkenes to azodicarbonyl compounds. A novel facile route to the 1,2,3,4-tetrazine system (SC) 696 [G.E. 757]
Cycloaddition reagent, 3-Bromo-3-methyl-2-trimethylsiloxy-1-butene—a new ~ (SC) 163 [G.E. 178]
Cyclobutadiene, Electrophilic behavior of tri-tert-butyl-~ (SC) 308 [G.E. 327]
~-metal complexes as potential intermediates in alkyne metathesis: flash vacuum pyrolysis of substituted η^4-~-η^5-cyclopentadienylcobalt complexes (SC) 409 [G.E. 439]

Cyclobutane, Multiple cyclopropylmethyl-cyclobutyl rearrangements in a pentaspirohexadecanol (SC) 868 [G.E. 927]
Influence of 1,2-functionalization with —C≡N, —CH=NR, or —CH=O on the stability of the ~ system (SC) 872 [G.E. 930]
γ-Cyclodextrin, Complexes with crown ethers, cryptands, coronates, and cryptates (SC) 623 [G.E. 676]
Cyclodiaza-λ^6-thianes—syntheses and structures (SC) 235 [G.E. 231]
4-Cycloheptenones, Synthesis of cis-2-vinylcyclopropyl ketones; a new synthesis of ~ (SC) 791 [G.E. 857]
2,4-Cyclohexadienones, Spectroscopic identification of polymethyl-substituted ~ (SC) 556 [G.E. 584]
Question of π^*,n- and π^*,π selective photochemistry of 2,4-cyclohexadienones (SC) 557 [G.E. 585]
Cyclohexanones, Asymmetric synthesis of 2-alkyl-~ on solid phases (SC) 221 [G.E. 255]
Cyclooctatetraene, Chemistry of ~ and its derivatives (Book Review) 236
Cyclooctene, Mechanistic aspects of the palladium-catalyzed cyclization of 5-methylene-~ (SC) 867 [G.E. 925]
Cyclooligocondensation of amino acids: macrocyclic amides of β-alanine (SC) 74 [G.E. 79]
Cyclopentacyclononene, Facile ring enlargement of azulene to give the ~ system by dipolar cycloaddition (SC) 162 [G.E. 175]
Cyclopentadiene, Tricyclo[4.2.2.1^{2,5}]undeca-3,7,9-triene: the [4+4]cycloadduct of benzene and ~. Reaction sequence of its retrocleavage (SC) 224 [G.E. 254]
Intermolecular exchange of substituents via ions (ion pairs) in cyclopentadienyl- and cyclononatetraenyl-trimethylstannane (SC) 218 [G.E. 228]
Cyclopentannelating agent, (Bromoacetylmethylene)triphenylphosphorane—a novel ~ (SC) 940 [G.E. 1005]
Cyclopeptides, Boat conformation of cyclo-[L-Pro$_2$-D-Pro] 538 [G.E. 573]
Cyclophane, [2.2.2.2](1,2,3,4)-~ (SC) 329 [G.E. 336]
Cyclopropane, Bonding properties of ~ and their chemical consequences (FP) 809 [G.E. 867]
Cyclopropanediazonium ions, Stereochemistry of nucleophilic substitution at ~ (SC) 228 [G.E. 240]
Cyclopropenes, Vinyl ketenimines by nucleophilic ring cleavage of ~ with tert-butyl isocyanide (SC) 67 [G.E. 62]
Cyclopropenylium ions, Structure and formation of triorganylphosphonio-~ (SC) 472 [G.E. 505]
Cyclopropenylium salt, Synthesis of a donor-substituted tris(cyclopropenylio)-~ (SC) 473 [G.E. 506]
Cyclopropylalkadienes, Facile synthesis (SC) 231 [G.E. 239]
Cyclopropylidene, Carbene-carbene rearrangements of cis- and trans-2-(1,3-butadienyl)-~ (SC) 396 [G.E. 424]
Cyclopropylmethyl-cyclobutyl rearrangements, Multiple ~ in a pentaspirohexadecanol (SC) 868 [G.E. 927]
Cycloreversions, 1,3-Dipolar ~ (FP) 721 [G.E. 781]
Tricyclo[4.2.2.1^{2,5}]undeca-3,7,9-triene, the [4+4]-cycloadduct of benzene and cyclopentadiene. Reaction sequence of its retrocleavage (SC) 224 [G.E. 254]
cyclo-Triphosphorus ligand, [(triphos)Co(μ-P$_3$)Cr$_2$(CO)$_{10}$]: A trinuclear heterometal complex containing cyclo-triphosphorus as μ_3-ligand (SC) 81 [G.E. 93]
Cyclotristannatellurane, 2,2,4,4,6,6-Hexamethyl-~, a Sn$_3$Te$_3$-ring with C$_2$-symmetry (SC) 677 [G.E. 740]

DEFECT chemistry, Applications of SEPIL to the solid state ~ of fluorites and ultra-trace inorganic analysis (FP) 738 [G.E. 765]
Degradation kinetics, Effects of long-chain branches on the ~ of polymers (SC) 321 [G.E. 341]
Dehydrating agents, Competition in the three-component system triphenylphosphane/azo ester/3-hydroxy-carboxylic acid: OH- versus COOH-activation (SC) 622 [G.E. 654]
Deprotection, Oxidative removal of the benzyl ether protecting group by homogeneous electron transfer (SC) 801 [G.E. 850]
Selective ~ of primary and secondary hydroxy functions by homogeneous electron transfer (SC) 802 [G.E. 851]
Desorption, Kinetics of sorption, ~, and diffusion in zeolites (FP) 266 [G.E. 309]
Deuteration, Selective ~ of enamines with deuterated formic acids (SC) 320 [G.E. 341]
Dianion and tetraanion of octalene (SC) 229 [G.E. 251]
Diastereomers, Extreme liquid chromatographic separation effects in the case of diastereomeric amides containing polar substituents (SC) 62 [G.E. 64]
Preparative scale directed resolution of enantiomeric carboxylic acids and lactones via liquid chromatography and neighboring-group assisted hydrolysis of diastereomeric amides (SC) 63 [G.E. 65]
Preparative scale directed resolution of enantiomeric amines via liquid chromatography of diastereomeric 4-hydroxybutyramides (SC) 65 [G.E. 66]
1H-1,2,3σ^2-Diazaphospholes—bond delocalization in σ^2-phospholes (SC) 413 [G.E. 442]
Diazoacetyl chloride, Synthesis and reactions—detection of diazoketene (SC) 947 [G.E. 1012]
α-Diazo carbonyl compounds, Cycloadditions to enamines (SC) 330 [G.E. 346]
1,4-Diazocine, 1,4-Dihydro-~ and N,N′-disubstitution products—a rational synthesis (SC) 962 [G.E. 1028]
1,4-Dihydro-~; N-substitution and structure ("aromaticity") (SC) 964 [G.E. 1030]
Diazo compounds, Cycloadditions of α-diazo carbonyl compounds to enamines (SC) 330 [G.E. 346]
Chemistry of functional groups. The chemistry of diazonium and diazo groups (Book Review) 804
Diazoketene, Synthesis and reactions of diazoacetyl chloride—detection of ~ (SC) 947 [G.E. 1012]
(Diazomethyl)cyclopropenes—synthesis, isomerization, and carbene reactions (SC) 531 [G.E. 566]
Diazonium ions, Chemistry of functional groups. The chemistry of diazonium and diazo groups (Book Review) 804
Diazonium salts, Alkene-~: a new chapter of classical organic chemistry (FP) 259 [G.E. 279]
Thermolysis of arenediazonium pentacarbonylcyano-6A-metalates in various media: a route to novel α-functionalized isocyanides (SC) 75 [G.E. 80]
α,α-Dichloroamines, Synthesis and intramolecular 1,3 Cl,H disproportionation of ethyl 2,2-dichloro-2-(dimethylamino)acetate (SC) 615 [G.E. 650]
Dicyanophosphide ion, Structure of the ~ in a crown-ether sodium salt (SC) 934 [G.E. 998]
Dicyclobuta[b,e]pyridine, 1,2,4,5-Tetrahydro-~ (SC) 411 [G.E. 440]
Dienynyl trifluoromethanesulfonate, Formation of phenyl cations in the solvolysis of a ~ (SC) 870 [G.E. 928]
1-(Diethylamino)propyne, Surprising transformation of azulene by cycloaddition with ~ (SC) 161 [G.E. 173]
Diffusion, Kinetics of sorption, desorption, and ~ in zeolites (FP) 266 [G.E. 309]
1,4-Dihydro-1,4-diazocine, ~ and N,N′-disubstitution products—a rational synthesis (SC) 962 [G.E. 1028]
~; N-substitution and structure ("aromaticity") (SC) 964 [G.E. 1030]
1,2-Dihydro-4,6-dimethyl-2-thioxo-3-pyridinecarbonitrile, Ester and lactone formation with the reagent ~ (SC) 308 [G.E. 330]
1,8a-Dihydroindolizines as components of novel photochromic systems (SC) 945 [G.E. 1010]
1,4-Dihydronicotinic acid, Synthesis of ~ derivatives by photochemical cycloaddition (SC) 540 [G.E. 575]
Dihydropyranones, Novel highly stereoselective rearrangements of chiral ~ (SC) 936 [G.E. 1001]
Dihydropyrene, 8,16-Methano[2.2]metacyclophane-1,9-diene. A valence isomer of 10b,10c-methano-cis-10b,10c-~ (SC) 946 [G.E. 1011]
Dihydropyridines, Metalation of pyrans and ~: when is an 8π-system cost effective? (SC) 489 [G.E. 515]
1,8-Dihydroxyanthraquinone, Mono- and bis(η^3-allylnickel) derivatives of ~ and of some 1,3,5-triketones (SC) 681 [G.E. 742]
α,α′-Dihydroxy ketones, Lactide contraction—a method for the synthesis of ~ from α-hydroxy carboxylic acids (SC) 310 [G.E. 329]
1,2-Dioxetanes, A 3-imino-1,2-dioxetane via singlet oxygenation of a ketenimine (SC) 788 [G.E. 855]
Diradical hybridization, Polar [4+2]- and [4+4]-photocycloadditions: effects of hybridization in diradicals (SC) 881 [G.E. 943]
Diradicals, First spectroscopic detection of ~ in photocycloreversions (SC) 215 [G.E. 232]
Disaccharides, Facile, high selective synthesis of α- and β-~ from 1-O-metalated D-ribofuranoses (SC) 466 [G.E. 497]
Disulfide bridges, Fully active insulin by selective formation of the ~ between a synthetic A-chain and natural B-chain (SC) 536 [G.E. 571]
η-Disulfido complexes, Generation of the triangulo-group Mo^V-η-S$_2$ in the "condensation" of [Mo^{VI}O$_2$S$_2$]$^{2-}$ to [Mo$^V_2$O$_2$S$_2$(S$_2$)$_2$]$^{2-}$ (SC) 530 [G.E. 565]
1,3-Di-tert-butylcyclooctatetraene (SC) 544 [G.E. 578]
1,3-Dithiane 1-oxides, Facile regeneration of carbonyl compounds from ~ via 1-ethoxy-1,3-dithianium salts (SC) 165 [G.E. 179]
1,3-Dithianium salts, Facile regeneration of carbonyl compounds from 1,3-dithiane 1-oxides via 1-ethoxy-~ (SC) 165 [G.E. 179]
Dithiiranes and thiosulfines as reactive intermediates (SC) 941 [G.E. 1006]
Dithiocarboxylato-metal complexes, CS$_2$- and CS$_3$-bridged transition metal complexes—directed synthesis of metallo-~ (SC) 626 [G.E. 661]
Dithionite formation, The double salt Na$_2$S$_2$O$_5$·NaOOCH as intermediate in sodium ~ by reduction of SO$_2$ with sodium formate (SC) 313 [G.E. 333]
Dithiophosphato complex, (−)$_{579}$-Bis[(S)-(+)-O,O′(1,1′-binaphthyl-2,2′-diyl)dithiophosphato]nickel(II)—The first ~ to have axial chirality (SC) 415 [G.E. 448]
Donor-acceptor approach to molecular interactions (Book Review) 560
Double bond, Synchronous mechanism of the 1,1-cycloaddition of nitrile ylides to C=C ~-s (SC) 167 [G.E. 168]
Mesityl(diphenylmethylene)arsane (SC) 395 [G.E. 423]

ELECTROCHEMISTRY, Selective electrochemical removal of protecting groups in nucleotide synthesis (SC) 148 [G.E. 155]
Model system for the electrochemical reduction of the carbon-halogen bond (SC) 938 [G.E. 1002]

Transient techniques in ~ (Book Review) 334
Electrolytes, Solid ~. General principles, characterization, materials, applications (Book Review) 884
Electronic effects, Separation of steric and ~ in the reaction enthalpies of association of phosphorus ligands (SC) 401 [G.E. 429]
Electronic structure of μ-methylenetransition metal complexes (SC) 554 [G.E. 591]
Electron transfer, Oxidative removal of the benzyl ether protecting group by homogeneous ~ (SC) 801 [G.E. 850]
Selective deprotection of primary and secondary hydroxy functions by homogeneous ~ (SC) 802 [G.E. 802]
(S)-Elenolide, Use of biogenetic key compounds for the biomimetic synthesis of natural products. ~ from secologanin (SC) 539 [G.E. 574]
Emissions, Rates of reactive removal of anthropogenic ~ in the atmosphere (FP) 663 [G.E. 707]
Enamines, Selective deuteration of ~ with deuterated formic acids (SC) 320 [G.E. 341]
Cycloadditions of α-diazo carbonyl compounds to ~ (SC) 330 [G.E. 346]
[3+2]-Cycloadditions of azoalkenes to ~—"criss-cross" cycloadditions to azoalkenes (SC) 695 [G.E. 756]
α-Aminoaldehydes from ~ and chloramine-T (SC) 933 [G.E. 997]
Enaminosulfonium salts, Morpholino(succinimido)bicyclo[n.1.0]alkanes from ~ (SC) 800 [G.E. 861]
Enantiomers, Preparative scale directed resolution of enantiomeric carboxylic acids and lactones via liquid chromatography and neighboring-group assisted hydrolysis of diastereomeric amides (SC) 63 [G.E. 65]
Preparative scale directed resolution of enantiomeric amines via liquid chromatography of diastereomeric 4-hydroxybutyramides (SC) 65 [G.E. 66]
Enantioselective oxidation by a chiral acylaminyl oxide (SC) 864 [G.E. 923]
Enantioselective synthesis of α-methyl-α-aminocarboxylic acids by alkylation of the lactim ether of cyclo-(L-Ala-L-Ala) (SC) 863 [G.E. 922]
Encyclopedia of chemical technology: Kirk-Othmer (Book Review) 237, 491, 704
Ene reactions, Intermolecular ~ in a high-pressure/high-temperature flow apparatus (SC) 70 [G.E. 74]
Thermal pericyclic reaction between alkynes and alkanes (SC) 71 [G.E. 75]
Energy storage, Criteria for the efficiency, stability, and capacity of abiotic photochemical solar ~ systems (FP) 652 [G.E. 696]
Enols, Acidity of acetophenone enol in aqueous solution (SC) 617 [G.E. 652]
β,γ-Enoximes, Ring-opening of 5-(bromomethyl)-2-isoxazolines to ~—a new principle for the γ-substitution of allyl bromides by α-functionalized alkyl groups (SC) 78 [G.E. 91]
Epoxidation, Asymmetric ~ of simple olefins with an optically active molybdenum(VI) peroxo complex (SC) 485 [G.E. 511]
ESR spectroscopy, Detection of heavy metal ions by ~ (SC) 943 [G.E. 1007]
Ester formation and lactone formation with the reagent 1,2-dihydro-4,6-dimethyl-2-thioxo-3-pyridinecarbonitrile (SC) 308 [G.E. 330]
Ethylene, Nickel(0)-induced synthesis of ethyllithium from lithium, hydrogen, and ~ (SC) 488 [G.E. 521]
Ethylenehydridometal complex, An example of the equilibrium ~ ⇌ ethylmetal complex (SC) 157 [G.E. 171]
Ethylmetal complex, An example of the equilibrium ethylene-hydridometal ⇌ ~ complex (SC) 157 [G.E. 171]
Explosion, Detonation of benzyl(triethyl)ammonium permanganate (SC) 786 [G.E. 852]
Stability of benzyl(triethyl)ammonium permanganate (SC) 787 [G.E. 852]

FERROCENE, Phase transfer catalyzed synthesis of ~ derivatives (SC) 792 [G.E. 858]
α-Ferrocenylalkylamines, One-pot syntheses ~ (SC) 956 [G.E. 1023]
Fischer-Tropsch synthesis, Catalytic alkylation of benzene with CO and H_2: A homogeneously catalyzed Fischer-Tropsch synthesis (SC) 77 [G.E. 83]
Flash thermolysis, Fragmentation of γ-hydroxyammonium compounds to unsaturated aldehydes by ~ (SC) 541 [G.E. 576]
Flash vacuum thermolysis of doubly unsaturated acyl halides to give phenols (SC) 170 [G.E. 163]
Flavines, Thermal generation of pteridines and ~ from amino acid mixtures (SC) 478 [G.E. 510]
Fluctuating ring size, Crown ethers with ~ ("breathing crown ethers") (SC) 311 [G.E. 331]
Fluorenone, Structure of the primary adduct of a phosphorus ylide and ~ (SC) 876 [G.E. 945]
Fluorides, Structural chemistry of ~ and oxide fluorides of nonmetals (FP) 186 [G.E. 199]
Fluorination, Diarylsulfur(VI) oxide difluoride by direct ~ of sulfoxides (SC) 880 [G.E. 941]
Fluorine compounds, Stable coordination compounds of "thiazyl fluoride": structure of $[Co(NSF)_6]^{2+}$ in the crystal (SC) 231 [G.E. 253]
Structure and reactions of methylenesulfur tetrafluoride (SC) 944 [G.E. 1008]
Fluorites, Applications of SEPIL to the solid state defect chemistry of ~ and ultra-trace inorganic analysis (FP) 738 [G.E. 765]
Fluorotellurates, $Xe(OTeF_5)_6$, a deep-colored noble gas compound, and $O{=}Xe(OTeF_5)_4$—the existence of $Kr(OTeF_5)_2$ (SC) 66 [G.E. 62]
Fluxional bonds, First 1,3,4,6-tetraphospha-1,5-hexadiene, a molecule with ~ (identical tetraphospha Cope rearrangement) and configurational isomerism (SC) 873 [G.E. 936]
Formaldehyde, Regioselective alkylation of 1,4,5-trihydroxy-9,10-anthraquinone with ~ and glyoxylic acid (SC) 621 [G.E. 658]
Formamides, Carbonylation of lithium monoalkylamides to give N-lithio(alkyl)formamides (SC) 85 [G.E. 72]
Formic acids, Selective deuteration of enamines with deuterated ~ (SC) 320 [G.E. 341]
Formic anhydride, (SC) 614 [G.E. 649]
ω-Formyl-carboxylic acids, ω-Formyl- and 4-oxocarboxylic acids in blood plasma (SC) 305 [G.E. 328]
Fragmentation, A fragmentational approach to macrolides: (5-E, 8-Z)-6-methyl-5,8-undecadien-11-olide (SC) 634 [G.E. 670]
Free-radical additions, Reversal of the selectivity principle in ~ to alkenes (SC) 154 [G.E. 167]
Fuels, Liquid ~ from coal (Book Review) 87
Functional groups, Direct removal of ~ by catalytic hydrogenolysis (SC) 939 [G.E. 1004]
Furan, Metalated 2-alkynyl- and 1,2-alkadienyl 2-tetrahydropyranyl ethers: versatile building blocks for ~ syntheses (SC) 875 [G.E. 938]

GAMMA rays, The ~ of the radionuclides (Book Review) 703
Gas chromatography with glass capillary columns (Book Review) 237
Geissoschizine, Thermodynamically controlled stereoselective synthesis (SC) 862 [G.E. 921]
Gels, Spatial structure formation in protein ~ (FP) 599 [G.E. 634]
Germanium phthalocyanines, trans-Bis(1-alkynyl)-4B-metal ~ (SC) 322 [G.E. 343]
Glycals, Novel ~ as synthons for saccharide syntheses (SC) 222 [G.E. 242]
β-Glycosides, Preferred β-glycoside formation by phase transfer catalysis in the synthesis of D-arabinofuranosyl-7-deazapurine nucleosides (SC) 536 [G.E. 570]
Gold compounds, Existence and bond energy of the cesium auride molecule (SC) 629 [G.E. 664]
Graphs, Nodal nomenclature—general principles (FP) 887 [G.E. 951]

HALF-SANDWICH complexes, η^5-Cyclopentadienyl(trinitrosyl)vanadium hexafluorophosphate, $[CpV(NO)_3]PF_6$ (SC) 220 [G.E. 241]
Halogenated carboxylic esters, New synthesis of amino acids from ~ (SC) 474 [G.E. 504]
Halogen compounds, Model system for the electrochemical reduction of the carbon-halogen bond (SC) 938 [G.E. 1002]
Heavy metal ions, Detection by ESR spectroscopy (SC) 943 [G.E. 1007]
Heptalene, An expeditious synthesis of ~ from naphthalene via a bis(bicyclo-[1.1.0]butane) intermediate (SC) 546 [G.E. 581]
Heptalenebis(tricarbonyliron) (SC) 545 [G.E. 579]
2,4,6-Heptanetrithionediate, Bis(η^3-allylnickel) 2,4,6-heptanetrithionediate (SC) 683 [G.E. 744]
Heteroaromatic compounds, From the principle of areno-analogy to heterocyclopolyaromatic compounds (FP) 1 [G.E. 1]
Heterocyclopolyaromatic compounds, From the principle of areno-analogy to ~ (FP) 1 [G.E. 1]
Heterometal cluster, Reversible opening of a trinuclear ~ (SC) 76 [G.E. 82]
Hexachloroantimonate, Tris(trichlorophosphoranediylamino)carbenium ~, $[C(NPCl_3)_3]^+SbCl_6^-$ (SC) 693 [G.E. 735]
High-pressure liquid chromatography, Liquid column chromatography with chemical derivatizations after separation (FP) 180 [G.E. 192]
Hindered rotation at the triple bond (SC) 159 [G.E. 163]
Homoallyl alcohols, Diastereoselective synthesis of β-methyl ~ (SC) 306 [G.E. 329]
Homolysis, Anchimerically accelerated bond ~ (FP) 173 [G.E. 185]
σ-Homotropilidenes, endo-Hydroxytrioxatris-~ (SC) 611 [G.E. 646]
Hormones, Molecular structure of Phe^2-TRH, an analogue of thyrotropin-releasing hormone (SC) 225 [G.E. 243]
Hydrido complex, New cationic binuclear tri-~ containing one four- and one five-coordinate platinum atom (SC) 155 [G.E. 169]
An example of the equilibrium ethylenehydridometal ⇌ ethylmetal complex (SC) 157 [G.E. 171]
Hydrocarbons, Oxidation of ~ with benzyl(triethyl)ammonium permanganate (SC) 68 [G.E. 77]
Regio- and stereospecific hydroxylation of alicyclic ~ with substituted perbenzoic acids (SC) 407 [G.E. 438]
Hydrogen, Six-coordinate ~: structure of $[(Ph_3P)_2N]^+[HCo_6(CO)_{15}]^-$ by single-crystal neutron diffraction analysis (SC) 80 [G.E. 86]
Colloidal redox catalysts for evolution of oxygen and for light-induced evolution of ~ from water (SC) 624 [G.E. 659]
Cyclic cleavage of water into ~ and O_2 by visible light with coupled redox catalysts (SC) 701 [G.E. 759]
Hydrogenation, Asymmetric ~ of (Z)-α-(acetylamino)cinnamic acid by a Rh/norphos catalyst (SC) 620 [G.E. 655]
Complexes with chiral alkylcyclopentadienyl ligands for homogeneous catalytic asymmetric ~ of 2-phenyl-1-butene (SC) 779 [G.E. 842]

Hydrogen-chlorine exchange, Synthesis and intramolecular 1,3 Cl,H disproportionation of ethyl 2,2-dichloro-2-(dimethylamino)acetate (SC) 615 [G.E. 650]
Intramolecular Cl,H disproportionation of an oxamide chloride. An entry to imidazole derivatives (SC) 616 [G.E. 651]
Hydrogen formation, Catalysis of ~ from an organic radical in aqueous solution by colloidal silver (SC) 418 [G.E. 449]
Hydrogenolysis, Direct removal of functional groups by catalytic ~ (SC) 939 [G.E. 1004]
Hydrosilane, Catalytic conversion of aldehydes into higher α-siloxy aldehydes by ~ and carbon monoxide (SC) 393 [G.E. 421]
Catalytic reactions with ~ and carbon monoxide (FP) 837 [G.E. 896]
α-Hydroxy carboxylic acids, Lactide contraction—a method for the synthesis of α,α'-dihydroxy ketones from ~ (SC) 310 [G.E. 329]
Hydroxylamido ligand, Synthesis of a hydroxylamido(2−)-O,N-(nitrosyl)molybdenum complex (SC) 549 [G.E. 583]
γ-Hydroxyammonium compounds, Fragmentation to unsaturated aldehydes by flash thermolysis (SC) 541 [G.E. 576]
Hydroxy carboxylic acids, Competition in the three-component system triphenylphosphane/azo ester/β-~: OH- versus COOH-activation (SC) 622 [G.E. 654]
Hydroxy functions, Selective deprotection of primary and secondary ~ by homogeneous electron transfer (SC) 802 [G.E. 851]
Hydroxylamine, Reactions of molybdate(VI) with ~ and N-methyl-~ (SC) 548 [G.E. 582]
Hydroxylation, Regio- and stereospecific ~ of alicyclic hydrocarbons with substituted perbenzoic acids (SC) 407 [G.E. 438]
endo-Hydroxytrioxatris-σ-homotropilidenes (SC) 611 [G.E. 646]

IMIDAZOLE derivatives, Intramolecular Cl,H disproportionation of an oxamide chloride. An entry to ~ (SC) 616 [G.E. 651]
Imides, Homogeneous catalytic vinylation of cyclic ~ and lactams for the synthesis of N-vinyl monomers (SC) 533 [G.E. 568]
Iminocarbene/ketenimine rearrangement (SC) 320 [G.E. 337]
3-Imino-1,2-dioxetane via singlet oxygenation of a ketenimine (SC) 788 [G.E. 855]
Imino-sulfur compounds, Cyclodiaza-λ⁶-thianes—syntheses and structures (SC) 235 [G.E. 231]
Inclusion compounds, Krypton and xenon ~ of complex metal cyanides (SC) 486 [G.E. 517]
Indolizines, 1,8a-Dihydro-~ as components of novel photochromic systems (SC) 945 [G.E. 1010]
Infrared spectroscopy, Infrared and Raman spectroscopy (Book Review) 237
Infrared and Raman spectra of inorganic and coordination compounds (Book Review) 639
Insect pheromones, Isopropyl carboxylates—a new class of ~ (SC) 796 [G.E. 843]
Insulin, Fully active ~ by selective formation of the disulfide bridges between a synthetic A-chain and natural B-chain (SC) 536 [G.E. 571]
Interdiffusion, Thin films—~ and reactions (Book Review) 560
Interfacial phenomena, Surfactants and ~ (Book Review) 419
Intermolecular interactions: from diatomics to biopolymers (Book Review) 418
Inversion, Internal rotation and ~. An introduction to large amplitude motions in molecules (Book Review) 419
Iodine azide, Chemistry of ~ (FP) 507 [G.E. 527]
Iodine compounds, Synthesis and properties of tetrabutylammonium octaiododirhenate(III), $[(n\text{-}C_4H_9)_4N]_2[Re_2I_8]$ (SC) 150 [G.E. 159]
Iodotrimethylsilane, Hexamethyldisilane/iodine: convenient in situ generation of ~ (SC) 612 [G.E. 648]
Ring-opening of lactones and cyclic carbonates with bromomethylsilane or ~ (SC) 689 [G.E. 749]
Ion cyclotron resonance studies on tert-butyl, 2-norbornyl, and 1- and 2-adamantyl cations (SC) 951 [G.E. 1018]
Ion pairs, Intermolecular exchange of substituents via ions (~) in cyclopentadienyl- and cyclononatetraenyl-trimethylstannane (SC) 218 [G.E. 228]
Iron complexes, Simple route to Li- or Zn-metalated η^5-cyclopentadienyliron-olefin complexes (SC) 549 [G.E. 590]
Tetrakis(ethylene)irondilithium and bis(η^4-1,5-cyclooctadiene)irondilithium (SC) 550 [G.E. 590]
Experiments on the HOMO-LUMO nature of metal-metal bonds (SC) 690 [G.E. 751]
New pathways to trinuclear complexes—structure of the tetradecker sandwich complex bis(η-thiadiborolenecobalt-μ,η-thiadiborolene)iron (SC) 949 [G.E. 1014]
Iron compounds, $FeCoMoWS(AsMe_2)Cp_2(CO)_7$: The first cluster to contain four different metal atoms (SC) 531 [G.E. 566]
Synthesis of metallacycles with reactive metal-carbon σ bonds (SC) 535 [G.E. 569]
Heptalenebis(tricarbonyliron) (SC) 545 [G.E. 579]
Island structure, Co^{II} with coordination number 3: $Na_4[CoO_3]$—the first oxocobaltate(II) with an ~ (SC) 542 [G.E. 577]
Isoadenylate, Directed synthesis of the trimeric ~ A2'p5'A2'p5'A (SC) 942 [G.E. 1007]
Isopropyl carboxylates, A new class of insect pheromones (SC) 796 [G.E. 843]
Isobacteriochlorin, Synthetic approach to the ~ macrocycle (SC) 675 [G.E. 752]
Isocyanates, α,β-Unsaturated ~ by thermolysis of N-(1-alkenyl)-N-alkylcarbamoyl chlorides (SC) 319 [G.E. 334]
Isocyanides, Vinyl ketenimines by nucleophilic ring cleavage of cyclopropenes with tert-butyl isocyanide (SC) 67 [G.E. 62]
Thermolysis of arenediazonium pentacarbonylcyano-6A-metalates in various media: a route to novel α-functionalized ~ (SC) 75 [G.E. 80]
Isoprene dimerization, Homogeneously catalyzed ~ to 2,7-dimethyl-2,trans-4,6-octatriene at chromium (SC) 324 [G.E. 344]
2-Isoxazolines, Ring-opening of 5-(bromomethyl)-~ to β,γ-enoximes—a new principle for the γ-substitution of allyl bromides by α-functionalized alkyl groups (SC) 78 [G.E. 91]

KEKULÉ, August ~—The architect of chemistry. Commemorating the 150th anniversary of his birth (FP) 641 [G.E. 685]
Kekulene, Molecular structure and spectroscopic properties of ~ (SC) 699 [G.E. 733]
Ketenes, Preparation of stable vinyl-~ by metal complex-induced olefination and carbonylation of alkynes (SC) 954 [G.E. 1021]
Ketenimine, Vinyl-~-s by nucleophilic ring cleavage of cyclopropenes with tert-butyl isocyanide (SC) 67 [G.E. 62]
Iminocarbene/~ rearrangement (SC) 320 [G.E. 337]
3-Imino-1,2-dioxetane via singlet oxygenation of a ~ (SC) 788 [G.E. 855]
Ketoacetal esters, Steric course of the reduction of ~ with alkali metals in liquid ammonia (SC) 637 [G.E. 673]
Ketones, Lactide contraction—a method for the synthesis of α,α'-dihydroxy ~ from α-hydroxy carboxylic acids (SC) 310 [G.E. 329]
Asymmetric synthesis of ant alarm pheromones—α-alkylation of acyclic ~ with almost complete asymmetric induction (SC) 397 [G.E. 425]
Key building blocks of natural product biosynthesis and their significance in chemistry and medicine (FP) 429 [G.E. 453]
Kinetics, Principles of chemical ~ (Book Review) 559
Chemical ~ and transport (Book Review) 885
Krypton and xenon inclusion compounds of complex metal cyanides (SC) 486 [G.E. 517]
Krypton compounds, $Xe(OTeF_5)_6$, a deep-colored noble gas compound, and $O{=}Xe(OTeF_5)_4$—the existence of $Kr(OTeF_5)_2$ (SC) 66 [G.E. 68]

LACTAMS, Homogeneous catalytic vinylation of cyclic imides and ~ for the synthesis of N-vinyl monomers (SC) 533 [G.E. 568]
Thermodynamically controlled stereoselective synthesis of geissoschizine (SC) 862 [G.E. 921]
Lactide contraction—a method for the synthesis of α,α'-dihydroxy ketones from α-hydroxy carboxylic acids (SC) 310 [G.E. 329]
Lactim ether, Enantioselective synthesis of α-methyl-α-aminocarboxylic acids by alkylation of the ~ of cyclo-(L-Ala-L-Ala) (SC) 863 [G.E. 922]
Lactone formation, Ester formation and ~ with the reagent 1,2-dihydro-4,6-dimethyl-2-thioxo-3-pyridinecarbonitrile (SC) 308 [G.E. 330]
Lactones, Preparative scale directed resolution of enantiomeric carboxylic acids and ~ via liquid chromatography and neighboring-group assisted hydrolysis of diastereomeric amides (SC) 63 [G.E. 65]
Ring-opening of ~ and cyclic carbonates with bromo- or iodotrimethylsilane (SC) 689 [G.E. 749]
Stereospecific synthesis of γ-~ by dyotropic Wagner-Meerwein rearrangement (SC) 793 [G.E. 840]
Lasalocid, ^{23}Na-NMR study of the competition of biogenic amines with sodium ion for binding to ~ (X-527 A) (SC) 153 [G.E. 166]
Laser chemistry, Megawatt infrared ~ (Book Review) 639
Lewis acid, Stepwise addition of a ~ and a Lewis base to a metal-metal bond (SC) 158 [G.E. 172]
Lewis base, Stepwise addition of a Lewis acid and a ~ to a metal-metal bond (SC) 158 [G.E. 172]
Ligand concentration-control in the system nickel(0)/triphenylphosphane/butadiene (SC) 400 [G.E. 428]
Ligands, Multidentate acyclic neutral ~ and their complexation (FP) 753 [G.E. 813]
Linear free-energy relationships, Empirical parameters of solvent polarity as ~ (FP) 98 [G.E. 119]
Lipids, Synthesis and biosynthesis of alkoxy-~ (FP) 493 [G.E. 550]
Liquid chromatography, Liquid column chromatography with chemical derivatizations after separation (FP) 180 [G.E. 192]
Liquids, Model of simple ~ (FP) 350 [G.E. 408]
α-Lithioacetic acid esters, Reaction with succinic anhydrides (SC) 632 [G.E. 656]
Lithiocarbenoids, Direct ^{13}C-NMR spectroscopic observation of cyclopropylidene bromo-~ (SC) 784 [G.E. 844]
Lithium, Nickel(0)-induced synthesis of ethyl-~ from ~, hydrogen, and ethylene (SC) 488 [G.E. 521]
Lithium compounds, Tetrakis(ethylene)irondilithium and Bis(η^4-1,5-cyclooctadiene)irondilithium (SC) 550 [G.E. 590]
^{13}C-NMR spectra of tribromomethyllithium and 1,1-dibromoethyllithium (SC) 785 [G.E. 845]
Lithium dialkylamides, Carbonylation to give carbamoyllithiums (SC) 83 [G.E. 73]
Lithium monoalkylamides, Carbonylation to give N-lithio(alkyl)formamides (SC) 85 [G.E. 72]

Lithium-nickel polynuclear complex, New ~: $Ni(C_{12}H_{17}NiLi)_2(THF)_4$ (SC) 487 [G.E. 520]

MACROLIDES, Fragmentational approach to ~: (5-E, 8-Z)-6-methyl-5,8-undecadien-11-olide (SC) 634 [G.E. 670]
Fragmentational approach to ~: (5-E, 9-E)-6-methyl-5,9-undecadien-11-olide (SC) 636 [G.E. 672]
Maleic anhydride, Radical complexes of palladium and platinum with bisphosphane derivatives of ~ (SC) 677 [G.E. 754]
Manganese compounds, Manganese-containing heterocycles having a λ^4-thia-λ^5-phosphanorbornadiene skeleton (SC) 534 [G.E. 568]
Synthesis of metallacycles with reactive metal-carbon σ bonds (SC) 535 [G.E. 569]
Synthesis and crystal structure of a chiral complex containing a non-linear heterotrimetal chain: $PtMn_2(\mu_2\text{-}PPh_2)_2(CO)_9$ (SC) 797 [G.E. 859]
Mass spectrometry, Chemistry of isolated cations (FP) 451 [G.E. 484]
Mast cell degranulating peptide, Synthesis of ~ from bee venom (SC) 147 [G.E. 156]
MCD Peptide, Synthesis of ~ from bee venom (SC) 147 [G.E. 156]
Medical laboratory, Methodische Fortschritte im medizinischen Laboratorium (Book Review) 86
Membrane, Permeability of the outer ~ of bacteria (FP) 337 [G.E. 394]
Mesityl(diphenylmethylene)arsane (SC) 395 [G.E. 423]
Metal anions, Compounds of alkali ~ (FP) 587 [G.E. 613]
Metalation of pyrans and dihydropyridines: when is an 8π-system cost effective? (SC) 489 [G.E. 515]
Metal clusters, Reversible opening of a trinuclear hetero-~ (SC) 76 [G.E. 82]
Metallacycles, Synthesis of ~ with reactive metal-carbon σ bonds (SC) 535 [G.E. 569]
Metalloporphyrin containing carbyne-like carbido carbon: 5,10,15,20-Tetraphenylporphyrinato [bis(μ-carbidotricarbonylrhenium)]tin(IV) (SC) 83 [G.E. 85]
Metal-metal bond, Stepwise addition of a Lewis acid and a Lewis base to a ~ (SC) 158 [G.E. 172]
Novel titanium halides containing ~-s: Ti_7Cl_{16} and Ti_7Br_{16} (SC) 325 [G.E. 343]
An easily prepared, air-stable compound with a triple (MoMo) ~ (SC) 462 [G.E. 496]
Experiments on the HOMO-LUMO nature of ~-s (SC) 690 [G.E. 751]
Metathiophosphoric acid, Synthesis of a platinum complex with a derivative of monomeric ~ as η^2-ligand (SC) 953 [G.E. 1020]
8,16-Methano[2.2]metacyclophane-1,9-diene. A valence isomer of 10b,10c-methano-cis-10b,10c-dihydropyrene (SC) 946 [G.E. 1011]
Methionine, Enantioselective synthesis of the hydroxy-analogues of D- and L-~ (SC) 797 [G.E. 858]
7-Methylenebicyclo[2.2.2]octa-2,5-diene, Bicyclo[2.2.2]octa-5,7-diene-2-carboxylic acid and ~ (SC) 470 [G.E. 500]
5-Methylenecycloоctene, Mechanistic aspects of the palladium catalyzed cyclization of ~ (SC) 867 [G.E. 925]
Methylenesulfur tetrafluoride, Structure and reactions (SC) 944 [G.E. 1008]
μ-Methylene transition metal complexes, Electronic structure (SC) 554 [G.E. 591]
β-Methyl homoallyl alcohols, Diastereoselective synthesis (SC) 306 [G.E. 329]
Molecular interactions, The donor-acceptor approach to ~ (Book Review) 560
Molybdate, Reactions of ~-(VI) with hydroxylamine and N-methylhydroxylamine (SC) 548 [G.E. 582]
Molybdenum compounds, S_2^{2-} as simultaneous end-on and side-on bonded ligand in the novel transition-metal complex $[Mo_4(NO)_4S_{13}]^{4-}$ (SC) 168 [G.E. 158]
Oxidative addition to a quadruple bond. The complete X-ray structure of $[Mo_2Cl_8H]^{3-}$ (SC) 332 [G.E. 356]
An easily prepared, air-stable compound with a triple metal-to-metal (MoMo) bond (SC) 462 [G.E. 496]
Generation of the triangulo-group Mo^V-η-S_2 in the "condensation" of $[Mo^{VI}O_2S_2]^{2-}$ to $[Mo_2^{V}O_2S_2(S_2)_2]^{2-}$ (SC) 530 [G.E. 565]
$FeCoMoWS(AsMe_2)Cp_2(CO)_7$: The first cluster to contain four different metal atoms (SC) 531 [G.E. 566]
Synthesis of a hydroxylamido(2-)-O,N-(nitrosyl)molybdenum complex (SC) 549 [G.E. 583]
Synthesis and X-ray structure analysis of a Mo complex with η^2-coordinated benzaldehyde; transformation of a CO ligand by double α-addition (SC) 861 [G.E. 920]
Molybdenum(VI) peroxo complex, Asymmetric epoxidation of simple olefins with an optically active ~ (SC) 485 [G.E. 511]
Monolayer assemblies, Photochemical reactions of surfactant molecules in condensed ~—environment control and modification of reactivity (FP) 440 [G.E. 472]
Morpholino group as stereoindicator in aminobicyclo[4.1.0]heptanes (SC) 798 [G.E. 860]
Morpholino(succinimido)bicyclo[n.1.0]-alkanes from enaminosulfonium salts (SC) 800 [G.E. 861]
MO theory, Circular dichroism and absolute conformation: application of qualitative ~ to chiroptical phenomena (FP) 363 [G.E. 380]

NAPHTHALENE, An expeditious synthesis of heptalene from ~ via a bis(bicyclo-[1.1.0]butane) intermediate (SC) 546 [G.E. 581]
Naphthalene oxides, New entry to ~ (SC) 304 [G.E. 325]
Natural products, Key building blocks of natural product biosynthesis and their significance in chemistry and medicine (FP) 429 [G.E. 453]
Neurohypophysial hormones, Neurophysins: molecular and cellular aspects (FP) 846 [G.E. 905]
Neurophysins: molecular and cellular aspects (FP) 846 [G.E. 905]
Nickel catalysts, Ligand concentration-control in the system nickel(0)/triphenylphosphane/butadiene (SC) 400 [G.E. 428]
Nickel complexes, $(-)_{579}$-Bis[(S)-(+)-O,O'(1,1'-binaphthyl-2,2'-diyl)dithiophosphato]nickel(II)—The first dithiophosphato complex to have axial chirality (SC) 415 [G.E. 448]
Tetrahedro-tetraphosphorus as monodentate ligand in a nickel(0) complex (SC) 469 [G.E. 510]
Mono- and bis(η^3-allylnickel) derivatives of 1,8-dihydroxyanthraquinone and of some 1,3,5-triketones (SC) 681 [G.E. 742]
Bis(η^3-allylnickel) 2,4,6-heptanetrithionediate (SC) 683 [G.E. 744]
Nickel-olefin complexes, New lithium-nickel polynuclear complex: $Ni(C_{12}H_{17}NiLi)_2(THF)_4$ (SC) 487 [G.E. 520]
Nickel(0)-induced synthesis of ethyllithium from lithium, hydrogen, and ethylene (SC) 488 [G.E. 521]
Nitrenes, Developments in arylnitrene chemistry: syntheses and mechanisms (FP) 900 [G.E. 965]
Nitrile ylides, Synchronous mechanism of the 1,1-cycloaddition of ~ to C=C double bonds (SC) 167 [G.E. 168]
Nitrogen complexes, Photochemical behavior of ~: photoluminescence of trans-$(N_2)_2W(diphos)_2$ and trans-$(CO)_2W(diphos)_2$ (SC) 328 [G.E. 335]
Nitrogen compounds, Structure and bonding in cyclic sulfur-nitrogen compounds (FP) 101 [G.E. 112]
SN ring with di-, tri-, and tetra-coordinated sulfur atoms by nucleophilic substitution (SC) 415 [G.E. 444]
$S_5N_6(CH_2)_4$—the first spirocyclic 1'λ^6-thiacyclopentane derivative of a sulfur-nitrogen compound (SC) 780 [G.E. 846]
Nitrogen-sulfur compounds, Cyclodiaza-λ^6-thianes—syntheses and structures (SC) 235 [G.E. 231]
Nitrogen-sulfur-fluorine compound, Stable coordination compounds of "thiazyl fluoride": structure of $[Co(NSF)_6]^{2+}$ in the crystal (SC) 231 [G.E. 253]
Nitrogen ylides, Synthesis of a Zeise salt derivative with a phosphorus-nitrogen ylide as chelate ligand (SC) 234 [G.E. 238]
Nitrosylated metal cations, η^5-Cyclopentadienyl(trinitrosyl)vanadium hexafluorophosphate, $[CpV(NO)_3]PF_6$ (SC) 220 [G.E. 241]
Nitrosyl ligands, η^5-Cyclopentadienylchromium complexes with thiocarbonyl ligands and ~ (SC) 631 [G.E. 662]
Nitroxides, Enantioselective oxidation by a chiral acylaminyl oxide (SC) 864 [G.E. 923]
NMR spectroscopy, Direct ^{13}C-NMR spectroscopic observation of cyclopropylidene bromolithiocarbenoids (SC) 784 [G.E. 844]
^{13}C-NMR spectra of tribromomethyllithium and 1,1-dibromoethyllithium (SC) 785 [G.E. 845]
Nodal nomenclature—general principles (FP) 887 [G.E. 951]
Nomenclature, Nodal ~—general principles (FP) 887 [G.E. 951]
Nucleophilic substitution, Stereochemistry of ~ at cyclopropanediazonium ions (SC) 228 [G.E. 240]
Nucleosides, Preferred β-glycoside formation by phase transfer catalysis in the synthesis of D-arabinofuranosyl-7-deazapurine ~ (SC) 536 [G.E. 570]
Nucleotide synthesis, Selective electrochemical removal of protecting groups in ~ (SC) 148 [G.E. 155]

OCTAIODODIRHENATE(III), Synthesis and properties of tetrabutylammonium ~, $[(n\text{-}C_4H_9)_4N]_2[Re_2I_8]$ (SC) 150 [G.E. 159]
Octalene, Dianion and tetraanion of ~ (SC) 229 [G.E. 251]
Octatriene, Homogeneously catalyzed dimerization of isoprene to 2,7-dimethyl-2,trans-4,6-~ at chromium (SC) 324 [G.E. 344]
Olefination, Preparation of stable vinylketenes by metal complex-induced ~ and carbonylation of alkynes (SC) 954 [G.E. 1021]
Olefins, Polycyclic azoalkanes via dipolar cycloaddition of 4-phenyl-1,2,4-triazoline-3,5-dione with strained bicyclic ~ (SC) 468 [G.E. 512]
Asymmetric epoxidation of simple ~ with an optically active molybdenum(VI) peroxo complex (SC) 485 [G.E. 511]
Metal complexes of Bredt ~: synthesis and structure of bicyclo[4.2.1]non-1(8)-ene-bis(triphenylphosphane)platinum(0) (SC) 685 [G.E. 746]
Cyclic systems by palladium-catalyzed oxidation of di-~ (SC) 866 [G.E. 924]
One-dimensional conductors, Highly conducting one-dimensional solids (Book Review) 884
Onium salts, New synthetic reactions based on the ~ of aza-arenes (FP) 707 [G.E. 798]
Optical materials, Plastics as ~ (FP) 49 [G.E. 52]
Orbital symmetry, A basis for ~ rules (FP) 377 [G.E. 363]
Organometallic chemistry, Organometallic mechanisms and catalysis (Book Review) 804
Orthocarbonic acid, Planar tetracoordinate silicon (SC) 553 [G.E. 588]
Ortho esters, Directed synthesis of acyl ~ (SC) 309 [G.E. 337]

Orthonitrate, Crystal structure of Na_3NO_4 (SC) 698 [G.E. 762]
Orthosilicic acid, Structure and reactivity of the orthocarbonic and ~ esters of pyrocatechol (SC) 551 [G.E. 587]
Planar tetracoordinate silicon (SC) 533 [G.E. 588]
Oxamide chloride, Intramolecular Cl,H disproportionation of an ~. An entry to imidazole derivatives (SC) 616 [G.E. 651]
Oxetanes, Unusually high asymmetric induction in photochemical formation (SC) 868 [G.E. 926]
Oxidation, ~ of hydrocarbons with benzyl(triethyl)ammonium permanganate (SC) 68 [G.E. 77]
~ of ethers with benzyl(triethyl)ammonium permanganate (SC) 69 [G.E. 78]
Cyclic systems by palladium-catalyzed ~ of diolefins (SC) 866 [G.E. 924]
Oxidative addition to a quadruple bond. The complete X-ray structure of $[Mo_2Cl_8H]^{3-}$ (SC) 332 [G.E. 356]
Oxidative elimination, Redox addition/elimination processes of cluster-bound ligands: ~ of CO from $Co_3(CO)_9C$—OH and reductive addition of acetylene to $Co_3(CO)_9H$ (SC) 619 [G.E. 657]
Oxide fluorides, Structural chemistry of fluorides and ~ of nonmetals (FP) 186 [G.E. 199]
4-Oxocarboxylic acids, ω-Formylcarboxylic acids and ~ in blood plasma (SC) 305 [G.E. 328]
Oxocobaltate(II), Co^{II} with coordination number 3: $Na_4[CoO_3]$—the first ~ with an island structure (SC) 542 [G.E. 577]
Oxygen, Cyclic cleavage of water into H_2 and ~ by visible light with coupled redox catalysts (SC) 701 [G.E. 759]
Oxygenation, A 3-imino-1,2-dioxetane via singlet ~ of a ketenimine (SC) 788 [G.E. 855]
Ozonation in organic chemistry (Book Review) 492

PALLADIUM complexes, Structural isomers of ~ of type $C_5H_5Pd(2\text{-}RC_3H_4)L$—A case of simultaneous π/σ and σ/π rearrangement of two organic ligands (SC) 416 [G.E. 447]
Radical complexes of palladium and platinum with bisphosphane derivatives of maleic anhydride (SC) 677 [G.E. 754]
ortho-Palladated complex of 2,5-diphenyl-1,6,6aλ⁴-trithiapentalene (SC) 684 [G.E. 745]
Cyclic systems by palladium-catalyzed oxidation of diolefins (SC) 866 [G.E. 924]
Mechanistic aspects of the palladium catalyzed cyclization of 5-methylenecyclooctene (SC) 867 [G.E. 925]
Synthesis and structural dynamics of bis(cyclopentadienyl)phosphane-~ (SC) 948 [G.E. 1013]
Pentaspirohexadecanol, Multiple cyclopropylmethyl-cyclobutyl rearrangements in a ~ (SC) 868 [G.E. 927]
Peptide antibiotics, Sequences of membrane-modifying peptide antibiotic trichotoxin A-40 (SC) 476 [G.E. 508]
Peptide protecting groups, Solubilizing acid-labile ~ (SC) 686 [G.E. 747]
Peptides, Boat conformation of cyclo-[L-Pro_2-D-Pro] (SC) 538 [G.E. 573]
Peptide synthesis, Synthesis of the mast cell degranulating (MCD) peptide from bee venom (SC) 147 [G.E. 156]
Synthesis of thymosin α_1, a polypeptide of the thymus (SC) 394 [G.E. 422]
Perbenzoic acids, Regio- and stereospecific hydroxylation of alicyclic hydrocarbons with substituted ~ (SC) 407 [G.E. 438]
Permanganate, Oxidation of hydrocarbons with benzyl(triethyl)ammonium ~ (SC) 68 [G.E. 77]
Oxidation of ethers with benzyl(triethyl)-ammonium ~ (SC) 69 [G.E. 78]
Detonation of benzyl(triethyl)ammonium ~ (SC) 786 [G.E. 852]
Stability of benzyl(triethyl)ammonium ~ (SC) 787 [G.E. 852]
Permeability of the outer membrane of bacteria (FP) 337 [G.E. 394]
pH values, pH-Wert-Berechnungen (Book Review) 703
Pharmaceutical chemistry, Einführung in die Pharmazeutische Chemie (Book Review) 334
Phase transfer catalysis, Preferred β-glycoside formation by ~ in the synthesis of D-arabinofuranosyl-7-deazapurine nucleosides (SC) 536 [G.E. 570]
Phase transfer catalyzed synthesis of ferrocene derivatives (SC) 792 [G.E. 858]
~ in organic chemistry (Book Review) 559
Phase transfer reagents, Long-chain alkylammonium ions as ~ for the synthesis of mixed-ligand complexes of the platinum metals (SC) 151 [G.E. 160]
Phenols, Flash vacuum thermolysis of doubly unsaturated acyl halides to give ~ (SC) 170 [G.E. 163]
Phenyl cations, Formation in the solvolysis of a dienynyl trifluoromethane sulfonate (SC) 870 [G.E. 928]
Pheromones, Asymmetric synthesis of ant alarm ~—α-alkylation of acyclic ketones with almost complete asymmetric induction (SC) 397 [G.E. 425]
Phosgene, Stepwise reaction of phenylbis(trimethylsilyl)phosphane with ~—isolation of a (phosphinomethylene)phosphane (SC) 469 [G.E. 497]
Phosphane, Ligand concentration-control in the system nickel(0)/triphenyl-~/butadiene (SC) 400 [G.E. 428]
Competition in the three-component system triphenyl-~/azo ester/3-hydroxy-carboxylic acid: OH- versus COOH-activation (SC) 622 [G.E. 654]
Synthesis, resolutions, and characterization of an amino-~ rotamer pair (SC) 679 [G.E. 741]
Novel polycyclic ~-s and arsanes: $P_{11}(SiMe_3)_3$ and $As_7(SiMe_3)_3$ (SC) 679 [G.E. 755]
Phosphanepalladium complexes, Synthesis and structural dynamics of bis(cyclopentadienyl)-~ (SC) 948 [G.E. 1013]
λ²-Phospholes, 1H-1,2,3λ²-diazophospholes—bond delocalization in ~ (SC) 413 [G.E. 442]
Phosphorane, Stabilization of an arsanediyl-~ (SC) 233 [G.E. 244]
(Bromoacetylmethylene)triphenyl-~—a novel cyclopentannelating agent (SC) 940 [G.E. 1005]
Phosphoranediylamino compounds, Tris(trichlorophosphoranediylamino)carbenium hexachloroantimonate, $[C(NPCl_3)_3]^+SbCl_6^-$ (SC) 693 [G.E. 735]
Phosphorus compounds, [(Triphos)Co(μ-P_3)$Cr_2(CO)_{10}$]: A trinuclear heterometal complex containing cyclo-triphosphorus as μ_3-ligand (SC) 81 [G.E. 93]
Bis(chlorophenylphosphoranediyl)methane (SC) 169 [G.E. 177]
Problem of the structure of carbodiphosphoranes, R_3PCPR_3: new aspects (SC) 408 [G.E. 437]
Cyanohalophosphates(III)-hypervalent anions containing λ⁵-phosphorus(III) (SC) 411 [G.E. 441]
Structure and formation of triorganylphosphoniocyclopropenylium ions (SC) 472 [G.E. 505]
Methylidynetris(dimethylphosphane) (SC) 484 [G.E. 518]
Radical complexes of palladium and platinum with bisphosphane derivatives of maleic anhydride (SC) 677 [G.E. 754]
Experiments on the HOMO-LUMO nature of metal-metal bonds (SC) 690 [G.E. 751]
Chemistry of the $H_3B(CH_3)_2P$ group: unusual properties of some simple reference compounds (SC) 781 [G.E. 847]
Synthesis and crystal structure of a salt containing the anion $[H_3B(CH_3)_2P{\cdots}CH{\cdots}P(CH_3)_2BH_3]^-$; precursors and related compounds (SC) 782 [G.E. 848]
The first 2,3,5,6-tetraphosphabicyclo[2.2.0]hexane (SC) 872 [G.E. 935]
First 1,3,4,6-tetraphospha-1,5-hexadiene, a molecule with fluxional bonds (identical tetraphospha Cope rearrangement) and configurational isomerism (SC) 873 [G.E. 936]
Five-coordinate tervalent phosphorus in the tricyanobromo- and -iodophosphate(III) ion (SC) 935 [G.E. 1000]
Phosphorus ligands, Separation of steric and electronic effects in the reaction enthalpies of association of phosphorus ligands (SC) 401 [G.E. 429]
Phosphorus-nitrogen ylide, Synthesis of a Zeise salt derivative with a ~ as chelate ligand (SC) 234 [G.E. 238]
Phosphorus ylide, A ~ with symmetrical resonance-stabilized sp^2-carbanion (SC) 484 [G.E. 519]
Structure of the primary adduct of a ~ and fluorenone (SC) 876 [G.E. 945]
Photochemical cycloaddition, Synthesis of 1,4-dihydronicotinic acid derivatives by ~ (SC) 540 [G.E. 575]
Photochemical reactions of surfactant molecules in condensed monolayer assemblies—environment control and modification of reactivity (FP) 440 [G.E. 472]
Photochemistry, Criteria for the efficiency, stability, and capacity of abiotic photochemical solar energy storage systems (FP) 652 [G.E. 696]
Characterization of short-lived photoproducts by pulse Raman spectroscopy (SC) 323 [G.E. 348]
Question of π*, n- and π*, π selective ~ of 2,4-cyclohexadienones (SC) 557 [G.E. 585]
Colloid redox catalysts for evolution of oxygen and for light-induced evolution of hydrogen from water (SC) 624 [G.E. 659]
Unusually high asymmetric induction in the photochemical formation of oxetane (SC) 868 [G.E. 926]
Photochromic systems, 1,8a-Dihydroindolizines as components of novel ~ (SC) 945 [G.E. 1010]
Photocycloadditions, Polar [4+2]- and [4+4]-~: effects of hybridization in diradicals (SC) 881 [G.E. 943]
Photocycloreversions, First spectroscopic detection of diradicals in ~ (SC) 215 [G.E. 232]
Photoelectron spectroscopy, Conformational analysis by ~ (FP) 826 [G.E. 885]
Photoluminescence, Photochemical behavior of N_2-complexes: ~ of trans-$(N_2)_2W(diphos)_2$ and trans-$(CO)_2W(diphos)_2$ (SC) 328 [G.E. 335]
Photoreactions, Adiabatic ~ of organic molecules (FP) 572 [G.E. 597]
Phthalocyanine, trans-Bis(1-alkynyl)-4B-metal ~-s (SC) 322 [G.E. 343]
Cobalt(I)-~ as vitamin B_{12s}-model: selectivity in reactions with electrophiles (SC) 794 [G.E. 841]
Plasmalogens, Synthesis and biosynthesis of alkoxylipids (FP) 493 [G.E. 550]
Plastics as optical materials (FP) 49 [G.E. 52]
Platinum complexes, Long-chain alkylammonium ions as phase transfer reagents for the synthesis of mixed-ligand complexes of the platinum metals (SC) 151 [G.E. 160]
New cationic binuclear trihydrido complex containing one four- and one five-coordinate platinum atom (SC) 155 [G.E. 169]
CS_2- and CS_3-bridged transition metal complexes—directed synthesis of metallodithiocarboxylato-metal complexes (SC) 626 [G.E. 661]
Radical complexes of palladium and platinum with bisphosphane derivatives of maleic anhydride (SC) 677 [G.E. 754]
Metal complexes of Bredt olefins: synthesis and structure of bicyclo[4.2.1]non-1(8)-enebis(triphenylphosphane)platinum(0) (SC) 685 [G.E. 746]

Synthesis and crystal structure of a chiral complex containing a non-linear heterotrimetal chain: $PtMn_2(\mu_2\text{-}PPh_2)_2(CO)_8$ (SC) 797 [G.E. 859]
Synthesis of a platinum complex with a derivative of monomeric metathiophosphoric acid as η^2-ligand (SC) 953 [G.E. 1020]
Polarity, Empirical parameters of solvent ~ as linear free-energy relationships (FP) 98 [G.E. 119]
Polyblends, Polymer alloys—their structure, morphology, and properties (FP) 273 [G.E. 286]
Polyethers, Multidentate acyclic neutral ligands and their complexation (FP) 753 [G.E. 813]
Spherical wrapping of a linear polyether around a cation—1,20-Bis(8-quinolyloxy)-3,6,9,12,15,18-hexaoxaeicosane·RbI (SC) 226 [G.E. 234]
S-shaped binuclear cation complex of a linear polyether: 1,5-Bis 2-[5-(2-nitrophenoxy)-3-oxapentyloxy]phenoxy-3-oxapentane · 2 KSCN (SC) 227 [G.E. 237]
Polymer alloys—their structure, morphology, and properties (FP) 273 [G.E. 286]
Polymer analysis, Hummel/Scholl: Atlas of polymer and plastics analysis (Book Review) 702
Polymers, Effects of long-chain branches on the degradation kinetics of ~ (SC) 321 [G.E. 341]
Inorganic ~ (Book Review) 559
Polysilanes, Homologous series of cyclic ~ from $(Me_2Si)_5$ to $(Me_2Si)_{35}$ (SC) 955 [G.E. 1022]
Potassium complexes, S-shaped binuclear cation complex of a linear polyether: 1,5-Bis-2-[5-(2-nitrophenoxy)-3-oxapentyloxy]phenoxy-3-oxapentane·2 KSCN (SC) 227 [G.E. 237]
Proline, Boat conformation of cyclo-[L-Pro_2-D-Pro] 538 [G.E. 573]
Propyne, Surprising transformation of azulene by cycloaddition with 1-(diethylamino)-~ (SC) 161 [G.E. 173]
Protecting groups, Selective electrochemical removal of ~ in nucleotide synthesis (SC) 148 [G.E. 155]
Solubilizing acid-labile peptide ~ (SC) 686 [G.E. 747]
Oxidative removal of the benzyl ether protecting group by homogeneous electron transfer (SC) 801 [G.E. 850]
Selective deprotection of primary and secondary hydroxy functions by homogeneous electron transfer (SC) 802 [G.E. 851]
Protein gels, Spatial structure formation in ~ (FP) 599 [G.E. 634]
Pteridines, Thermal generation of ~ and flavines from amino acid mixtures (SC) 478 [G.E. 510]
Pulse Raman spectroscopy, Characterization of short-lived photoproducts by ~ (SC) 323 [G.E. 348]
Pyrans, Metalation of ~ and dihydropyridines: when is an 8π-system cost effective? (SC) 489 [G.E. 515]
Pyridine-3-carbonitrile, Ester and lactone formation with the reagent 1,2-dihydro-4,6-dimethyl-2-thioxo-~ (SC) 308 [G.E. 330]
Pyridines, Regiospecific nucleophilic attack at the γ-position of 1-(2,6-dimethyl-4-oxo-1,4-dihydro-1-pyridyl)pyridinium compounds; novel synthesis of 4-substituted ~ (SC) 792 [G.E. 856]
Pyrocatechol, Structure and reactivity of the orthocarbonic and orthosilicic acid esters of ~ (SC) 551 [G.E. 587]
Planar tetracoordinate silicon (SC) 553 [G.E. 588]

QUADRUPLE bond, Oxidative addition to a ~. Complete X-ray structure of $[Mo_2Cl_8H]^{3-}$ (SC) 332 [G.E. 356]
Tetracarbanilanilidodichromium(II): A clue to the understanding of the CrCr ~ (SC) 874 [G.E. 937]
Quinazoline, N^2-(Trichlorovinyl)amidines—new 1,3-biselectrophilic reagents (SC) 333 [G.E. 355]

RADICAL complexes of palladium and platinum with bisphosphane derivatives of maleic anhydride (SC) 677 [G.E. 754]
Radical reactions, Anchimerically accelerated bond homolysis (FP) 173 [G.E. 185]
Radicals, Capto-dative substituent effects in syntheses with ~ and radicophiles (FP) 917 [G.E. 982]
Reversal of the selectivity principle in free-radical additions to alkenes (SC) 154 [G.E. 167]
First spectroscopic detection of di-~ in photocycloreversions (SC) 215 [G.E. 232]
Catalysis of hydrogen formation from an organic radical in aqueous solution by colloidal silver (SC) 418 [G.E. 449]
Enantioselective oxidation by a chiral acylaminyl oxide (SC) 864 [G.E. 923]
Polar [4+2]- and [4+4]-photocycloadditions: effects of hybridization in di-~ (SC) 881 [G.E. 943]
Radicophiles, Capto-dative substituent effects in syntheses with radicals and ~ (FP) 917 [G.E. 982]
Radionuclides, The gamma rays of the ~ (Book Review) 703
Raman spectroscopy, Characterization of short-lived photoproducts by pulse ~ (SC) 323 [G.E. 348]
Infrared and ~ (Book Review) 237
Infrared and Raman spectra of inorganic and coordination compounds (Book Review) 639
Reaction enthalpies, Separation of steric and electronic effects in the ~ of association of phosphorus ligands (SC) 401 [G.E. 429]
Reaction rates, A basis for orbital symmetry rules (FP) 377 [G.E. 363]
Reactivity Umpolung, Methods of ~ (FP) 239 [G.E. 259]
d^3-Reagent, Metalated allylurea with sterically protected carbonyl group as novel ~ (SC) 399 [G.E. 427]
Rearrangements, Stereochemistry of [2,3]sigmatropic ~ (FP) 563 [G.E. 625]
Thermal "walk"-~ in the bicyclo[2.1.0]pent-2-ene system (SC) 674 [G.E. 738]
Multiple cyclopropylmethyl-cyclobutyl ~ in a pentaspirohexadecanol (SC) 868 [G.E. 927]
Spontaneous rearrangement of a carbene-to a carbyne complex: C,Cr migration of a $Sn(C_6H_5)_3$ group (SC) 871 [G.E. 929]
Novel highly stereoselective ~ of chiral dihydropyranones (SC) 936 [G.E. 1001]
Redox addition/elimination processes of cluster-bond ligands: oxidative elimination of CO from $Co_3(CO)_9C$—OH and reductive addition of acetylene to $Co_3(CO)_9H$ (SC) 619 [G.E. 657]
Redox catalysts, Colloid ~ for evolution of oxygen and for light-induced evolution of hydrogen from water (SC) 624 [G.E. 659]
Cyclic cleavage of water into H_2 and O_2 by visible light with coupled ~ (SC) 701 [G.E. 759]
Reduction, Steric course of the ~ of ketoacetal esters with alkali metals in liquid ammonia (SC) 637 [G.E. 673]
Model system for the electrochemical ~ of the carbon-halogen bond (SC) 938 [G.E. 1002]
Reductive addition, Redox addition/elimination processes of cluster-bond ligands: oxidative elimination of CO from $Co_3(CO)_9C$—OH and ~ of acetylene to $Co_3(CO)_9H$ (SC) 619 [G.E. 657]
Regioselective alkylation of 1,4,5-trihydroxy-9,10-anthraquinone with formaldehyde and glyoxylic acid (SC) 621 [G.E. 658]
Regiospecific synthesis of disubstituted benzene derivatives (SC) 402 [G.E. 430]
Relaxation, Fundamentals of chemical ~ (Book Review) 171
Transient techniques in electrochemistry (Book Review) 334
Rhenium compounds, A metalloporphyrin containing carbyne-like carbido carbon: 5,10,15,20-Tetraphenylporphyrinato [bis(μ-carbidotricarbonylrhenium)]tin(IV) (SC) 83 [G.E. 85]
Synthesis and properties of tetrabutylammonium octaiododirhenate(III), $[(n\text{-}C_4H_9)_4N]_2[Re_2I_8]$ (SC) 150 [G.E. 159]
Synthesis of metallacycles with reactive metal-carbon σ bonds (SC) 535 [G.E. 569]
Rhodium complexes, Asymmetric hydrogenation of (Z)-α-(acetylamino)cinnamic acid by a Rh/norphos catalyst (SC) 620 [G.E. 655]
D-Ribofuranoses, Facile, highly selective synthesis of α- and β-disaccharides from 1-O-metalated ~ (SC) 466 [G.E. 497]
Ring enlargement, Facile ~ of azulene to give the cyclopentacyclononene system by dipolar cycloaddition (SC) 162 [G.E. 175]
Ring-opening, ~ of 5-(bromomethyl)-2-isoxazolines to β,γ-enoximes—a new principle for the γ-substitution of allyl bromides by α-functionalized alkyl groups (SC) 78 [G.E. 91]
~ of lactones and cyclic carbonates with bromo- or iodotrimethylsilane (SC) 689 [G.E. 749]
Rotamers, Synthesis, resolution, and characterization of an aminophosphane rotamer pair (SC) 679 [G.E. 741]
Rotation, Hindered ~ at the triple bond (SC) 159 [G.E. 163]
Internal ~ and inversion. An introduction to large amplitude motions in molecules (Book Review) 419
Rubidium compounds, Spherical wrapping of a linear polyether around a cation—1,20-Bis(8-quinolyloxy)-3,6,9,12,15,18-hexaoxaeicosane·RbI (SC) 226 [G.E. 234]

SACCHARIDE syntheses, Novel glycals as synthons for ~ (SC) 222 [G.E. 242]
Safety, Verordnung über gefährliche Arbeitsstoffe (Book Review) 236
Secologanin, Use of biogenetic key compounds for the biomimetic synthesis of natural products. (S)-Elenolide from ~ (SC) 539 [G.E. 574]
Selectivity, "Multi-loop crown ethers" with multiple ~ (SC) 219 [G.E. 230]
Selectivity principle, Reversal of ~ in free-radical additions to alkenes (SC) 154 [G.E. 167]
Selenium compounds, New synthesis of carbonyl selenide (SC) 691 [G.E. 760]
Reactions of carbonyl selenide with amines and aminoalcohols to produce ureas and carbamates (SC) 692 [G.E. 760]
Thiocarbonyl-metal complexes from CSSe (SC) 865 [G.E. 930]
Separation effects, Extreme liquid chromatographic ~ in the case of diastereomeric amide containing polar substituents (SC) 62 [G.E. 64]
SEPIL, Applications to the solid state defect chemistry of fluorites and ultra-trace inorganic analysis (FP) 738 [G.E. 765]
Silabenzene, 1,4-Di-tert-butyl-~: generation and trapping reactions (SC) 789 [G.E. 863]
Silane, Hexamethyldi-~/iodine: convenient in situ generation of iodotrimethyl-~ (SC) 612 [G.E. 648]
Homologous series of cyclic poly-~-s from $(Me_2Si)_5$ to $Me_2Si)_{35}$ (SC) 955 [G.E. 1022]
Silicate, $Ag_{10}Si_4O_{13}$—the first tetra-~ (SC) 464 [G.E. 500]
Silicon carbide, Chemical vapor deposition of ~ and silicon nitride—chemistry's contribution to modern silicon ceramics (FP) 295 [G.E. 316]
Silicon ceramics, Chemical vapor deposition of silicon carbide and silicon nitride—chemistry's contribution to modern ~ (FP) 295 [G.E. 316]

Silicon compounds, Catalytic reactions with hydrosilane and carbon monoxide (FP) 837 [G.E. 896]
Novel polycyclic phosphanes and arsanes: $P_{11}(SiMe_3)_3$ and $As_7(SiMe_3)_3$ (SC) 679 [G.E. 755]
Ring-opening of lactones and cyclic carbonates with bromo- or iodotrimethylsilane (SC) 689 [G.E. 749]
Silicon nitride, Chemical vapor deposition of silicon carbide and ~—chemistry's contribution to modern silicon ceramics (FP) 295 [G.E. 316]
Silicon phthalocyanines, trans-Bis(1-alkynyl)-4B-metal phthalocyanines (SC) 322 [G.E. 343]
α-Siloxy aldehydes, Catalytic conversion of aldehydes into higher ~ by hydrosilane and carbon monoxide (SC) 393 [G.E. 421]
Silver, Catalysis of hydrogen formation from an organic radical in aqueous solution by colloidal ~ (SC) 418 [G.E. 449]
Silver atoms, Complexes of nitrogen-containing crown ether surfactants with stable ~ (SC) 630 [G.E. 669]
Silver fir, Abietospiran, the triterpene from the bark of the ~ (Abies alba) (SC) 698 [G.E. 751]
Silylamines, Bis(dichloroboryl)-~ and tris(dichloroboryl)amine (SC) 326 [G.E. 357]
Singlet oxygen, reactions with organic compounds and polymers (Book Review) 335
Sodium, ^{23}Na-NMR study of the competition of biogenic amines with ~ ion for binding to lasalocid (X-537 A) (SC) 153 [G.E. 166]
Sodium dithionite, The double salt $Na_2S_2O_5 \cdot NaOOCH$ as intermediate in the formation of ~ by reduction of SO_2 with sodium formate (SC) 313 [G.E. 333]
Sodium orthonitrate, Crystal structure (SC) 698 [G.E. 762]
Solar energy, Criteria for the efficiency, stability, and capacity of abiotic photochemical ~ storage systems (FP) 652 [G.E. 696]
Solid state chemistry, Applications of SEPIL to the solid state defect chemistry of fluorites and ultra-trace inorganic analysis (FP) 738 [G.E. 765]
Solvent polarity, Empirical parameters of ~ as linear free-energy relationships (FP) 98 [G.E. 119]
Solvents, Ureas as ~ for chemical investigations (FP) 503 [G.E. 560]
Solvent effects in organic chemistry (Book Review) 803
Sorption, Kinetics of ~, desorption, and diffusion in zeolites (FP) 266 [G.E. 309]
Spectroscopy, Collision ~ (Book Review) 171
The spectrum in chemistry (Book Review) 560
7-Stannanorbornane, The first stable derivative of ~ and its thermolysis (SC) 543 [G.E. 577]
Stereochemistry, ~ of [2,3]sigmatropic rearrangements (FP) 563 [G.E. 625]
~ of nucleophilic substitution at cyclopropanediazonium ions (SC) 228 [G.E. 240]
Stereochemie und Konformationsanalyse (Book Review) 419
Stereoselective synthesis of Z-α,β-unsaturated aldehydes (SC) 687 [G.E. 748]
Steric effects, Separation of electronic and ~ in the reaction enthalpies of association of phosphorus ligands (SC) 401 [G.E. 429]
Structure reports (Book Review) 87
Substituent effects, Capto-dative ~ in syntheses with radicals and radicophiles (FP) 917 [G.E. 982]
Succinic anhydrides, Reaction of α-lithioacetic acid esters with ~ (SC) 632 [G.E. 656]
(Succinimido)bicyclo[n.1.0]alkanes, Morpholino-~ from enaminosulfonium salts (SC) 800 [G.E. 861]
Sugar amino acids, N-Nitroso-~ (SC) 878 [G.E. 940]
Sulfone pyrolysis as a synthetic method (FP) 515 [G.E. 534]
Sulfoxides, Diarylsulfur(VI) oxide difluoride by direct fluorination of ~ (SC) 880 [G.E. 941]
Sulfur, Detection of large-ring ~ molecules in liquid ~: simple preparation of S_{12}, α-S_{18}, and S_{20} from S_8 (SC) 152 [G.E. 165]
Sulfur compounds, Facile regeneration of carbonyl compounds from 1,3-dithiane 1-oxides via 1-ethoxy-1,3-dithianium salts (SC) 165 [G.E. 179]
Bond switch with participation of π-bonded S^{IV} in thiathiophthene-analogous systems (SC) 166 [G.E. 176]
S_2^{2-} as simultaneous end-on and side-on bonded ligand in the novel transition-metal complex $[Mo_4(NO)_4S_{13}]^{4-}$ (SC) 168 [G.E. 158]
Elemental sulfur/alkali metal hydroxide/dimethyl sulfoxide—a new "reagent" for preparing organic ~ (SC) 217 [G.E. 228]
Cyclodiaza-λ^6-thianes—syntheses and structures (SC) 235 [G.E. 231]
CS_2- and CS_3-bridged transition metal complexes—directed synthesis of metallodithiocarboxylato-metal complexes (SC) 626 [G.E. 661]
$(C_5H_5)_3Co_3(CS)(S)$; the first complex to have a μ_3-thiocarbonyl bridge (SC) 627 [G.E. 663]
Structure and reactions of methylene-sulfur tetrafluoride (SC) 944 [G.E. 1008]
Sulfur dioxide, Double salt $Na_2S_2O_5 \cdot NaOOCH$ as intermediate in the formation of sodium dithionite by reduction of ~ with sodium formate (SC) 313 [G.E. 333]
Sulfur-fluorine compounds, Stable coordination compounds of "thiazyl fluoride": structure of $[Co(NSF)_6]^{2+}$ in the crystal (SC) 231 [G.E. 253]
Sulfur-nitrogen compounds, Structure and bonding in cyclic ~-s (FP) 91 [G.E. 112]
$S_5N_6(CH_2)_4$—the first spirocyclic $1'\lambda^6$-thiacyclopentane derivative of a ~ (SC) 780 [G.E. 846]
SN ring with di-, tri-, and tetra-coordinated sulfur atoms by nucleophilic substitution (SC) 415 [G.E. 444]
Sulfur(VI) oxide difluoride, Diaryl-~ by direct fluorination of sulfoxides (SC) 880 [G.E. 941]
Sulfur trioxide, Formal criss-cross cycloaddition of ~ to cyanogen (SC) 223 [G.E. 243]
Surfactants, Photochemical reactions of surfactant molecules in condensed monolayer assemblies—environment control and modification of reactivity (FP) 440 [G.E. 472]
~ and interfacial phenomena (Book Review) 419
Synthetic methods, Triphase catalysis (FP) 421 [G.E. 464]
Pyrolysis of sulfones as a synthetic method (FP) 515 [G.E. 534]
New synthetic reactions based on the onium salts of aza-arenes (FP) 707 [G.E. 798]
Catalytic reactions with hydrosilane and carbon monoxide (FP) 837 [G.E. 896]
Specialist periodical reports: general and ~ (Book Review) 884
Symmetry, A basis for orbital ~ rules (FP) 377 [G.E. 363]
TARTARIC acid, Chiral reagents from ~—1-benzyloxy-3,4-epoxy-2-butanol, a versatile intermediate for the synthesis of enantiomers (SC) 958 [G.E. 1025]
Technical chemistry, Ullmanns Enzyklopädie der technischen Chemie (Book Review) 88, 491
Tellurates $Xe(OTeF_5)_6$, a deep-colored noble gas compound, and $O{=}Xe(OTeF_5)_4$—the existence of $Kr(OTeF_5)_2$ (SC) 66 [G.E. 68]
Tellurium catalyzed reactions of amines with carbon monoxide (SC) 547 [G.E. 582]
Tellurium compounds, 2,2,4,4,6,6-Hexamethylcyclotristannatellurane, a Sn_3Te_3-ring with C_2-symmetry (SC) 677 [G.E. 740]
Tetraanion, Dianion and ~ of octalene (SC) 229 [G.E. 251]
1,2,4,5-Tetrahydrodicyclobuta[b,e]pyridine (SC) 411 [G.E. 440]
2-Tetrahydropyranyl ethers, Metalated 2-alkynyl- and 1,2-alkadienyl: ~ versatile building blocks for furan syntheses (SC) 875 [G.E. 938]
2,3,5,6-Tetraphosphabicyclo[2.2.0]hexane, The first ~ (SC) 872 [G.E. 935]
1,3,4,6-Tetraphospha-1,5-hexadiene, The first ~, a molecule with fluxional bonds (identical tetraphospha Cope rearrangement) and configurational isomerism (SC) 873 [G.E. 936]
Tetrasilicate, $Ag_{10}Si_4O_{13}$—the first ~ (SC) 464 [G.E. 500]
Tetrathiosquarate dianion, Transition metal complexes with the ~ as bridging bischelate ligand (SC) 463 [G.E. 499]
1,2,3,4-Tetrazine, [4+2]-Cycloadditions of azoalkanes to azodicarbonyl compounds. A novel facile route to the ~ system (SC) 696 [G.E. 757]
Thallium, Quantitative trace analysis in biological material (SC) 882 [G.E. 944]
Thermolysis, Flash vacuum ~ of doubly unsaturated acyl halides to give phenols (SC) 170 [G.E. 163]
$1'\lambda^6$-Thiacyclopentane, $S_5N_6(CH_2)_4$—the first spirocyclic ~ derivative of a sulfur-nitrogen compound (SC) 780 [G.E. 846]
Thiadiborolene, New pathways to trinuclear complexes—structure of the tetradecker complex bis(η-~-cobalt-μ,η-~)iron (SC) 949 [G.E. 1014]
λ^4-Thia-λ^5-phosphanorbornadiene, Manganese-containing heterocycles having a ~ skeleton (SC) 534 [G.E. 568]
Thiathiophthene, Bond switch with participation of π-bonded S^{IV} in ~-analogous systems (SC) 166 [G.E. 176]
Thiazyl fluoride, Stable coordination compounds of "~": structure of $[Co(NSF)_6]^{2+}$ in the crystal (SC) 231 [G.E. 253]
Thieno[3,4-d][1,3]dioxol-2-one 5,5-dioxide, Economic synthesis of activated N-tert-butyloxycarbonyl amino acid esters (SC) 307 [G.E. 326]
Thin films—interdiffusion and reactions (Book Review) 560
Thiocarbonyl bridge, $(C_5H_5)_3Co_3(CS)(S)$; the first complex to have a μ_3-~ (SC) 627 [G.E. 663]
Thiocarbonyl ligands, η^5-Cyclopentadienylchromium complexes with ~ and nitrosyl ligands (SC) 631 [G.E. 662]
Thiocarbonyl-metal complexes from CSSe (SC) 865 [G.E. 930]
Thiosulfines, Dithiiranes and ~ as reactive intermediates (SC) 941 [G.E. 1006]
Thymosin, Synthesis of ~ α_1, a polypeptide of the thymus (SC) 394 [G.E. 422]
Thyrotropin-releasing hormone, Molecular structure of Phe^2-THR, an analogue of ~ (SC) 225 [G.E. 243]
Tin compounds, Synthesis and structure of the nido-cluster $(CH_3)_5C_5Sn^+$ (SC) 59 [G.E. 81]
A metalloporphyrin containing carbyne-like carbido carbon: 5,10,15,20-tetraphenylporphyrinato [bis(μ-carbidotricarbonylrhenium)]tin(IV) (SC) 83 [G.E. 85]
Intermolecular exchange of substituents via ions (ion pairs) in cyclopentadienyl- and cyclononatetraenyl-trimethylstannane (SC) 218 [G.E. 228]
β-Stannylated ynamines as aminoethynylation reagents (SC) 405 [G.E. 432]
2,2,4,4,6,6-Hexamethylcyclotristannatellurane, a Sn_3Te_3-ring with C_2-symmetry (SC) 677 [G.E. 740]
Spontaneous rearrangement of a carbene-to a carbyne complex: C,Cr migration of a $Sn(C_6H_5)_3$ group (SC) 871 [G.E. 929]
Tin phthalocyanines, trans-Bis(1-alkynyl)-4B-metal phthalocyanines (SC) 322 [G.E. 343]

Titanium compounds, Complexes with chiral alkylcyclopentadienyl ligands for homogeneous catalytic asymmetric hydrogenation of 2-phenyl-1-butene (SC) 779 [G.E. 842]
Titanium halides, Novel ~ containing metal-metal bonds: Ti_7Cl_{16} and Ti_7Br_{16} (SC) 325 [G.E. 343]
Titanocene, 1,1'-Trimethylenebis(η^5-3-tert-butylcyclopentadienyl)titanium(IV) dichloride, a chiral ansa-~ derivative (SC) 777 [G.E. 837]
Titanocene dichloride—the first metallocene with cancerostatic acitivity (SC) 477 [G.E. 509]
Titration, From classical end points to modern differential and dynamic analysis (FP) 20 [G.E. 20]
Trace analysis, Applications of SEPIL to the solid state defect chemistry of fluorites and ultra-trace inorganic analysis (FP) 738 [G.E. 765]
Quantitative ~ of thallium in biological material (SC) 882 [G.E. 944]
Transform techniques in chemistry (Book Review) 420
Transition metal complexes with the tetrathiosquarate dianion as bridging bischelate ligand (SC) 463 [G.E. 499]
Transport processes, Chemical kinetics and transport (Book Review) 885
Triazine, N^2-(Trichlorovinyl)amidines—new 1,3-biselectrophilic reagents (SC) 333 [G.E. 355]
Triazole, N^2-(Trichlorovinyl)amidines—new 1,3-biselectrophilic reagents (SC) 333 [G.E. 355]
1,2,4-Triazoline-3,5-dione, Polycyclic azoalkanes via dipolar cycloaddition of 4-phenyl-~ with strained bicyclic olefins (SC) 468 [G.E. 512]
Tri-tert-butylcyclobutadiene, Electrophilic behavior (SC) 308 [G.E. 327]
N^2-(Trichlorovinyl)amidines—new 1,3-biselectrophilic reagents (SC) 333 [G.E. 355]
Trichotoxin A-40, Sequences of the membrane-modifying peptide antibiotic ~ (SC) 476 [G.E. 508]
Tricyclo[4.2.2.$1^{2,5}$]undeca-3,7,9-triene, the [4+4]cycloadduct of benzene and cyclopentadiene. Reaction sequence of its retrocleavage (SC) 224 [G.E. 254]
1,3,5-Triketones, Mono- and bis(η^3-allylnickel) derivatives of 1,8-dihydroxyanthraquinone and of some ~ (SC) 681 [G.E. 742]
Trinuclear complexes, New pathways to ~—structure of the tetradecker sandwich complex bis(η-thiadiborolenecobalt-μ,η-thiadiborolene)iron (SC) 949 [G.E. 1014]
Trioxatris-σ-homotropilidenes, endo-Hydroxy-~ (SC) 611 [G.E. 646]
Triphase catalysis (FP) 421 [G.E. 464]
Triple bond, Hindered rotation at the ~ (SC) 159 [G.E. 163]
An easily prepared, air-stable compound with a metal-to-metal (MoMo) ~ (SC) 462 [G.E. 496]
Chemistry of functional groups. Chemistry of the carbon-carbon ~ (Book Review) 639
Triterpene, Abietospiran, the ~ from the bark of the white fir (Abies alba) (SC) 698 [G.E. 751]
1,6,6aλ^4-Trithiapentalene, An ortho-palladated complex of 2,5-diphenyl-~ (SC) 684 [G.E. 745]
Tungsten compounds, Complex-stabilized hydroxy(p-tolyl)acetylene by reaction of trans-chlorotetracarbonyl(tolylcarbyne)-tungsten with acetylacetone (SC) 327 [G.E. 345]
Photochemical behavior of N_2-complexes: photoluminescence of trans-$(N_2)_2W(diphos)_2$ and trans-$(CO)_2W(diphos)_2$ (SC) 328 [G.E. 335]
Unsymmetrical binuclear complexes of tungsten with three OR bridges, η^3-$C_7H_7(CO)_2W(OR)_3W(CO)_2$-$\eta^4$-$C_7H_8$ (SC) 404 [G.E. 432]
$FeCoMoWS(AsMe_2)Cp_2(CO)_7$: The first cluster to contain four different metal atoms (SC) 531 [G.E. 566]
$[\{Cu_3WS_3Cl\}(PPh_3)_3O]$, directed synthesis of a compound containing different metal atoms in a cubane-like skeleton (SC) 628 [G.E. 656]

ULLMANNS Encyklopädie der technischen Chemie (Book Review) 88, 491
Umpolung, Methods of reactivity ~ (FP) 239 [G.E. 259]
5,8-Undecadien-11-olide, Fragmentational approach to macrolides: (5-E, 8-Z)-6-methyl-~ (SC) 634 [G.E. 670]
5,9-Undecadien-11-olide, Fragmentational approach to macrolides: (5-E,9-E)-6-methyl-~ (SC) 636 [G.E. 672]
Ureas, ~ as solvents for chemical investigations (FP) 503 [G.E. 560]
Reactions of carbonyl selenide with amines and aminoalcohols to produce ~ and carbamates (SC) 692 [G.E. 760]
Uroporphyrinogen, Enzymatic formation of ~ I and III from a substituted bilane (SC) 778 [G.E. 838]

VACUUM thermolysis, Flash ~ of doubly unsaturated acyl halides to give phenols (SC) 170 [G.E. 163]
Vanadium complexes, η^5-Cyclopentadienyl(trinitrosyl)vanadium hexafluorophosphate, $[CpV(NO)_3]PF_6$ (SC) 220 [G.E. 241]
Vapor deposition, Chemical ~ of silicon carbide and silicon nitride—chemistry's contribution to modern silicon ceramics (FP) 295 [G.E. 316]
Vinylation, Homogeneous catalytic ~ of cyclic imides and lactams for the synthesis of N-vinyl monomers (SC) 533 [G.E. 568]
Vinyl cation, [2+2]-Cycloaddition (SC) 614 [G.E. 649]
cis-2-Vinylcyclopropyl ketone, Synthesis of ~: a new synthesis of 4-cycloheptenones (SC) 791 [G.E. 857]
Vinylketenes, Preparation of stable ~ by metal complex-induced olefination and carbonylation of alkynes (SC) 954 [G.E. 1021]
Vinylketenimines by nucleophilic ring cleavage of cyclopropenes with tert-butyl isocyanide (SC) 67 [G.E. 62]
N-Vinyl monomers, Homogeneous catalytic vinylation of cyclic imides and lactams for the synthesis of ~ (SC) 533 [G.E. 568]
Vitamin B_{12}, Cobalt(I)-phthalocyanine as vitamin B_{12s}-model: selectivity in reactions with electrophiles (SC) 794 [G.E. 841]

WAGNER-Meerwein rearrangement, Stereospecific synthesis of γ-lactones by dyotropic ~ (SC) 793 [G.E. 840]
Walk rearrangement, Thermal ~ in the bicyclo[2.1.0]pent-2-ene system (SC) 674 [G.E. 738]
Water, Colloidal redox catalysts for evolution of oxygen and for light-induced evolution of hydrogen from ~ (SC) 624 [G.E. 659]
Cyclic cleavage of ~ into H_2 and O_2 by visible light with coupled redox catalysts (SC) 701 [G.E. 759]
White fir, Abietospiran, the triterpene from the bark of the ~ (Abies alba) (SC) 698 [G.E. 751]
Wittig reaction, New evidence for zwitterionic intermediates in the ~ (SC) 633 [G.E. 675]

XENON compounds, $Xe(OTeF_5)_6$, a deep-colored noble gas compound, and $O{=}Xe(OTeF_5)_4$—the existence of $Kr(OTeF_5)_2$ (SC) 66 [G.E. 68]
Krypton and xenon inclusion compounds of complex metal cyanides (SC) 486 [G.E. 517]

YLIDES, Synchronous mechanism of the 1,1-cycloaddition of nitrile ~ to C=C double bonds (SC) 167 [G.E. 168]
Synthesis of a Zeise salt derivative with a phosphorus-nitrogen ylide as chelate ligand (SC) 234 [G.E. 238]
Phosphorus ylide with symmetrical resonance-stabilized sp^2-carbanion (SC) 484 [G.E. 519]
Ynamines, β-Stannylated ~ as aminoethynylation reagents (SC) 405 [G.E. 432]

ZEISE salt, Synthesis of a ~ derivative with a phosphorus-nitrogen ylide as chelate ligand (SC) 234 [G.E. 238]
Zeolites, Kinetics of sorption, desorption, and diffusion in ~ (FP) 266 [G.E. 309]
Zinc compounds, Bis(trimethylsilyl)zinc and -cadmium (SC) 60 [G.E. 62]